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FREQUENCY OF IL 12B GENE POLYMORPHISM AMONG PATIENTS WITH CHRONIC RHINOSINUSITIS POLYPOSIS

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ABSTRACT

Analyzing the prevalence of genotypic variants of this polymorphism, we revealed a direct association of the C/C monogenotype of the A1188C rs3212227 polymorphism in the IL12B gene with the development of polyposis processes. In addition, these data emphasize the prognostic significance of the C/C genotype of the rs1800896 polymorphism of the IL-12B gene in the development of CPMS. In carriers of this genotype, the relative risk of developing CPMS increases by more than 3 times, compared with carriers of other genotypic variants of the rs3212227 polymorphism of the IL12B gene.

Key words: paranasal sinuses, polyp, allele, genotyping.

INTRODUCTION

Diseases of the paranasal sinuses are among the most common pathologies in otorhinolaryngology, which is facilitated by the current environmental situation, the prevalence of allergic and viral respiratory diseases, and a decrease in local and general immunity. All researchers agree that in recent years there has been a tendency in the world to increase the incidence of chronic sinusitis, including chronic polypous rhinosinusitis (CPRS) [1,2,3].

Epidemiological studies of CPRS in Russia, which were conducted with an interval of 5 years, indicate that the prevalence of the disease does not change

significantly in selected time intervals in each specific region. Due to a number of reasons (environmental situation, social and drug load, changes in the functional parameters of the most important homeostatic systems of the human body, etc.), it is not necessary to expect a decrease in the incidence of CPRS. Leading otolaryngologists consider the stability of CPRS incidence rates, regardless of regional characteristics or other external factors, to be the basis for a more detailed study of the causes of this nosology [4], primarily the genetic predisposition to the development of CPRS. Many facts speak in favor of the genetic hypothesis of the development of CPRS. It has been proven that the risk of developing CPRS in the presence of polypous heredity is 25 times higher, with a heterozygous carrier of the MZ phenotype (deficiency of alpha-1 antitrypsinase) - 4 times, with a dry type of earwax - 3 times [5]; changes in karyotypes of peripheral blood cells in patients with CPRS were found [6]. Since chromosomal polymorphism can determine individual sensitivity to the occurrence of any disease, i.e. the individual response of the body to a damaging factor, persons with karyotype variants that differ from the norm are at risk of developing certain diseases depending on hypo-, hyper, or normosensitivity of the hereditary apparatus [7,8,9,10].

Numerous studies of the last decade have demonstrated the dependence of the immune response on the allelic polymorphism of cytokine genes. The result of such work in vitro is the identification of individual alleles of genes associated with increased or decreased production of the corresponding cytokine [11]. The data obtained to date suggest that polymorphic cytokine genes are able to take an active part in the formation of a specific immune response to human pathological conditions. Individual allelic variants may be associated with the level of production of the corresponding protein, which also affects the course of the disease and the development of a number of complications. However, it remains unclear which mutations and which cytokines are of decisive importance in the development of individual diseases. Therefore, a promising direction of molecular genetic research is the study of the contribution of specific alleles to the tendency to infection in the development of pathology [12,13,14,15,16].

The current stage in the development of cytology, histology, and clinical anatomy, as well as progress in diagnostic technologies, has led to the concept of the nasal cavity as a complex morphofunctional system [17]. The modern knowledge of anatomy, histology and physiology, as well as the morphogenesis of various pathological processes in the nasal cavity and paranasal sinuses, obtained in the course of scientific research, has significantly expanded the understanding of the functional significance of these structures in the adaptive capabilities of the

nasal cavity to respiratory conditions, their role in the respiratory system in in general [18,19].

Modern histological and clinical-functional studies have made it possible to ascertain the growth of chronic diseases of the mucous membrane of the nasal cavity and paranasal sinuses, the formation of various endonasal formations [20]. This is due to the deterioration of the ecological and social situation, increased virulence of the microbial flora, changes in its composition and resistance to antibacterial drugs. In the pathogenesis of diseases of the ENT organs, in addition to the infectious agent, the leading role belongs to the immune system of the mucous membranes of the nose and pharynx, as well as the general reactions of humoral and cellular immunity [21].

The body's resistance to exogenous and endogenous pathological factors is largely associated with the ability to quickly adapt to changing environmental conditions. The mucous membrane of the nasal cavity serves as the first protective barrier where local immunity reactions take place.

It is known that in many organs and tissues, including the nasal mucosa of the human body, there are neuroendocrine cells that belong to the link of autonomic regulation of organs. Moreover, the structural and functional features of neuroendocrine cells and their bioamine profile in patients with signs of polypous rhinosinusitis are practically not studied. Therefore, the study of the morphophysiological organization of the nasal mucosa in humans is an urgent problem of modern cytology, histology, and cell biology.

Given the above, we conducted a study of the genetic polymorphism of cytokine genes in patients with CPRS, the results of which demonstrate genetically determined features of the immune response that contribute to the development of CPRS, as well as determining some of the clinical features of the disease.

Material and methods:

In accordance with the purpose of the study and to fulfill the tasks set, clinical studies were conducted in 140 patients with CPRS and chronic rhinosinusitis, who were examined and treated in the ENT department of the multidisciplinary clinic of the Tashkent Medical Academy in 2017-2019. The examined patients met the following criteria: the presence of polypous tissue in the nasal cavity, wiping the common nasal passage completely or not less than 50%; complaints of prolonged difficulty in nasal breathing; according to the patient, the disease significantly reduces the quality of his life; absence of acute inflammatory pathology; written informed consent for surgical treatment and morphological examination of the surgical material (attached to the medical history).

To study the diallelic polymorphism of the promoter regions of the genes of the studied interleukins, 50 healthy (without CPRS) donors, men and women, were examined. The average age of the examined donors was 51.3±1.44 years.

For real-time PCR, a commercial kit with SYBRGreen I dye (Litekh, Russia) was used. Polymorphism of five positions of the IL10 gene rs1800895 592C>A was studied. Genotyping of samples was carried out using real-time allele-specific polymerase chain reaction (PCR) on a DT-96 device (DNA-Technology) using SYBR Green I intercalating dye. The reaction mixture corresponded to the manufacturer's recommendations.

The reaction started with the activation phase of Taq polymerase (93°C, 1 min.). The next 35 PCR cycles consisted of denaturation (93°C, 10 sec), annealing (64°C, 15 sec), and elongation (72°C, 20 sec) phases. The signal was read at the elongation stage.

Results and discussion.

The values of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 1-2 group and control presented in table 1.

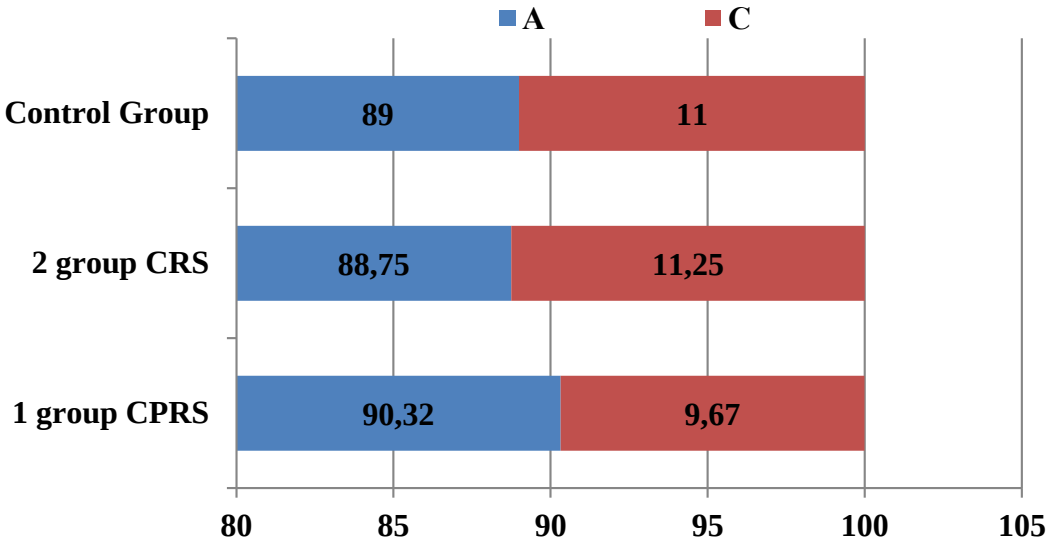
Table 1

The frequency of distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in groups of patients and controls

	Group	Allele frequency				Frequency distribution of genotypes					
		A		C		A\A		A\C		C\C	
		n	%	n	%	n	%	n	%	n	%
	CPRS n=31	56	90.32	6	9.67	25	80.64	6	19.35	0	0
	CRS n=40	71	88.75	9	11.25	31	77.5	9	22.5	0	0
	Control group n=73	130	89.0	16	11.0	57	78.1	16	21.9	0	0

Taking into account the fact that the detection of allele A prevailed in all groups of the study. It should be taken into account that in the frequency of detection of allele A in the 1st group slightly prevailed, relative to its values in the 2nd and control groups. The frequency of allele C, on the contrary, was slightly higher among patients of group 2, relative to its frequency in group 1 and the population sample.

The study of the distribution of genotypes showed that the homozygous A/A genotype was slightly, almost 1.2 times more often detected in group 1 (80.64%), while the frequency of detection of the heterozygous A/C genotype was insignificantly 1.1 times higher among patients with HRS 2 groups. The reverse situation could be observed in the study of the homozygous C/C genotype, which was not detected among all study groups (Figure 1.2).



Pic.1. The frequency of distribution of alleles of the A1188C rs3212227 polymorphism in the IL 12B gene in groups of patients and controls

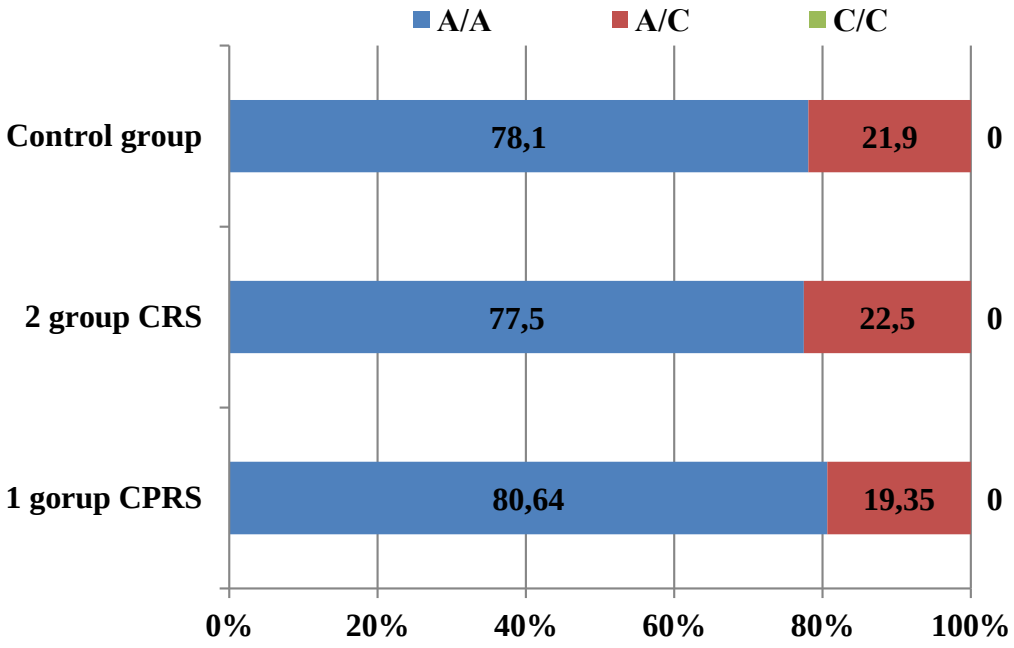


Fig. 2. Distribution frequency of A1188C rs3212227 polymorphism genotypes in IL 12B gene groups and subgroups of patients and controls

In table 2 presents the results of the analysis of the distribution of alleles and genotypes among representatives of the population sample and patients in groups 1-2.

Table 2

Differences in the frequency of occurrence of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 1st and control groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi^2	p	RR	+ 95%CI	OR	+95% CI
	CPRS		Control							
	n	%	n	%						
A	56	90,32	130	89,04	0,076	0,273	1,014	4,130	1,149	3,093
C	6	9,68	16	10,96	0,076	0,727	0,986	1,683	0,871	2,332
A/A	25	80,65	57	78,08	0,086	0,273	1,033	4,550	1,170	3,347
A/C	6	19,35	16	21,92	0,086	0,305	0,883	3,890	0,855	2,440

The analysis showed that if the frequency of allele A detection did not have statistically significant differences in detection in groups 1 and control, however, there was a tendency to increase its detection among patients with CPRS ($\chi 2$ = 0.07; P = 0.2; RR = 1.01; OR =1.14; 95% CI: 4.13-3.09), while allele C, on the contrary, was characterized by a tendency to increase its occurrence among conditionally healthy individuals ($\chi 2$=0.07; P=0.7; RR=0.98; OR=0.87; 95% CI: 1.68-2.33).

An analysis of the frequencies of detection of the A/A genotype showed that among patients with CPRS this genotype was detected statistically insignificant less than 1.1 times more often than in the group of conditionally healthy individuals ($\chi 2$=0.08; P=0.2; RR=1.03; OR=1.17; 95% CI: 4.55-3.34). The study of the distribution of the A/C genotype showed the same picture, according to which a slight and statistically insignificant prevalence was found - 1.1 times the frequency of its detection in the control group of conditionally healthy individuals, relative to the detection values of this genotype in patients of group 1 with CRRS ($\chi 2$=0.08; P=0.3; RR=0.88; OR=0.85; 95% CI: 3.890-2.44).

The results of the analysis of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene presented in Table 3 demonstrate the same indicators in patients with CRS and among conditionally healthy individuals.

Analysis of the distribution of A and C alleles showed a slight less than 1.0 times and statistically insignificant predominance of the A allele in the control

sample (χ2=0.004; P= 0.36; RR=0.99; OR=0.97; 95% CI: 2.95-2.30), and there was also a statistically insignificant, less than 1.0 times, predominance of the allele C among patients with CRS (χ2=0.04; P=0.6; RR=1.0; OR=1.03; 95% CI: 1.84-2.45).

It was found that the A/A genotype among conditionally healthy individuals is insignificant, less than 1.0 times higher than its frequency of detection among patients with CRS (χ2 = 0.005; P = 0.35; RR = 0.99; OR = 0.96; 95% CI: 3.18-2.43).

Table 3

Differences in the frequency of occurrence of alleles and genotypes of the A1188C rs3212227 polymorphism in the IL 12B gene in the 2nd and control groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi^2	p	RR	+ 95%CI	OR	+95% CI
	CRS		Control							
	n	%	n	%						
A	71	88,75	130	89,04	0,004	0,360	0,997	2,959	0,971	2,305
C	9	11,25	16	10,96	0,004	0,640	1,003	1,846	1,030	2,454
A/A	31	77,5	57	78,08	0,005	0,360	0,993	3,184	0,967	2,432
A/C	9	22,5	16	21,92	0,005	0,352	1,027	3,293	1,034	2,592

It was also found that the heterozygous A/C genotype of the A1188C rs3212227 polymorphic locus in the IL 12B gene was evenly distributed in group 2 and in the control group, and its detection frequency was practically the same in both studied samples, with extremely low and statistically insignificant prevalence in the subgroup of patients with CRS (χ2 =0.005; P=0.3; RR=1.02; OR=1.03; 95% CI: 3.29-2.59).

The results of the analysis of the distribution of alleles and genotypes of the A1188C rs3212227 polymorphic locus in the IL 12B gene among patients with CPMS in comparison with group 2 are presented in table 4.

Analysis of the distribution of alleles A and G did not reveal statistically significant differences in the frequency of their detection in the 1b subgroup and in the control sample. Thus, the G genotype did not have significant and statistically significant differences in both studied groups, being practically at the same level in them, only slightly prevailing among conditionally healthy individuals.

Table 4

Differences in the frequency of occurrence of alleles and genotypes of polymorphism A1188C rs3212227 in the IL 12B gene in the 1- and 2-groups

Alleles and genotypes	Number of examined alleles and genotypes				Xi^2	p	RR	+ 95%CI	OR	+95% CI
	CPRS		CRS							
	n	%	n	%						
A	56	90,32	71	88,75	0,091	0,400	1,018	3,639	1,183	3,516
C	6	9,68	9	11,25	0,091	0,600	0,983	2,333	0,845	2,517
A/A	25	80,65	31	77,5	0,104	0,400	1,041	3,985	1,210	3,861
A/C	6	19,35	9	22,5	0,104	0,446	0,860	3,292	0,827	2,628

However, it was noted that the A genotype, which also had no significant and significant differences in the frequency of its distribution, slightly prevailed among patients with CPRS ($\chi 2$=0.09; P=0.4; RR=1.01; OR=1.18; 95% CI: 3.63-3.51).

The frequency of the A/A genotype was statistically insignificant, less than 1.0 times, prevailed among patients with CPRS relative to patients with CRS ($\chi 2$=0.1; P=0.40; RR=1.04; OR=1.21; 95% CI: 3.985 -3.86).

The A/C genotype, on the contrary, was insignificantly 1.1 times more likely to be detected among patients with CRS ($\chi 2$ =0.1; P=0.44; RR=0.86; OR=0.82; 95% CI: 3.292-2.62).

Conclusion

Thus, our data confirm the complexity of the genetic mechanism for the development of polyposis processes in patients with CPRS and indicate the need and importance of understanding complex gene interactions in the analysis of the development and clinical stage of the pathology under study. Analyzing the prevalence of genotypic variants of this polymorphism, we revealed a direct association of the C/C monogenotype of the A1188C rs3212227 polymorphism in the IL12B gene with the development of polyposis processes.

In addition, these data emphasize the prognostic significance of the C/C genotype of the rs1800896 polymorphism of the IL-12B gene in the development of CPRS. In carriers of this genotype, the relative risk of developing CPMS increases by more than 3 times compared with carriers of other genotypic variants of the rs3212227 polymorphism of the IL12B gene.

The absence of significant differences in the prevalence of IL12B gene genotypes among conditionally healthy donors and CRS patients may be due to the fact that the presence of an unfavorable polymorphism, in itself, is not enough for the development of this disease. In genetically predisposed persons, CPRS will develop according to the scheme of interaction in the "genotype-phenotype"

system (gene-environment). At the same time, the presence of unfavorable genotypic variants can influence the clinical course of the disease.

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GENDER AND AGE CHARACTERISTICS OF CHILDREN HOSPITALIZED WITH CORONAVIRUS INFECTION IN UZBEKISTAN

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ABSTRACT

At the beginning of the pandemic of the new coronavirus infection SARS-CoV 2, researchers drew attention to the fact that the proportion of children among those infected with COVID-19 was significantly lower than other age groups. **The purpose of the study:** to determine the gender and age patterns of coronavirus infection in the children's contingent of hospitalized patients (on the example of Tashkent city). **Research material and methods:** The study was conducted based on the 3rd city Infectious diseases Hospital in Tashkent city during the years 2020-2021 the time periods when this medical institution was transformed into a covid hospital. **Conclusion:** Thus, among hospitalized children with COVID-19 (on the example of the 3rd city infectious diseases hospital in Tashkent city) during the second wave of the pandemic (I the year of 2021), an increase in the proportion of children under 1 year old was noted, due to the emergence of new strains of the virus characterized by greater involvement in the epidemic process of the children's contingent, as well as the mitigation of quarantine restrictions and, consequently, an increased risk of infection in family clusters.

Key words: COVID-19, Gender, infectious diseases, virus.

INTRODUCTION

At the beginning of the pandemic of the new coronavirus infection SARS-CoV 2, researchers drew attention to the fact that the proportion of children among those infected with COVID-19 was significantly lower than other age groups. In addition, it was also noted that children have a milder course of the disease and complications and adverse outcomes are much less common. *[11, 12, 13, 14, 15]*

With the advent of new strains of coronavirus, the situation has changed significantly and now it is possible to observe a significant increase in the proportion of the children's contingent in the overall structure of the sick. There are very scattered data in the literature on the age structure of children infected with COVID-19. Thus, according to Zhang Y.P, 0.9% of the cases were children 0-9 years old, 1.2% - 10-18 years old. *[16]*. По результатам анализа Dong Y Mo и соавт. [*17]*. 17.6% of patients were children younger than 1 year, 23% - 1-5 years, 24.5% - 6-10 years, 19.3% - 11-15 years, 15.6% - older than 15 years. The Lu X Zhang study indicates that 18.1% of patients were younger than 1 year, 23.4% - 1-5 years, 33.9% - 6-10 years, 24.6% - 11-15 years. [18]. According to Wu Z. Et al., children under 9 years of age and from 10 to 19 years of age accounted for 1% of the total number of registered cases of coronavirus infection. [*19]*

At the same time, the data of different authors differ from each other, in connection with which the study of the sex and age characteristics of the new coronavirus infection in children in Uzbekistan was of fundamental interest.

The purpose of the study: to determine the gender and age patterns of coronavirus infection in the children's contingent of hospitalized patients (on the example of Tashkent city).

Research material and methods: The study was conducted based on the 3rd city Infectious diseases Hospital in Tashkent city during the years 2020-2021 the time periods when this medical institution was transformed into a covid hospital. The study included only hospitalized children who received inpatient treatment at this infectious diseases hospital. During the entire period of operation of the institution as a covid hospital, 1,434 children aged 0 to 18 years were treated.

The design of the study is cross-sectional.

Statistical processing was carried out using standard nonparametric statistical methods.

Results and discussion:

We conducted a comparative analysis of the distribution of children by age in the year 2020 and 2021. The results obtained are shown in Fig. 1 and 2.

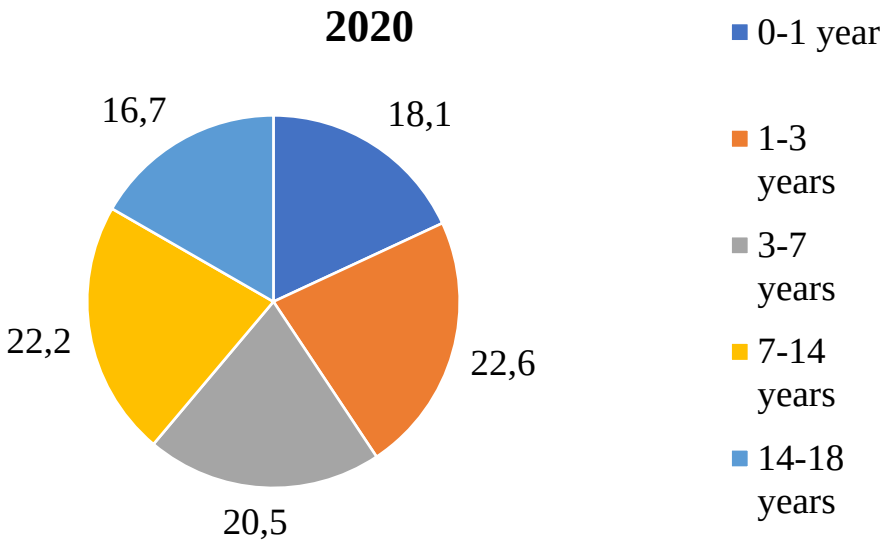

Fig. 1 Distribution of hospitalized children by age (the year 2020)

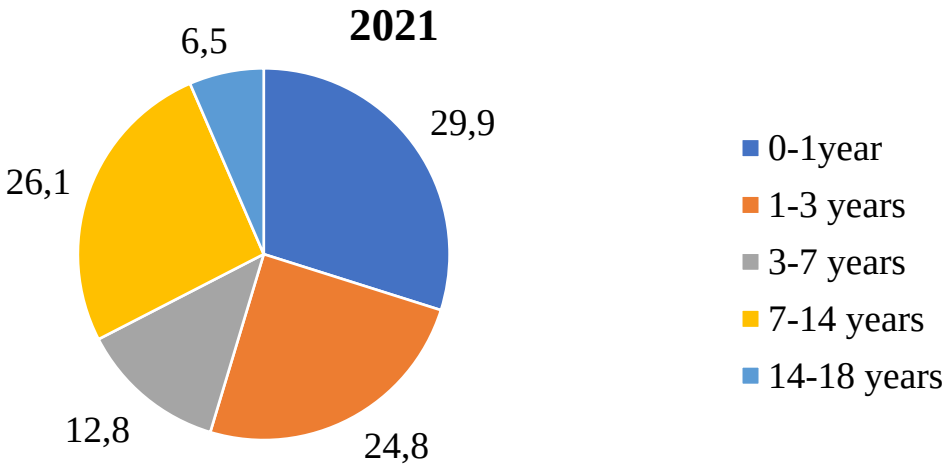

Fig. 2. Distribution of hospitalized children by age (the year 2021)

As can be seen from the data of diagrams 1 and 2, compared with the year 2020, the proportion of young children increased in the year 2021 (29.9% in 2021 versus 18.1% in 2020), and the proportion of adolescents aged 14 to 18 decreased (6.5% in the year 2021 versus 16.7% in 2020). The increase in the proportion of children under 1 year is explained, in our opinion, by a number of reasons. In 2021, quarantine restrictions were significantly relaxed, and therefore opportunities for intra-family contacts expanded, which explains the increased proportion of young children. In addition, it is necessary to take into account the fact that the clinical manifestation of COVID-19 in various age groups and its severity largely depends on the strain of the virus. Thus, the Wuhan strain was distinguished by the fact that in childhood clinical manifestation was either absent or minimal. In this regard, not all cases of coronavirus infection in children have been identified. It cannot be excluded that in the year 2021, after the successful introduction of coronavirus vaccination among adults, vaccination of adolescents was started, which could also affect the ratio of age groups of patients.

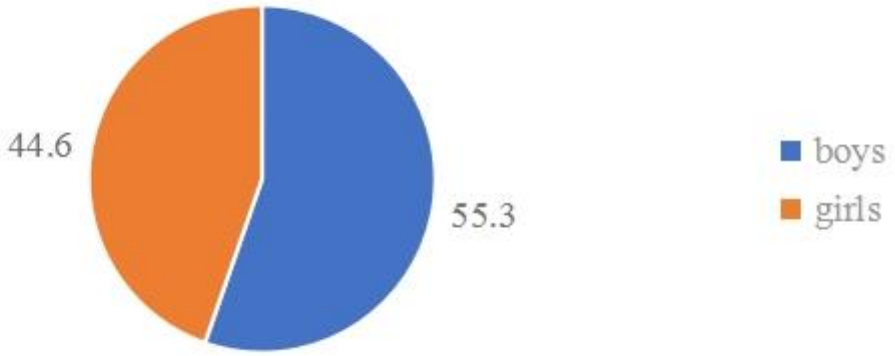

Figure 3. Distribution of children with COVID-19 by gender

As can be seen from Figure 1, in our study, the proportion of male patients was slightly higher (55.3%).

Next, we analyzed the cases of registration of coronavirus infection in children, depending on gender and age. The results obtained are shown in Table 1

Table 1

The year	The year 2020				The year 2021			
Gender	Boys (n=143)		Girls (n=145)		Boys (n=650)		Girls (n=495)	
Age	abs	%	abs	%	abs	%	abs	%
0-1 year old	26	18,2	26	17,9	193	29,7	149	30,1
1-3 years old	32	22,4	33	22,8	173	26,6	111	22,4
3-7 years old	30	21,0	29	20,0	70	10,8	76	15,4
7-14 years old	35	24,5	29	20,0	179	27,5	120	24,2
14-18 years old	20	14,0	28	19,3	35	5,4	39	7,9
P-meaing	0,752				0,033			
	0,015							

Note: If p=values less than 0.05 is valid

When combining data on gender and age, we obtained the following results. In the year 2020, the predominant group of cases were boys of high school age (7-14 years old). In the year 2021 – boys and girls under the age of 1 year (29.7 and 30.1%, respectively).

CONCLUSION

Thus, among hospitalized children with COVID-19 (on the example of the 3rd city infectious diseases hospital in Tashkent city) during the second wave of the pandemic (I the year of 2021), an increase in the proportion of children under 1 year old was noted, due to the emergence of new strains of the virus characterized by greater involvement in the epidemic process of the children's contingent, as well as the mitigation of quarantine restrictions and, consequently, an increased risk of infection in family clusters.

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AUTOIMMUNE DIATHESIS END RHEUMATOID ARTHRITIS IN CHILDREN

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ABSTRACT

In this article, the authors reviewed the literature, as a result, it was revealed that the pathogenesis of autoimmune diathesis, rheumatoid arthritis and rheumatoid nephritis in children has a general immunopathological nature. However, autoimmune diathesis is an important risk factor for the onset and progression of rheumatoid arthritis and the subsequent development of renal amyloidosis based on immunopathological reactions in these patients.

Key words: nephropathy, autoimmune diathesis, rheumatoid arthritis.

INTRODUCTION

Currently, rheumatoid arthritis (RA) has become medical and social problem it attracts serious attention of rheumatologists and pediatricians, which is due to a noticeable increase in cases of diseases among children, often with a severe and progressive course with a tendency to early disability of patients. According to WHO 1/10 of incapacity for work and 1/3 of disability accounted for by rheumatic diseases [1, 33, 86]. In recent years, some progress has been made in diagnostics and therapy for RA. Despite this, many aspects of this problem remain unclear. So, a lot of work remains to be done to determine the main risk factors, pathogenesis, clinical features of RA in children, finding out the reason for the chronicity of the inflammatory process, improvement of diagnostic criteria and treatment methods, which has great importance for the prevention of early disability among population. Renal damage at the onset of RA is prognostic an unfavorable sign indicating a high degree activity and severity of the course, high risk of poor

outcome of the disease, which often proceeds latently, has a tendency to progress and its result is a secondary contracted kidney with the development of chronic renal failure and death of the patient from uremia. Currently, the definition of clinical and laboratory markers, typical for different types of RA in comorbidity with different pathologies, including autoimmune diathesis (A&D) and early prevention of complications remains a priority area of scientific research.

The Republic of Uzbekistan pays special attention to mother and child's health protection, to improve efficiency, quality and availability health care, support for a healthy lifestyle and prevention diseases, including through the formation of a system of medical standardization, introduction of high-tech diagnostic methods, treatment and effective models of clinical examination [45, 51]. In this plan improving the health of children, especially in early childhood, improving diagnosis, treatment and early prevention of complications of autoimmune diseases in the most modern ways is important in medical practice.

Modern understanding of autoimmune diathesis in children

The constitution is a set of relatively stable morphological and functional properties of a person, due to heredity, age, as well as long-term and intense environmental influences, which determines the functional ability and the reactivity of the organism [8, 9, 19, 23, 26]. Diathesis is a genetically determined feature of the body, determining the originality of his adaptive reactions and predisposing to 3 a certain group of diseases, i.e. "Hereditary predisposition". The risk factors for the formation of many diseases are not only in the influence of the environment, but sometimes, largely, in constitutional characteristics of the body. It is believed that the majority chronic diseases is based on the constitution of the sick. In that, sense of diathesis is considered as a pre-disease. Isolation of this or that type of diathesis helps in the development of recommendations for primary prevention of possible future diseases [2, 3, 49, 50, 58]. Thus, diathesis is a predisposition, pre-illness, pre-insufficiency of certain metabolic mechanisms. Define predisposition and degree of risk of the disease much more difficult than making a diagnosis of an already developed disease, even in cases of its minimal manifestations Predisposition (or diathesis) to diseases is determined by the characteristics of the structure and function one or several body systems: immune, central nervous system, neuro-humoral [8, 14, 16, 18, 59]. The amplitude of fluctuations in the "normal" functioning of the body very individual. Extreme indicators of the norm and compensated metabolic defects are the essence of predisposition (diathesis). In cases where the body cannot provide adaptation to changing environmental conditions, the disease realizes the predisposition. In currently, there are about 20 types of diathesis, combined into groups: I.

Immunopathological: atopic, autoimmune, lymphatic, infectious and allergic. II. Dysmetabolic: uric acid, oxalate, diabetic, hemorrhagic, adiposodiathesis. III. Organotopic: nephrotic, intestinal, hypertensive, cardioischemic, atherosclerotic. IV. Neurotopic: psycho-asthenic, vegetative-dystonic [16, 22, 23, 26, 37, 58]. The basis of autoallergic diathesis is the inability to the formation or maintenance of immunological tolerance for four in relation to their own antibodies (own cells, proteins or nucleic acids) under the influence of various, most often infectious stimuli (cytomegalovirus) [46, 47, 71]. Distinguish between organospecific form (lupoid diathesis), causing a predisposition to the occurrence in children of systemic lupus erythematosus, rheumatoid arthritis, some connective tissue diseases, immunohemopathies, and organ-specific, underlying the formation of organ pathology such as autoimmune thyroiditis, orchitis, encephalitis, etc. [42, 50, 60, 63].

Autoimmune diathesis - (autoimmune reactions, "lupoid diathesis") hypersensitivity of the skin to ultraviolet irradiation, a significant increase in the level of gamma globulins in the blood, often identification of LE cells, antinuclear factors, in a state of complete clinical well-being, polyclonal activation of B-lymphocytes, and also T-helpers with a decrease in the activity of T-suppressors, increased, spontaneous blast transformation of lymphocytes or its activation by tissue antigens, elevated IgM levels, hypocomplementemia (especially deficiency of C3 complement [26, 56, 70, 86]. According to American authors, congenital tendency to autoimmune diseases is traced in 10% of the US population penetrance among women is 2 times higher than among men [52, 55, 64]. Study the role of persistent viral infections in provoking the transformation of diathesis into an autoimmune disease.

Prevention of diseases to which children with diathesis should begin before the birth of the child [30]. Even before pregnancy, it is necessary to take care of the treatment of chronic genital and extragenital pathology in the expectant mother. Pregnant woman must follow a rational diet. Elimination is essential from the first 7 months of pregnancy, occupational hazards, excessive sun exposure, cessation of active and passive smoking, adverse effects of various radiation, medicines. Should keep in mind that prolonged breastfeeding is an important factor in the prevention of many diseases. Questions and answers nutrition of children with diathesis are key to prevent the development of diseases such as atopic dermatitis, bronchial asthma, food allergies. Nutrition also plays an important role in preventing development of metabolic diseases [2, 13, 14, 16, 30, 60, 62].

An essential point in preventing the development of diseases environmental control. It is known that frequent infectious diseases, allergic diseases are directly

related to unfavorable conditions in the environment [14, 16, 58]. Strengthening the immunological reactivity of the body of such children by hardening, organization of a rational lifestyle, the use of adapagens, immunomodulators will help reduce the incidence of infectious diseases and pathological conditions to which children with diathesis [32, 37, 41, 43]. Data from sources suggests that children with autoimmune diathesis have a higher risk of developing various autoimmune diseases in the future. From a pathogenetic point of view, comorbid the course of autoimmune diseases, including rheumatoid arthritis with autoimmune diathesis, accelerates the development of visceral changes (nephropathy) [76]. New views on immunopathological processes in rheumatoid arthritis in children Rheumatoid arthritis (RA) in both adults and children is is a common disease from the group of collagenoses, which is based on immunological processes and characterized by cyclic prolonged or a chronic course with systemic damage to the connective tissue, mainly of the musculoskeletal system [1, 4, 5, 12, 20]. The social significance of this disease is extremely high, because it tends to become more widespread throughout the world, leads to early disability and disability of patients [33, 52, 54, 86].

RA is registered in all countries of the world with different climatic and geographical conditions with a frequency of 0.6 to 1.5% [1, 28, 31, 36, 56]. Moreover, the disease develops more often in women than in men. By data from sources in various climatic and geographical zones of the CIS RA suffer from 0.24 to 1.5% of the adult population, and abroad - from 1 to 3.3% population. A particularly high incidence of RA was found among relatives. First degree of relationship (3.5%), and the highest incidence rate (5.1%) found in women of the first degree of relationship [33]. In families of patients RA is much more common than in the general population, rheumatic fever and other autoimmune and infectious-allergic diseases, i.e. family aggregation is observed, which may be due to a hereditary predisposition to influences environmental factors (past infectious diseases, physical and psychological trauma, hypothermia, etc.). According to epidemiological studies, the incidence of RA among children in the USA it was up to 10 cases, in Europe - 5-10 cases, in Finland - 19.6, in England - 16-27 cases per 10,000 child population [67, 68, 69, 70, 74, 79]. Among the child population in Uzbekistan, the RA ranges from 0.08% to 2.1% cases [1].

In children with RA, in about half of cases, it begins before the age of 5-7 age, much less often before the first year of life and after 13 years. Wherein, girls get sick 1.5-2 times more often than boys [1, 70]. Increased degree of age risk, predominant spread of the disease in girls, apparently associated with early physiological hormonal abnormalities of the body. The factors contributing to the

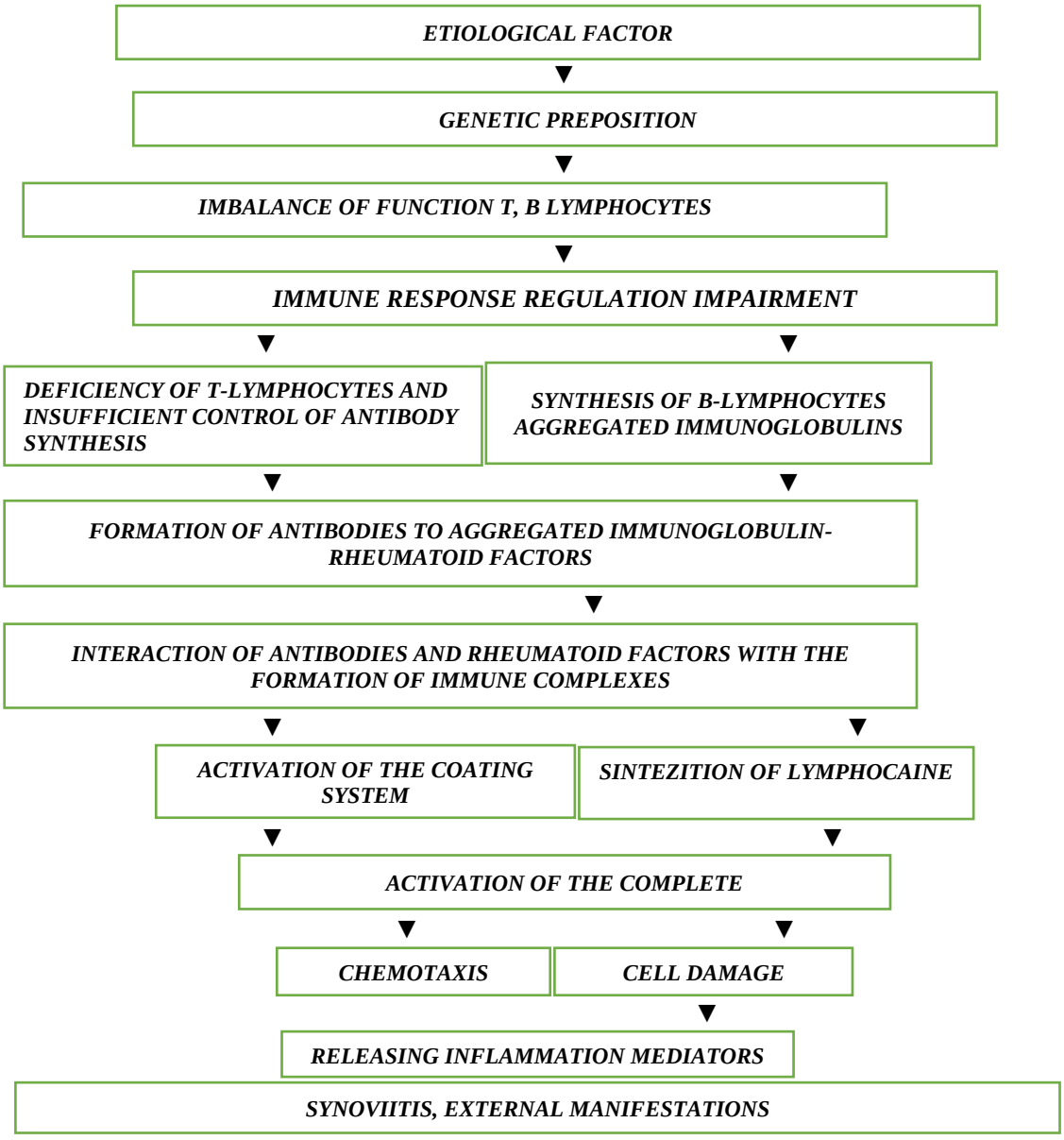
onset of RA are numerous. A number of authors point to the etiological role of streptococci, staphylococci, diphtheroids, clostridia, chlamydia, yersinia infections, mycoplasmas, rickettsiae as possible causative agents of RA [80, 81, 82]. Other researchers believe that RA is caused by parvoviruses, hepatitis B viruses, rubella viruses. Many authors cite information that the causative agents of the disease are Epstein-Barr viruses, localized in B-lymphocytes and having the ability disrupt the synthesis of immunolobulins [48, 83].

However, to date, no convincing data have been received indicating the specificity of any particular of the above microorganisms as the causative agent of RA. In some cases, a factor that provokes the development of RA in children, there may be joint injury. Some researchers dismiss the decisive the role of food agents and unfavorable social and living conditions in the occurrence of RA. A number of authors believe that in the development of the RA a large importance belongs to endogenous factors - age, genetic and endocrine [70, 72, 73, 74, 77, 78]. According to these researchers, various adverse environmental influences (intercurrent diseases, hyperinsolation, physical trauma, psychological factors, the use of some medicines, etc.) activate the initial infectious agent, which is a trigger in the development of immune response reactions in the body, predisposed to the development of pathological process.

Currently, the vast majority of researchers recognize the great role of hereditary predisposition in development RA in children. Research by scientists has shown that the likelihood of the risk of development diseases in children in families where there are patients with any collagen diseases increases by 4.7 times. In the research of S.A. Rakhimov [31] also emphasizes the importance and great role of the family factor in the occurrence of RA in children. The development of this pathological process is associated not so much with features of the primary agent, how much with an individual reaction organism on its impact. This reaction is largely genetically determined. Therefore, in recent years, when learning the role of hereditary mechanisms in the pathogenesis of RA is attention to the study of antigens of the main histocompatibility complex. Quite a number of studies point to the presence of an associative relationship of HLA antigens with clinical signs diseases, which indicates their predictive value in relation to the nature of the course and outcome of the disease [70, 72, 77, 78]. It is noteworthy that a number of researchers [73, 74] found the presence of the same antigenic associations of the HLA complex in children and adults suffering from RA, this confirms the unity pathogenetic mechanisms in this disease in children and adults, since there is no such form of RA in adults that would not occur in children; the difference lies only in the frequency of specific clinical forms diseases in adults and children.

Therefore, it is reasonable to view a number of authors on RA as a heterogeneous disease in adults and children [1, 4, 5]. Currently, the overwhelming majority of researchers believe that the pathogenesis of RA is based on an immunoregulation disorder various etiological factors on the body, which is different genetic predisposition to the development of the disease (Fig. 1), [33].

Fig. 1. SCHEME OF RHEUMATOID PATHOGENESIS ARTHRITIS



Modern features of kidney damage in rheumatoid arthritis in children

In the overwhelming majority of cases, the pathological process with RA is localized at the beginning of the synovial membrane of the joints, but in further changes in the connective tissue of other organs are observed. At the heart of the defeat of many organs and systems are vasculitis, which immunocomplex character [1, 4, 5, 12, 57, 67]. The severity of clinical and laboratory manifestations of

damage to other organs and systems in RA depends on the clinical form of the disease. In patients, predominantly the articular form of the disease in the clinical picture appears at the first plan to damage the joints, while manifestations of damage to other organs absent or very weakly expressed, and with articular-visceral form, along with articular syndrome, already at the onset of the disease there are clear signs of damage to various organs and systems [9, 24, 54]. Lymph node involvement may occur in patients with RA (lymphadenopathy), nervous system, spleen and gastrointestinal tract (amyloidosis, gastritis, enteritis, colitis), liver (hepatitis, dystrophy, necrosis, cell sclerosis), muscular system (degeneration, atrophy), lungs (interstitial pneumonia, pneumosclerosis), heart (carditis), major endocrine glands - pituitary gland, thyroid gland, adrenal glands, pancreas and eyes [2, 3, 36, 42, 43, 44, 48]. The defeat of these organs and systems contributes to a more severe course of the disease, creates additional difficulties in treating patients and aggravates the prognosis pathological process. [12, 15, 25, 29, 32, 39, 66].

In recent years, the attention of researchers has attracted more functional state of the kidneys in RA. It has been established that the kidneys are the disease is affected in about 50-60% of cases and their involvement in the pathological process can manifest itself in the form of amyloidosis [15, 29, 38, 42, 52], glomerulonephritis, nephroangiosclerosis, interstitial nephritis and eleven pyelonephritis [6, 7, 21, 63, 64]. It was found that nephropathy in patients RA often presents with varying degrees of proteinuria, microhematuria and leukocyturia, signs of renal failure, but often clinical signs were absent, which was the basis to the allocation of the subclinical stage of the renal process in patients with RA. Later studies using immunohistochemical and electron microscopic methods made it possible to detect in patients RA is practically all morphological types of glomerulonephritis [46, 53]. Clinical and laboratory symptoms of kidney damage in RA can be manifested by swelling of the face, scrotum, legs and feet or only proteinuria of varying severity or hematuria, arterial hypertension, nephrotic syndrome or and isolated urinary syndrome. Kidney damage in RA can be prolonged time to pass latently, or to progress steadily and rapidly, the result of which is a secondary contracted kidney with a clinical picture chronic renal failure [13, 56, 60]. A number of authors suggest that the occurrence of glomerulonephritis in RA is a pre-stage of renal amyloidosis [36, 67, 68, 69]. According to H.L. F. Currey and J. Woodlend Prescribing Prednisolone in Patients with RA lesions kidneys led to an improvement in the condition of patients and the elimination of clinical and laboratory manifestations of glomerulonephritis. However, many scientists do not found positive dynamics of the renal process in RA patients when prescribing corticosteroid drugs, and according to some authors,

use of anti-inflammatory drugs and corticosteroids can even lead to an increase in clinical and morphological symptoms of kidney damage in this disease [39, 70, 72, 73, 74]. Some authors, based on the results of their own studies also concluded that the appointment of non-steroidal anti-inflammatory drugs can in some cases aggravate kidney damage in RA [56, 75]. In addition, the literature provides 12 messages, the authors of which link the occurrence of nephropathy in patients with RA with the appointment of gold preparations, D-penicillamine, cyclosporin A, levamisole [77, 78, 79]. However, most researchers consider kidney damage in this disease ai pathognomonic sign, which is one of the manifestations immunocomplex pathology [31, 69]. The incidence of AA-amyloidosis of the kidneys in RA in children is from 0.8 to 2.0%, in adults with RA duration of 28.3 years - 8.9% [5, 85, 86]. IN In recent years, against the background of immunobiological therapy, the frequency of AA-amyloidosis of the kidneys in adults has decreased to 2.5% [67, 72, 76, 81]. On the to date, the main mechanism of development of AA amyloidosis has been established, which consists in a constant or periodic increase serum amyloid A (SAA) concentration. It was found that the synthesis SAA is influenced by pro-inflammatory cytokines: IL-1, IL-2, IL-11, IL-6, TNF-α and others. To realize the amyloidogenic potential of SAA, it is necessary not only the effect of the inflammatory process in the body, but also its duration. The role of genetic factors in the development of AA-amyloidosis of the kidneys in RA. AA-renal amyloidosis most often develops in children with a systemic form, in adults – with systemic and polyarticular forms of RA. The first symptom of AA renal amyloidosis is isolated proteinuria, which transforms into nephrotic syndrome [17, 34, 35, 87]. Features of the nephrotic syndrome are in the absence in most cases hypercholesterolemia, combined in some patients with arterial hypertension, hematuria, impaired renal function [48, 61, 62, 84]. The main method for confirming the diagnosis of AA-renal amyloidosis, is an intravital morphological study of the kidneys. Enhancement blood SAA level in children with RA reflects the degree of the inflammatory process and is considered as a risk factor for the development of AA-amyloidosis of the kidneys [10, 27, 13 28]. In this case, the use of immunobiological drugs (tocilizumab, anakinra) has therapeutic efficacy [11, 88]. Along with joint damage in patients with RA, involvement in pathological process of other organs and systems [17]. One of pathognomonic visceral signs of the process, a number of authors consider kidney damage, which can manifest itself as an overt clinical picture, but more often it proceeds latently and is diagnosed only when application of special research methods [65, 71]. Kidney involvement in the pathological process is an unfavorable prognostic sign, since the result of kidney damage in these patients

may be development of chronic renal failure [38, 40, 44, 45]. Summarizing the above data of the special literature, one can conclude that damage to joints and other organs in RA is a consequence of the development of immunopathological reactions in individuals genetically predisposed to the onset of this disease. Immune the nature of RA is confirmed by the identification of rheumatoid factor in patients, various autoantibodies, immune complexes sensitized to components of the connective tissue of lymphocytes, the similarity of focal pathological changes with the manifestation of immune inflammation, impossibility of detecting an infectious agent and ineffectiveness anti-infectious therapy with the effectiveness of treatment of patients immunosuppressive drugs [80, 82, 84]. However, literature data on the pathogenesis and nature of clinical and laboratory manifestations of renal disorders in this disease in adults are few in number and contradictory, while the renal pathology in children with RA remains generally poorly understood problem and until now there have been no comprehensive studies in the comorbid course of RA in children with immunodeficiency pathologies, including AID, which remains relevant in pediatric and adult rheumatology. Fourteen Thus, the presented data indicate that pathogenesis of autoimmune diathesis, rheumatoid arthritis and rheumatoid nephritis in children has a general immunopathological nature. But autoimmune diathesis is an important risk factor for the occurrence and progression of rheumatoid arthritis and subsequent development amyloidosis of the kidneys based on immunopathological reactions in such patients.

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PATHOPHYSIOLOGICAL SUBSTANTIATION OF THE USE OF A NEW DRUG BASED ON G. LUCIDUM AND ALKHADIA IN THE TREATMENT OF CORONAVIRUS INFECTION CAUSED BY SARS COV-2.

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ABSTRACT

The current outbreak of coronavirus disease (COVID-19) is a global emergency as its rapid spread and high mortality rate have caused severe disruption. The number of people infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, is rapidly increasing worldwide. Patients with COVID-19 may develop pneumonia, severe symptoms of acute respiratory distress syndrome (ARDS) and multiple organ failure.

Key words: coronavirus infection, pathogenesis, acute respiratory syndrome, G. lucidum, Alkhadaya.

INTRODUCTION

The current outbreak of coronavirus disease (COVID-19) is a global emergency as its rapid spread and high mortality rate have caused severe disruption. The number of people infected with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, is rapidly increasing worldwide. Patients with COVID-19 may develop pneumonia, severe symptoms of acute respiratory distress syndrome (ARDS) and multiple organ failure.

Coronavirus is an enveloped positive single-stranded RNA virus. It belongs to the subfamily Orthocoronavirinae, as the name suggests, with characteristic "crown" spines on their surface. Together with SARS-CoV, SARS-CoV of bats and others also fall into the genus of betacoronaviruses [6]. On January 15, 2019 in Taiwan, COVID-19 (caused by 2019-nCoV infection) is classified as a Category 5 Notifiable Infectious Disease. The genus of betacoronaviruses can be divided into several subgroups. 2019-nCoV, SARS-CoV, and bat SARS-like CoV belong to sarbecovirus, while MERS-CoV belongs to merbecovirus, having different biological characteristics and virulence [7, 10].

Immune models of COVID-19 include lymphopenia, lymphocyte activation and dysfunction, granulocyte and monocyte abnormalities, increased cytokine production, and elevated antibodies. Lymphopenia is a key feature in patients with COVID-19, especially in severe cases. CD69, CD38, and CD44 are highly expressed on patients' CD4+ and CD8+ T cells, and virus-specific T cells in severe cases show a central memory phenotype with high levels of IFN-γ, TNF-α, and IL-2. However, lymphocytes exhibit a depletion phenotype with activation of programmed cell death protein-1 (PD1), immunoglobulin T-cell domain and mucin domain-3 (TIM3), and cell lectin-like C-receptor subfamily member 1 (NKG2A) [2, 4]. The level of neutrophils is significantly higher in severe patients, while the percentage of eosinophils, basophils and monocytes is reduced. Increased production of cytokines, especially IL-1β, IL-6 and IL-10, is another key characteristic of severe COVID-19. IgG levels are also elevated and there is a higher titer of all antibodies [8].

Lymphopenia is a key feature in patients with COVID-19, especially in severe cases. Patients with severe COVID-19 are more likely to have lymphopenia on admission, indicating a significant predictor for severe patients. The percentage of lymphocytes has been found to be below 20% in severe cases. Further analysis showed a significant decrease in the number of T cells, especially CD8+ T cells, in severe cases compared to mild cases. Qin et al. reported that the percentage of memory T-helper cells (CD3+CD4+CD45RO+) is also reduced in severe cases compared to non-severe cases. These data indicate that lymphopenia can be used as an indicator of disease severity and prognosis in patients with COVID-19 [3, 5]. However, lymphopenia was present in some non-severe cases and pregnant women; however, the percentage of non-severe patients with lymphopenia is significantly lower than that of severe patients. Interestingly, the number of B cells is within the normal range, which is similar to the results of our study, indicating that damaged B cells are not as significant as damaged T or NK cells [1, 9]. There is also a growing focus on another natural product, the well-known mushroom G.

Lucidum. The composition of this natural product is very wide, including superoxide dismutase, which also reduces the pathogenetic effect of the “cytokine storm” without causing side effects on the liver [10].

Also, in recent years, more and more attention has been paid to another natural product of Alkhadaya, which is black cumin oil. I noticed that both G. Lucidum and Alkhadaya contain carboxyl groups in their composition, and they are not a continuation of nitro groups and sulfhydryl groups. These carboxyl groups originate from the phenolic rings of G. Lucidum and the benzene rings of Alkhadai, and the idea of creating a new drug based on G. Lucidum and Alkhadai was proposed, and given its importance not only in the treatment of coronavirus infection, but also in its safe use, this study is considered a hot topic and requires further study.

The aim of the study. Optimization of approaches in the diagnosis and treatment of coronavirus infection caused by COVID-19.

Materials and research methods. To achieve this goal, the results of treatment of 50 patients with coronavirus infection caused by COVID-19 were analyzed. All patients were divided into groups: group 1 - patients with coronavirus infection with a confirmed positive PCR test, treated with ivermectin at a dosage of 300 mg of body weight (n=12), group 2 - patients with coronavirus infection treated with baicalin at a dosage of 500 mg (n= 14), group 3 - patients with coronavirus infection treated with molnupiravir 25 mg/kg body weight, group 4 - patients with coronavirus infection treated with a new drug based on G. Lucidum and Alkhadaya.

The amplification reaction and analysis of PCR products were carried out in the mode real time cycler "Rotor-Gene 6000" ("Corbett Research", Australia). The reaction mixtures included oligonucleotide forward and reverse primers complementary to a specific fragment, fluorescent probes labeled with the FAM fluorophore (carboxyfluorescein) and fluorescence quencher (RTQ1), deoxyribonucleoside triphosphates (dNTPs), $MgCl_2$, buffer, Taq polymerase enzyme, and deionized sterile water. For the negative control, the same volume of distilled water was added to the test tube instead of the sample.

Positive samples were determined by the presence of a phase of the logarithmic growth of the fluorescence curve. Registration of results in real time (the value of the threshold cycle, Ct) was performed in tabular and graphical form using computer programs.

Statistical processing was carried out taking into account parametric and nonparametric research methods.

Research results. Taking into account the high analytical sensitivity and specificity of the developed BDags1F/BDags2R primers and the BDags-2P fluorescent probe for the identification of SARS CoV-2, at the next stage of the work, their diagnostic informativeness was studied in the simulation of coronavirus infection in white mice.

In addition, the study used human blood contaminated with SARS CoV-2 cells to evaluate whether primers can be used to diagnose the disease in humans. For this, a suspension of SARS CoV-2 viral cells in yeast form was used with a concentration of 1×10^5 cells/ml to 1×10 cells/ml.

As a result of the work, it was found that the BDags-1F/BDags-2R primers are able to detect virus DNA in the blood at a concentration of 1×10^4 cells/ml. To standardize the experiment in modeling infection, a yeast culture suspension was used at a concentration of 1×10^6 cells/ml. For the amplification reaction, the selection of sectional material from infected white mice was carried out on days 7, 14, 21, and 28 after infection. The study of biological samples using real-time PCR was carried out in parallel with the cultural (mycological) method.

Intraperitoneal infection in susceptible animals may develop a coronavirus infection. The autopsy of animals on the 7th day after infection is due to the fact that this period coincides with the period of manifestation of this coronavirus.

However, the autopsy of infected white mice revealed no macroscopic changes in the internal organs. SARS CoV-2 6/85 DNA was detected by PCR in 12.5% of spleen and blood samples. In the study of sectional material using the cultural method, the growth of SARS CoV-2 6/85 was detected in samples of the liver and spleen in 12.5%.

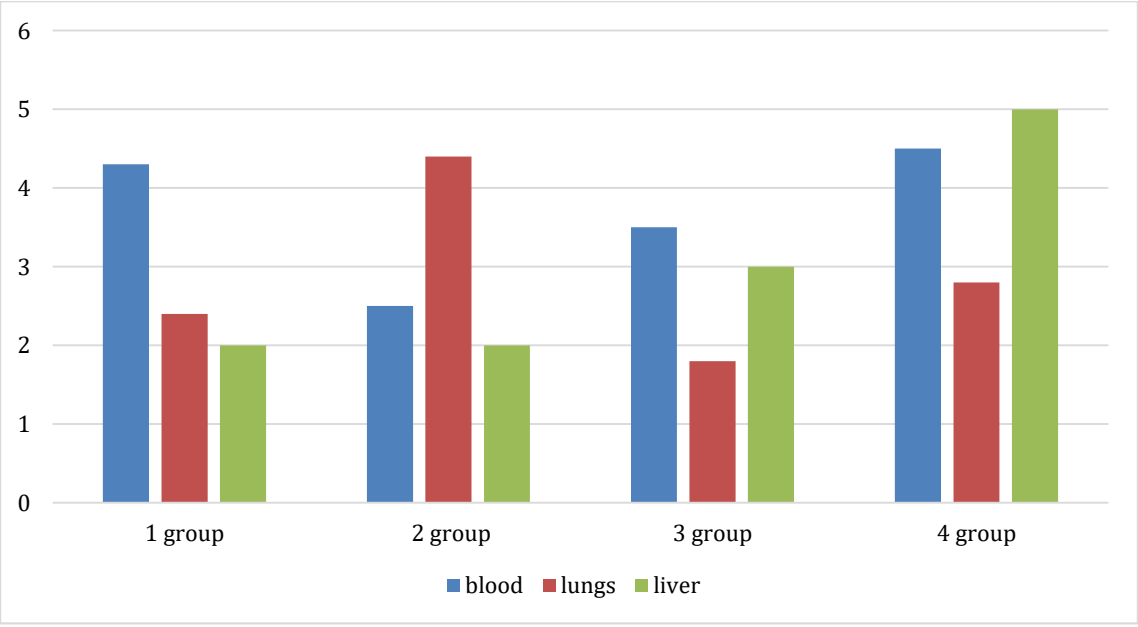

Fig. 1. Results of detection of SARS CoV-2 during experimental infection on the 7th day of the disease.

Thus, the content of T-cells in the norm is 0.8-2.5 109/l. The study revealed a decrease in the content of T-cells ≤0.8X109/l (Fig. 2).

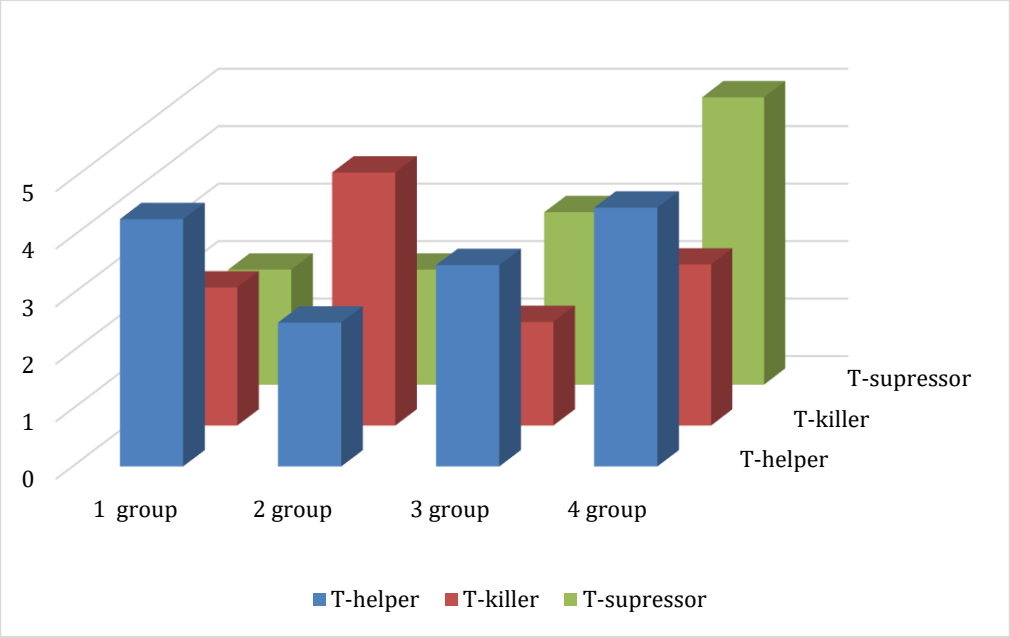

Fig. 2. The content of T-cells at the time of admission of the experimental animal.

Since an increase in the relative number of T-cells is more often observed with a sharply polarized Tx1 type of immune response to a viral antigen, we also observed an increased number of T-lymphocytes.

An increase in the relative number of T-helpers can be observed in the Tx2 type of immune response, which is due to an increase in the number of T-helpers in the Tx2 type of immune response.

Severe Acute Respiratory Syndrome Coronavirus (ARDS) is known to infect cells expressing surface angiotensin converting enzyme 2 (ACE2) and TMPRSS2 receptors, active replication and release of the virus causes the host cell to release damage-associated molecular structures including ATP, nucleic acids and ASC oligomers. They are recognized by neighboring epithelial cells, endothelial cells, and alveolar macrophages, causing the generation of pro-inflammatory cytokines and chemokines (including IL-6, IP-10, macrophage inflammatory protein 1α (MIP1α), MIP1β, and MCP1). These proteins attract monocytes, macrophages, and T cells to the site of infection, promoting further inflammation.

Figure 3 shows the content of B-lymphocytes in coronavirus infection.

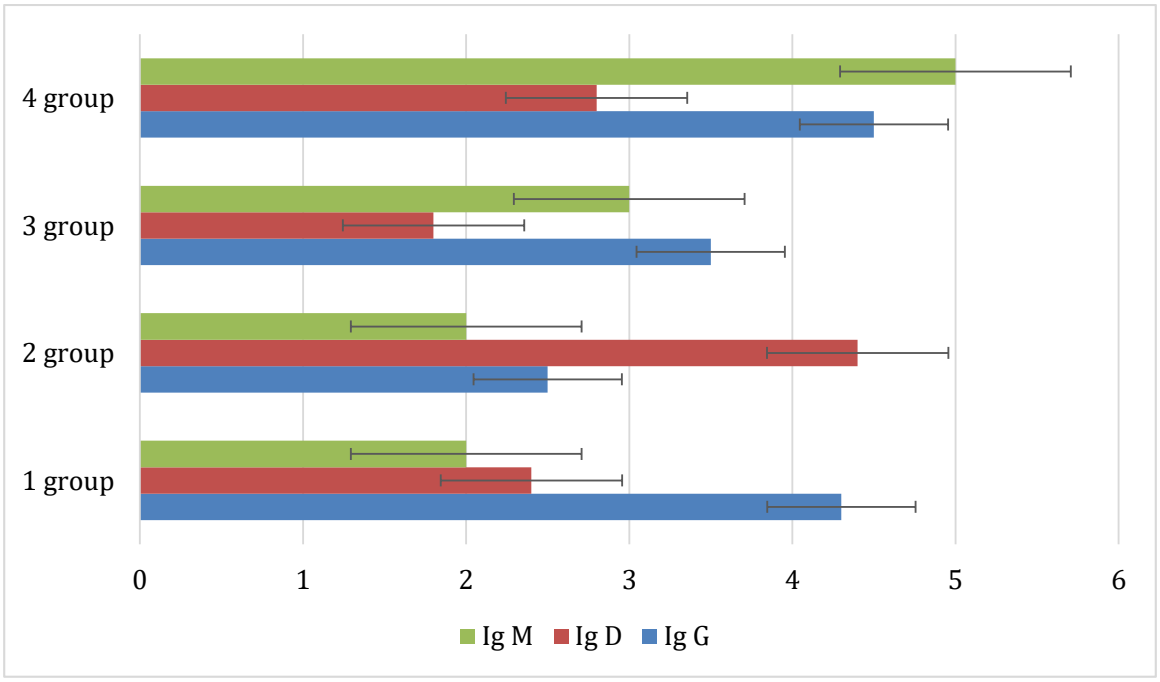

Fig. 3. The content of B-lymphocytes in the peripheral blood of experimental animals with coronavirus infection.

Since a decrease in the absolute number of B-lymphocytes can be the result of lymphopenia, it can be observed in the case of active antibody formation and in coronary infection caused by SARS CoV-2.

After treatment in the 1st study group, on day 14, 10 patients showed an improvement in PCR parameters, which was expressed in a decrease in the degree of detection of SARS CoV-2 in the subjects.

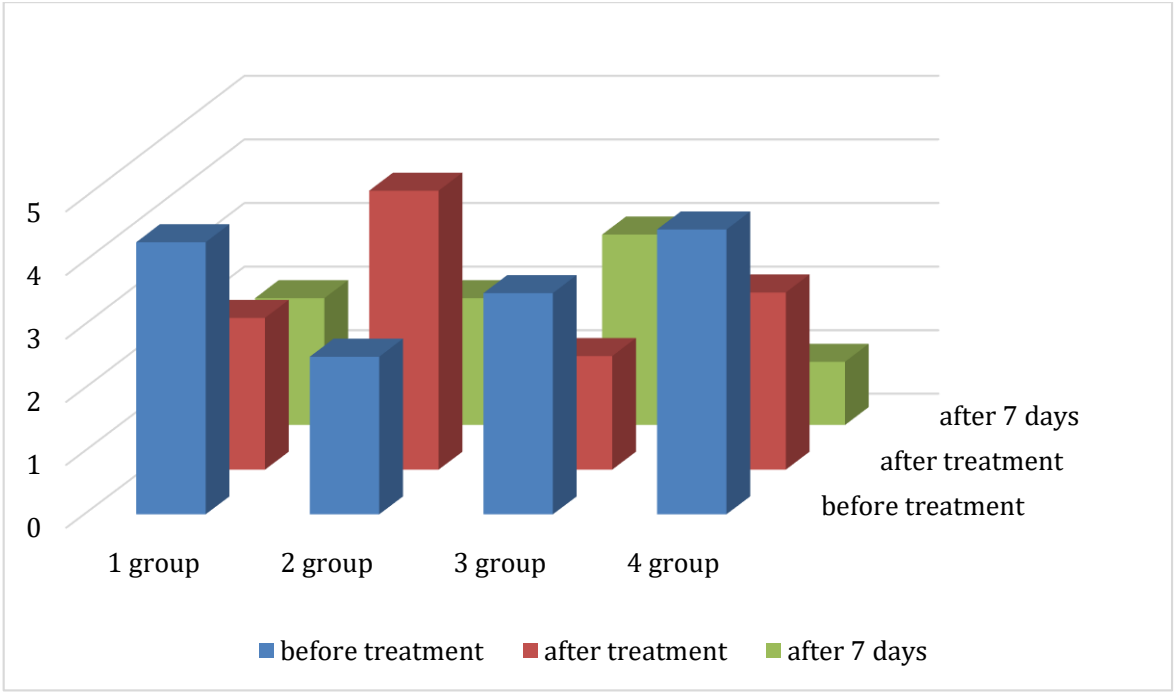

Fig. 4. Results of detection of coronavirus infection caused by SARS CoV-2 in subjects.

Moreover, on day 21, the causative agent of coronavirus infection was found in 25% of liver samples and 37.5% of spleen samples. When examining the abdominal organs of mice at autopsy, the presence of plethora and enlargement of the liver and spleen of infected animals was noted. SARS CoV-2 6/85 DNA was detected by PCR in 12.5% of liver, blood, and 25% of spleen samples.

When modeling an experimental infection, DNA of the causative agent of coronavirus infection by PCR was detected in 10 out of 32 infected mice (31%).

However, the bacteriological method required much more time for research. Visible growth of micromycete was observed only 10-14 days after taking the material for research. Another 7-10 days were required for the appearance of morphological features, with the help of which it was possible to identify the microorganism. Also, the results of PCR were not affected by the possible contamination of samples with foreign microflora.

Table 1.

Comparison of PCR results after treatment in the examined groups.

Groups	PCR results	
1 group	Positive at 6	Negative at 4
2 group	Positive at 9	Negative at 3
3 group	Positive at 8	Negative at 3
4 group	Positive at 1	Negative at 9

Thus, it can be seen that the use of a new drug based on G. Lucidum and Alkhadai is effective in the treatment of coronavirus infection.

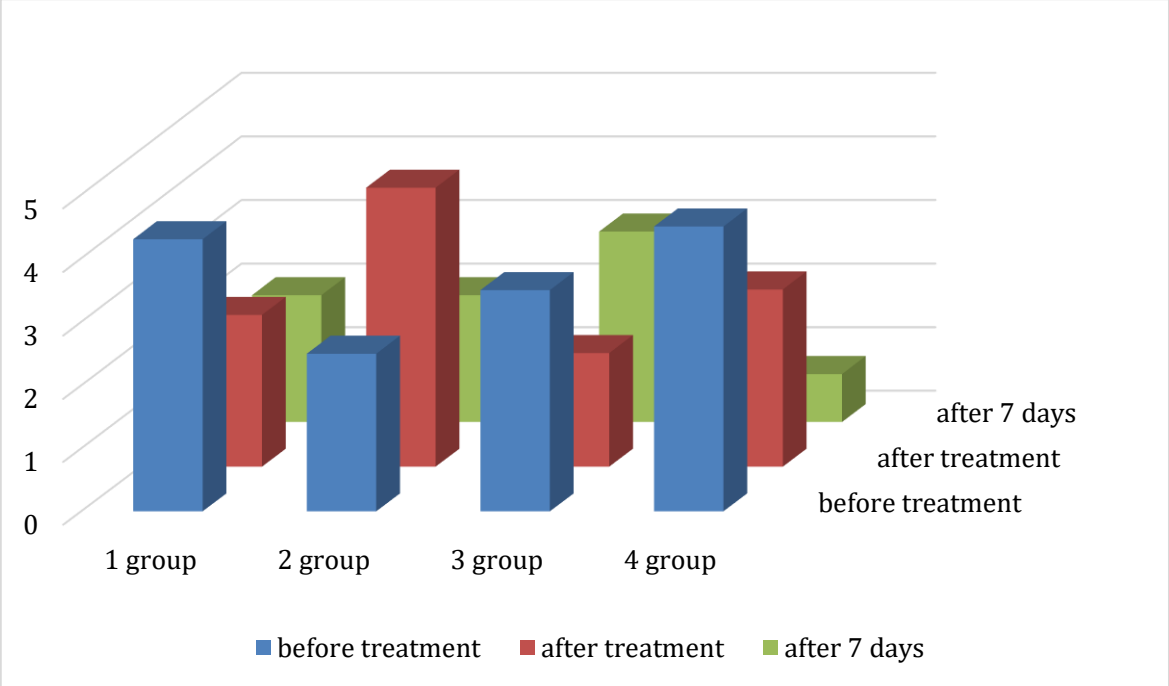

Fig. 5. The content of T-cells after treatment in the examined groups.

There was also an increase in the CD4/CD8 ratio due to an increase in T-helpers (with a normal number of T-killers) and a decrease in CD8 lymphocytes. Since an increase in the CD4 / CD8 ratio due to an increase in CD4 and a decrease in CD8 lymphocytes is usually detected with a mixed Tx1 / Tx2 response to the antigen.

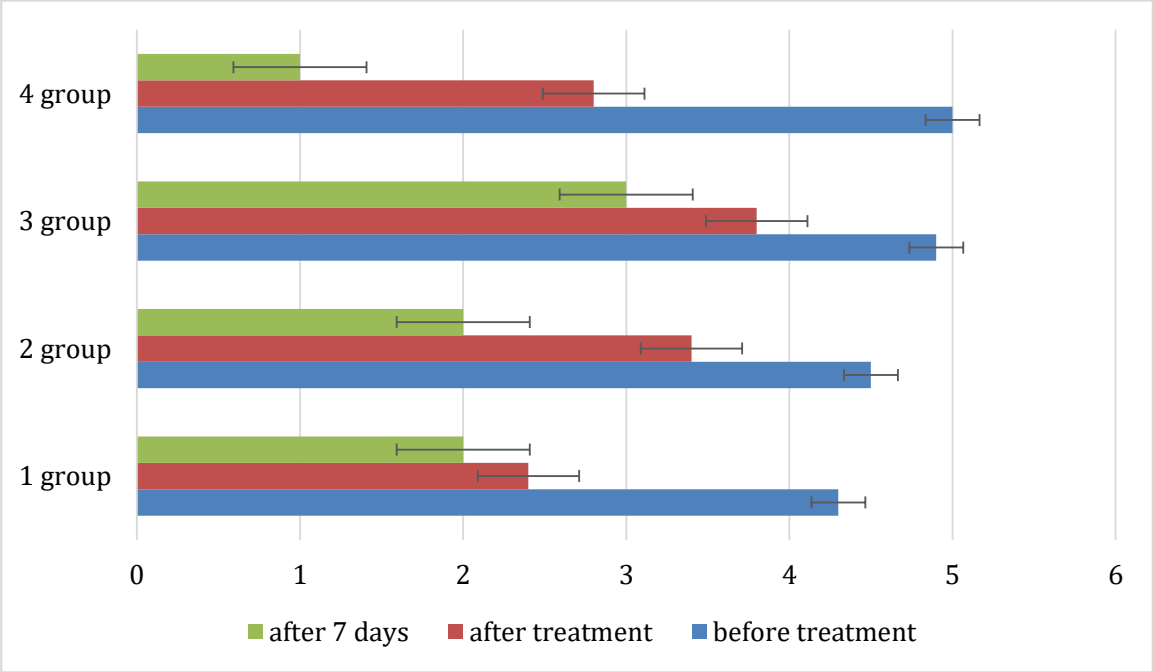

Fig. 6. The content of B-lymphocytes in peripheral blood after treatment.

The results of the presented studies indicate the fundamental possibility of using the polymerase chain reaction to detect SARS CoV-2 DNA. PCR was shown to be more informative in the analysis of blood samples, in comparison with the bacteriological method, which in real conditions can make it possible to detect the pathogen in the early stages of the disease.

Findings. Thus, the detection and elimination of coronavirus infection caused by SARS CoV-2 is achieved after the use of a new drug based on G. Lucidum and Alkhadai (95% CI = 1.3-5.6 at $\chi 2 = 0.9321007$, U (Mann- Winnie) = 0.8721093, N (Kruskes-Wallis test) = 0.9102385 at $p \leq 0.05$.

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Central Asian Journal of Medicine

ASSESSMENT OF COGNITIVE FUNCTIONS IN PATIENTS WITH POST-COVIDAL CEREBROASTENIC SYNDROME

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ABSTRACT

Aim of the study: We aimed to study the occurrence of cognitive impairment in post-covidal cerebroastenic syndrome in patients with various degrees of severity of COVID-19, to assess the severity of the asthenic syndrome, and develop optimal diagnostic approaches. **Materials and methods:** The presence of cognitive impairments was assessed based on the clinical symptom questionnaire, the MMSE scale (Mini Mnetal State Exam, Folstein, et al., 1975), and the MoCA test (The Montreal Cognitive Assessment, MoCa, 2005). The severity of asthenic manifestations was determined by ASS (Asthenic State Scale modified by L. D. Malkova and T. G. Chertova, 2014). **Conclusions:** In patients with post-covidal cerebroastenic syndrome, cognitive impairment was assessed using the MMSE scale. In the main group, 21 people had moderate dementia, 27 people had mild dementia, and 20 people had moderate cognitive impairment. In the control group, positive results were recorded within the standard values. The MoCA test revealed a decrease in cognitive functions in the form of moderate dementia in 23, mild dementia in 26 and moderate cognitive impairment in 19 in the main group. Whereas in the comparison group on the first day of admission to the hospital against the background of intoxication.

Key words: COVID-19, asthenic syndrome, cognitive functions, post-covidal cerebroastenic syndrome, dementia, cognitive impairment.

INTRODUCTION

The COVID-19 pandemic originated in our society as a severe unemployment crisis, a financial crisis in the healthcare system, and in many other areas. Numerous studies have shown that situations such as the death of family members and many physical consequences after COVID-19 caused psychological distress in

survivors of COVID-19 infection (Rogertz et al., 2020; Taquet et al., 2021), such as fatigue. (Garg et al., 2021; Stavem) (Townsend et al., 2020), impairment of cognitive disorders (Rakhimbaeva G.S., 2021), cognitive changes, or "slowing down of consciousness" / "areas of thinking" sometimes led to the development of a number of additional pathologies such as depressive conditions (Landau, 2021; Zhou et al., 2020). Based on the above data, we can say that this is clear evidence that the virus and psychosocial factors have a direct effect on the nervous system. SARS-CoV-2 causes neuropsychiatric effects on the human central nervous system, such as mood swings, psychosis, and neuromuscular dysfunctions during the acute and recovery periods.

Among the physical consequences of COVID-19, feeling tired is the most common complication. Available data indicate that fatigue ranges from 46 to 53% (Litas, Kee et al. 2020). The likelihood of fatigue and other complications depends on a number of factors and can occur independently (Townsend et al., 2020). In most cases, the onset of fatigue is also associated with factors such as anemia and vitamin B12 deficiency, female gender (Garg et al., 2021; Townsend et al., 2020). In addition, patients recovering from COVID-19 infection experience pathological processes such as cognitive impairment and dementia (Beaud et al. 2020; Zhou et al. 2020). Some studies point to mild to moderate cognitive impairment up to severe dementia (Di Pietro 2021; Vanderlind et al. 2021).

An asthenic syndrome is diverse clinical symptomatology, which includes a decrease in physical activity (endurance, performance), cognitive functions (memory, attention, perception of new information, speed of decision-making), rapidly increasing fatigue, and a persistent feeling of weakness. Asthenia is manifested by various psycho-emotional disorders (increased anxiety, irritability, mood swings, decreased motivational activity and interest in what is happening, fear of the future). Various diseases can be accompanied by asthenic symptoms, which indicates a significant decrease in the psychoemotional resources of the body.

Objective: To study the incidence of cognitive impairment in post-covidal cerebroastenic syndrome in patients with varying degrees of severity of COVID-19, to assess the severity of the asthenic syndrome, and to develop optimal diagnostic approaches.

Research materials: in the COVID-specialized center "Geologist" in the Karshi branch of the RSCEMA, 98 patients were treated, followed up for 120 days. All patients in the acute phase of the disease underwent clinical and neurological examination; among comorbid conditions, diabetes mellitus was noted - 26 (26.5%), arterial hypertension - 7 (7.1%), cerebral atherosclerosis - 5 (5.1%),

pneumonia - 42 (42.9%). All patients were divided into two groups. The main group included 77.5% (68) of patients who developed post-covidal cerebroastenic syndrome and other neurological complications after suffering from COVID-19. The control group included 22.5% (21) of patients with COVID-19 infection, but without functional or organic complications from the nervous system during the entire observation period. The patients underwent the following studies: COVID-19 was confirmed by polymer chain reaction analyzes and MSCT chest examination and other analyzes. The presence of cognitive impairments was assessed based on the clinical symptom questionnaire, the MMSE scale (Mini Mnetal State Exam, Folstein, et al., 1975), and the MoCA test (The Montreal Cognitive Assessment, MoCa, 2005). The severity of asthenic manifestations was determined by ASS (Asthenic State Scale modified by L. D. Malkova and T. G. Chertova, 2014). The patients were followed up for 14 days.

Research results: When analyzing the results obtained, the average age of patients in the main group was determined as 51.4 ± 3.1 years, and in the control group - 47.4 ± 2.5 years. In patients with post-covidal cerebroastenic syndrome, cognitive impairment was assessed using the MMSE scale. In the main group, 21 people (10-19 points) had moderate dementia, 27 people (20-24 points) had mild dementia, and 20 people (25-27 points) had moderate cognitive impairment. In the control group (above 28 points), positive results were recorded within the standard values. (Table 1).

Table 1.

Indicators of the MMSE scale in the study cohort of patients 1 day of admission to the covid hospital.

Indicators of the MMSE scale	Main results
Moderate dementia (10-19 points)	21/98
Mild dementia (20-24 points)	27/98
Moderate cognitive impairment (25-27 points)	20/98
Within normal limits (above 28 points)	30/98

The percentage of patients according to the MMSE scale criteria in the studied cohort of patients on the 1st day of admission to the covid hospital was shown in Diagram 1. As can be seen from the presented results on the 1st day of illness, only in 30.61% of patients, the indicators of cognitive functions according to the MMSE scale in the studied cohort corresponded to the parameters norms, while 60.39% of those examined against the background of acute coronavirus infection showed a slight and moderate decrease, sometimes approaching the indicators of dementia.

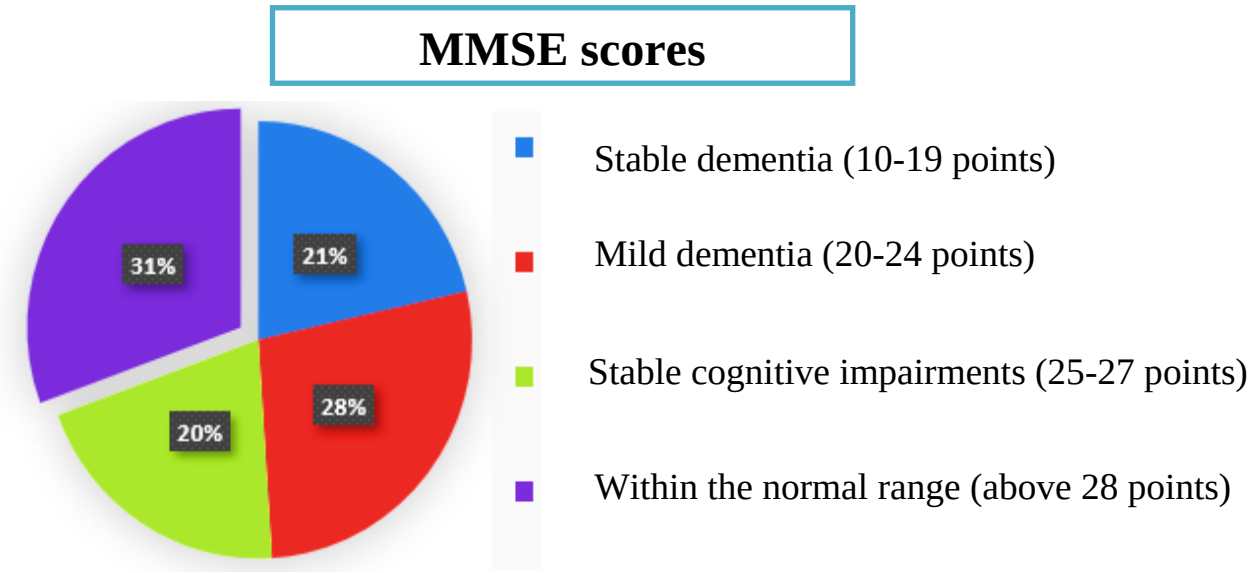

Fig. 1. Indicators of the percentage of cognitive impairment according to the MMSE scale in the studied cohort of patients.

Nervousness, fatigue and cognitive impairment were observed at the beginning of the observation in the main group, and these changes persisted in 41 (60%) patients during 120 days of observation. In the control group, no signs of neurological symptoms and asthenia were observed in patients even after 3 months from the onset of the disease (Table 2).

Table 2.

The ratio of patients in the study cohort on the 120th day of observation in relation to the formation of postcoid cerebro-asthenic syndrome.

Study cohort	1 day (inpatient treatment)	120 days (outpatient observation)
Main group	68/98	41/98
Control group	30	30

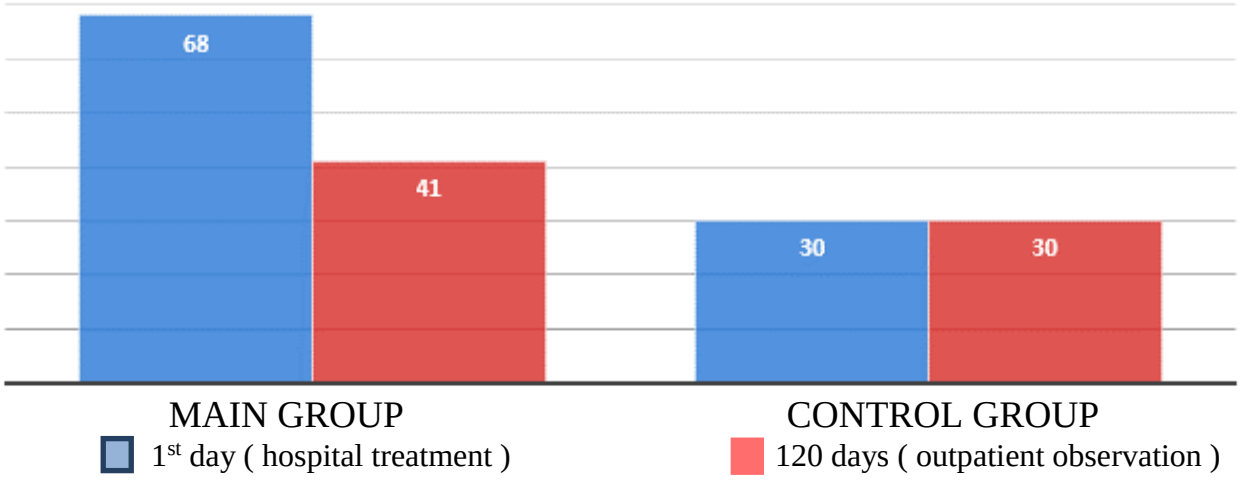

Fig. 2. Indicators of regression of cognitive impairments in the studied cohort of patients according to the MMSE scale on the 120th day of observation.

The MoCA test revealed a decrease in cognitive functions in the form of moderate dementia in 23 (20-17 points), mild dementia in 26 (24-21 points) and moderate cognitive impairment in 19 (27-24 points) in the main group. Whereas in the comparison group on the first day of admission to the hospital against the background of intoxication (table 3.).

Table 3.

Cognitive indices according to the Montreal scale MoCA test in the study cohort on the 1st day of admission to the covid hospital.

Graduation of points MoCA test	results
Moderate dementia (20-17 points)	23/98
Mild dementia (24-21 points)	26/98
Moderate cognitive impairments (27-24 points)	19/98
Within normal limits (30-28 points)	30/98

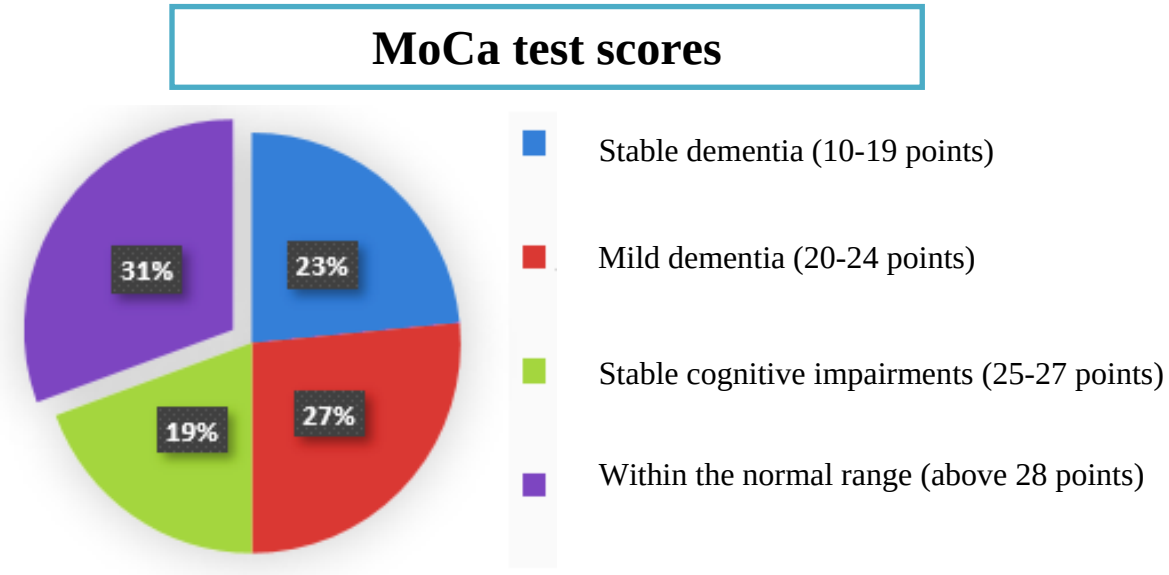

Fig. 3. Percentage of the Montreal MoCA test scores in the study cohort of patients upon admission to the hospital.

We also conducted a survey to determine how our patients assess their condition according to the ASS (asthenic state scale, Malkova L.D.).

Survey participants (n = 98).

The severity of asthenic manifestations in patients of the study and control groups varied from moderate to severe. (Fig. 4)

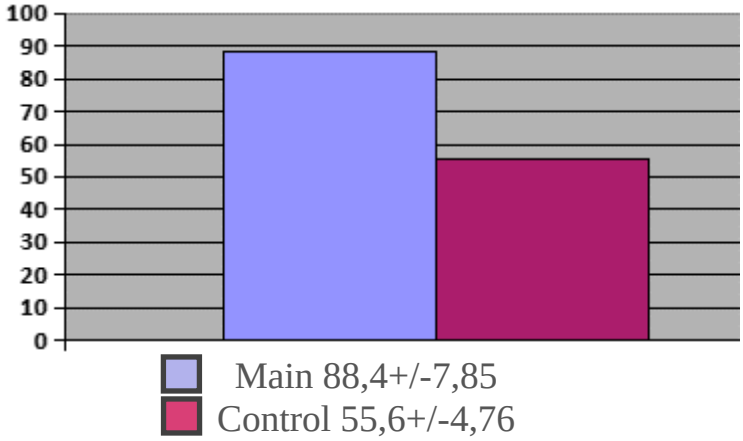

Fig 4. Dynamics of indicators of the asthenic state scale on the 1st and 120th day of observation of the studied cohort of patients with COVID - 19.

As can be seen from the figure, on the first day of admission to the hospital, patients were tested according to the ASS scale questionnaire, consisting of 30 items, 88.4% of patients in the first group noted increased fatigue, decreased mood, sleep disturbance, intolerance to loud sounds and bright light, and no desire to communicate with others, a sharply reduced mood background, in the comparison group in patients with mild and asymptomatic COVID-19, mild symptoms of asthenia were observed approaching the norm, which quickly returned to normal and were in the range for 120 days of observation in all the subjects. In the main group, the indicators of the ASS scale by the 120th day of the study also somewhat regressed from the indicators of severe to moderate asthenia. But only in 18 patients (15%) they corresponded to the norm.

Conclusion: Thus, the results of our study showed that coronavirus infection is accompanied from the very first day of the disease by a state of pronounced general weakness and the formation of post-covidal cerebroastenic syndrome in a significant part of patients with moderate and severe course of the disease, which is expressed not only by high indices of the ASS scale, but and a decrease in cognitive functions according to the MMSE and MoCa test scales, in severe cases of the disease bordering on dementia disorders. Our data are consistent with the results published by Qi, R. Et al. 2020, Townsend L. et al. 2020, which noted the phenomena of pronounced loss of strength and unusual asthenia in patients in the acute period of SARS-COVID - 19. The opinion that correction of asthenic and cognitive impairments, obligatory for patients with moderate and severe course of the disease, is emphasized by many practical researchers of the problem of post-covidal syndrome, noting not only neurological, but also a complex of neuropsychiatric syndromes in SARS-COVID-19 (Di Pietro, DA et al, 2021). Consequently, efforts carried out in this direction will help to reduce asthenic

phenomena and improve the quality of life in patients with post-covidal cerebroastenic syndrome.

The results of a 120-day open-label cohort comparative study allowed us to draw the following conclusions:

1) Test studies (ASS scale) have demonstrated a long-lasting cerebro-asthenic syndrome, the signs of which, without appropriate therapy, persist for 120 days or more of observation in patients who have undergone severe and moderately severe forms of COVID.

2) Studies of cognitive function according to the MMSE and MoCa test showed in the acute period moderate cognitive decline and mild dementia, developing against the background of acute intoxication in 60.39% of patients, regressing in the postcoid period and by the 120th day of observation are observed only in 23.5% requiring medical correction.

3) Assessment of the cognitive state of patients during 120 days of observation, early diagnosis of cerebro-asthenic syndrome and its timely correction will help prevent further possible consequences and aggravation of the process.

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ULINASTATIN IN THE CONSERVATIVE THERAPY OF CHRONIC PANCREATITIS

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ABSTRACT

The article presents the results of the anti-inflammatory efficacy of the new generation protease inhibitor ulinastatin in the treatment of exacerbation of chronic pancreatitis of moderate severity. It is shown that exacerbation of chronic pancreatitis of alimentary, alcoholic and biliary etiology was expressed by abdominal pain and dyspeptic symptoms. An increase in the level of serum aminotransferases, bilirubin and alpha amylase was noted, which was accompanied by a significant increase in the activity of pro-inflammatory cytokines. The use of ulinastatin in the complex of pharmacotherapy of chronic pancreatitis contributed to the effective relief of exacerbation of pancreatitis, which was due to the anticytokine effect of the drug.

Key words: chronic pancreatitis, etiology, treatment, clinical, adverse reaction.

INTRODUCTION

Among diseases of the pancreas, chronic pancreatitis (CP) occupies a significant place, which is characterized by various etiological factors, the presence

of focal necrosis in the pancreas against the background of segmental fibrosis with the development of functional insufficiency of varying severity. The progression of CP leads to the appearance and development of atrophy of the glandular tissue, fibrosis and replacement of the cellular elements of the pancreatic parenchyma with connective tissue. In the literature of recent years, there are publications that provide the opinions of some researchers on the stages of the course (progression) of CP. According to one of them, the initial period of the disease, the stage of exocrine (exocrine) pancreatic insufficiency and a complicated variant of the course of CP - tumors of this organ are distinguished; however, apparently, other variants of the course of the disease are also possible [1,2].

Treatment of patients with CP largely depends on the severity of its exacerbation (including the presence or absence of various complications), manifested by various, more or less pronounced symptoms in pain, dyspeptic, hypoglycemic, so-called "metabolic" and / or "icteric" options. Often it is not possible to accurately determine one or another clinical variant [3,4,5].

The appearance of complications of CP largely determines, as the disease progresses, and often significantly changes the clinical manifestations of chronic pancreatitis. In the treatment of patients with CP, depending on their condition, various drugs are used: those that reduce pancreatic secretion, most often proton pump inhibitors, anticholinergics, enzyme preparations, antispasmodics, prokinetics, painkillers, antibiotics, plasma-substituting solutions. At present, the use of drugs that suppress the activity of pancreatic enzymes (Contrykal, Gordox, Trasylol,etc.) in modern pancreatology has been significantly limited due to the emergence of more effective and safe antienzymatic drugs, one of which is an inhibitor of proinflammatory cytokine , tumor necrosis factor (TNFα) ulinastatin.

The purpose of the study: to study the clinical efficacy and tolerability of ulinastatin(the drug "ROAN" 100,000 IU. lyophilisate for the preparation of an injection solution in patients with chronic pancreatitis in the acute stage of mild to moderate degree.

Research objectives:

1. Evaluation of the clinical, diagnostic and laboratory efficacy of the study drug.

2. Evaluation of tolerability of the study drug based on patient complaints and monitoring of adverse reactions.

Materials and methods:

In the group that received the study drug, there were 20 patients with mild to moderate CP who were hospitalized, of both sexes (men 8, women 12), over the age of 18 years (mean age 52.5 $\pm$ 4.5 years) who agreed to participate in the study,

with a diagnosis of chronic biliary pancreatitis, alcoholic, alimentary or mixed etiology in the acute stage. When diagnosing CP, the classification M - ANNHEIM was used , where the main diagnostic criteria were: M - Multiple, A - Alcohol, N - Nicotin, N - Nutrition, H - Heredity, E – Efferent pancreatic duct factors, I- Immunological, M – Miscellaneous and Metabolic factors[1]. In this case, the diagnosis of CP implies the presence of a typical clinical picture (recurrent pancreatic attacks, abdominal pain, etc.), as well as the presence of a number of the following criteria:

"Definite" CP (at least 1 criterion): calcification of the pancreas; moderate or severe changes in the ducts of the pancreas (Cambridge, 1984); severe exocrine insufficiency; morphological picture typical for CP.

"Probable" CP (at least 1 criterion): mild changes in the ducts of the pancreas (Cambridge, 1984); pseudocyst (s) - constantly existing or recurrent; pathological results of functional tests (fecal elastase, coprogram); endocrine insufficiency.

"Borderline" CP : typical clinical presentation without "probable"/"definite" CP criteria; expected after the first episode of acute pancreatitis.

Before and after treatment, all patients underwent a clinical examination (scored), including a general examination, clinical and biochemical studies: complete blood count, bilirubin, AlAT, AsAT , alpha amylase. Pro- inflammatory cytokines : IL-6 and TNFα, and also carried out the determination of fecal elastase. Of the instrumental studies, all patients underwent ultrasound examination (ultrasound) or, according to indications, computed tomography (CT) of the pancreas, where imaging criteria (Cambridge) were used to diagnose mild to moderate CP - the presence of two or more pathological signs:

- GPP width 2-4 mm;
- uneven width of the ducts
- moderate increase in prostate (up to 2 times)
- heterogeneity of the parenchyma with areas of increased and decreased echogenicity
- cavities less than 10 mm
- increased echogenicity of the MPD wall
- irregular contour of the pancreas.

The patients were prescribed ulinastatin 100,000 IU intravenously, drip, previously diluted in 100 ml of 0.9% sodium chloride 1 time per day for 3 days. The patients were also prescribed drugs necessary for the treatment of the underlying disease: proton pump inhibitors, antispasmodics, analgesics, enzyme preparations according to indications. The dose of drugs taken remained

unchanged throughout the study period. If during the course of the study it became necessary to change the dose or prescribe a new drug, continuation of the study for this patient was allowed, provided that these changes do not have a significant positive or negative effect on the course of the underlying disease. A repeated clinical and instrumental study was performed 7 days after the start of therapy.

Results: In patients with CP, the etiological factors of exacerbation were calculous cholecystitis, alcoholic and alimentary factors, and in 3 patients a combination of alcoholic and alimentary factors (Table 1).

Table 1

Etiological characteristics of patients with chronic pancreatitis

Etiological factors of CP	Number of patients
Biliary	10 (50%)
Alcoholic	4 (20%)
Alimentary	3 (15%)
Mixed	3 (15%)

Determination of fecal elastase showed that exocrine pancreatic insufficiency (below 200 units) was noted only in 4 patients.

The effectiveness of the treatment was evaluated based on the improvement of the patient's clinical condition and the dynamics of laboratory tests. The conducted studies revealed high efficiency in patients in the form of reliable relief of abdominal pain and dyspeptic symptoms of exacerbation of CP (Table 2).

Table 2

Dynamics of clinical symptoms of patients before and after treatment, in points

Complaints	**Ulinastatin 100,000 IU, 3 days**	
	Before treatment	**After treatment**
Abdominal pain syndrome	2.8 ± 0.23	1.1 ± 0.05*
Nausea	2.9 ± 0.12	0.7 ± 0.04*
Vomit	2.2 ± 0.05	0.5 ± 0.05*
Flatulence	2.5 ± 0.06	0.7 ± 0.03*
Diarrhea	2.0 ± 0.06	0.5 ± 0.05*

Note: hereinafter* - the difference is significant in relation to the indicators before and after treatment ($p < 0.05$)

Points:

0- no symptoms

1-Moderately pronounced symptoms

2-Medium pronounced symptoms

3-Expressed symptoms

Analysis of the obtained results showed that in the general blood test in patients before treatment, a moderate increase in leukocytosis and ESR was noted (Table 3). In their biochemical parameters, a significant increase in the parameters of AlAT, AsAT, bilirubin and alpha amylase was also noted (Table 4).

Table 3

Dynamics of the main indicators of peripheral blood of patients before and after treatment

UAC indicators	Before treatment	After treatment
Hemoglobin , g/l	124,5 ± 3,42	120.5 ± 2.55
Erythrocytes , 10^{12}/l	4,8 ± 0,12	4.4 ± 0.17
Leukocytes , 10^{9} /l	12,5 ± 1,9	8.4 ± 0.20*
ESR mm / hour	1 5, 2 ±1 ,50	7.40 ± 0.90*

Table 4

Dynamics of hepatic transaminases and bilirubin in the blood of patients before and after treatment

	Before treatment	After treatment
AlAT , U/l	67,19 ± 4,20	37,2 ± 3,30*
AsAT , U/l	34,7 ± 2,85	17,8 ± 0,55*
Bilirubin , mmol /l	32,05 ± 3,02	19,05 ± 2,90 *
Alpha amylase, U/ l	323,5 ± 30,50	221,7 ± 22,40*

When studying the level of pro-inflammatory cytokines in the blood serum of patients with CP during the period of exacerbation, an increase in the levels of IL-6 and TNFα was found (Table 5).

Table 5

Dynamics of IL-6 and TNFα in patients before and after treatment

Interleukins	Before treatment	After treatment
IL-6 (pg / ml)	65,8±5,4	40,3±3,6*
TNFα (pg / ml)	124,0±7,4	66,5±5,2*

Tolerability of the drug was assessed on the basis of subjective symptoms and sensations reported by the patient and objective data obtained by the investigator during treatment. The dynamics of laboratory parameters, as well as the frequency and nature of adverse reactions, were taken into account. In our patients, no

adverse reactions from the drug therapy used were observed. The drug was well tolerated. Only in 3 patients, laboratory tests over time revealed a slight increase in AlAT, AsAT and bilirubin, which was associated with an attack of existing cholelithiasis, as a result of which an exacerbation of CP occurred. These patients, after consulting an abdominal surgeon, were recommended to undergo cholecystectomy in a planned manner.

Discussion: CP is still an urgent problem of modern gastroenterology. The standards of treatment for such patients included anti-enzyme drugs (Aprotinin). However, due to their low efficiency and the presence of pronounced side effects, indications for their use in modern pancreatology have been extremely reduced. According to modern guidelines for the diagnosis and treatment of CP, inhibitors of proinflammatory drugs are most often used to relieve exacerbations, cytokines, in particular ulinastatin [6,7,8,9].

The study to study the clinical efficacy and tolerability of ulinastatin included 20 patients with exacerbation of CP.

Of the 20 patients with exacerbation of CP, 10 patients with etiological factors of the disease had calculous cholecystitis and a complication in the form of biliary pancreatitis. In 4 patients, exacerbation of the disease was associated with the use of strong alcoholic beverages. In 3 patients, exacerbation of the disease was associated with frequent malnutrition (excessive consumption of fatty foods). Also, in 3 patients, exacerbation of CP was due to a combination of factors such as alcohol and fatty foods. The clinic of exacerbation of the disease was expressed by a combination of abdominal pain and dyspeptic manifestations. Pain in patients was more often localized in the epigastrium and in the left upper square of the abdomen with irradiation into the interscapular space. Dyspeptic symptoms were manifested by nausea, vomiting, often not leading to relief, and flatulence. 18 patients also had diarrhea (more than 3 times a day or more) with steatorrhea. In 12 patients, a manifestation of exocrine pancreatic insufficiency was noted, which was expressed by a decrease in the level of mild fecal elastase (below 200 units in 4 patients). In 9 patients, moderate leukocytosis, an increase in ESR (in 15 patients), a moderate increase in transaminases, and an increase in bilirubin (often due to direct fraction) were noted in the blood serum. In 12 patients, an increase in the activity of alpha amylase in the blood serum was noted. Also, the majority of patients (16) showed an increase in the activity of IL-6 and TNF-alpha more than twice.

Thus, the studies revealed that the study drug in patients with exacerbation of chronic pancreatitis during treatment contributed to the relief of pain and dyspeptic symptoms, as evidenced by a decrease in patients' complaints about abdominal

pain symptoms and dyspeptic disorders. Control studies of biochemical blood parameters 7 days after the start of treatment showed normalization of leukocytes and ESR. In blood plasma, a significant decrease in the level of serum transaminases, bilirubin and alpha amylase was recorded. Accordingly, there were significant decreases in IL-6 and TNFα levels. However, in three patients with CP, no significant dynamics of clinical manifestations and biochemical blood parameters was observed, which was associated with attacks of calculous cholecystitis. In these patients, on the recommendation of an abdominal surgeon, cholecystectomy was recommended in a planned manner.

CONCLUSIONS:

1. The anti-inflammatory efficacy of the protease inhibitor ulinastatin in the conservative pharmacotherapy of CP is associated with inhibition of the pro-inflammatory cytokines IL-6 (by 65%) and more than twofold TNFα.

2. The protease inhibitor ulinastatincan be effectively and safely used in the treatment of patients with chronic pancreatitis to relieve exacerbations of the disease.

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TREATMENT OF ACUTE EROSIVE-ULCERATIVE GASTRODUODENAL BLEEDING

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ABSTRACT

To date, the tactics of treating patients with acute erosive-ulcerative gastroduodenal bleeding remains one of the most actual problem of urgent surgery. According to various authors, acute erosion and ulcers of the mucous membrane of the gastroduodenal zone are detected about 5-10% during endoscopic examination [1, 2]. In most published works, bleeding from acute ulcers is often treated as a peptic ulcer, using the same therapeutic and tactical techniques. The clinical course of acute ulcers differs from the manifestations of peptic ulcer. **Material and methods:** We analyzed 215 clinical cases with acute erosive-ulcerative bleeding, which were received by the emergency surgery department of the clinic of the Tashkent Medical Academy for the period from 2014 to 2021 yy. The age of patients ranged from 18 to 83 years. **Results and discussion:** Among patients undergoing endoscopic manipulations, the final hemostasis was achieved in 53 (88.3%) cases. Recurrence bleeding was noted in 7 (11.7%) cases. After repeated endoscopic intervention in 3 cases, the bleeding was finally stopped. 4 (1.9%) patients, due to the inefficiency of endoscopic methods of hemostasis in an extremely serious condition, were taken for surgery ongoing bleeding. **Conclusions:** Endoscopic methods of hemostasis are effective for bleeding (especially F-I-A, F-I-B, F-II-A degrees) from acute ulcers and erosion of the upper gastrointestinal tract, with the frequency of final hemostasis up to 93.3%; The use of combined methods and retrograde hemostasis in the position on the “right side” made it possible to stop bleeding in 90% of cases; With the ineffectiveness of endoscopic methods, it is necessary to resort to open surgery.

Key words: hemostasis, acute ulcers, arterial bleeding, vomiting, pain.

INTRODUCTION

To date, the tactics of treating patients with acute erosive-ulcerative gastroduodenal bleeding remains one of the most actual problem of urgent surgery. According to various authors, acute erosion and ulcers of the mucous membrane of the gastroduodenal zone are detected about 5-10% during endoscopic examination [1, 2]. However, the actual frequency of gastroduodenal erosive-ulcerative processes has not yet been established. They are often found when patients are

examined for dyspeptic symptoms, but more often – with the appearance of complications such as bleeding (in 60–70% of cases) or perforation (in 0.5–3% of cases) [3]. The etiological factors of acute erosion and ulcers complicated by bleeding are injuries, burns and surgical interventions [4]. Cases of erosion and ulcers of the upper gastrointestinal tract after significant operations in patients who previously did not suffer from gastrointestinal tract diseases are described. Mortality in this category of patients, especially with severe concomitant pathologies, can reach up to 60%, with a relapse of bleeding this indicator is more than 80% [5, 6].

In most published works, bleeding from acute ulcers is often treated as a peptic ulcer, using the same therapeutic and tactical techniques. The clinical course of acute ulcers differs from the manifestations of peptic ulcer. Uncomplicated acute ulcers in most patients are asymptomatic. The appearance of pain in the epigastric region, nausea, vomiting, and pain during palpation of the anterior abdominal wall may indicate the formation of acute ulcers and erosion of the stomach or intestines. Diagnosis of uncomplicated ulcers presents certain difficulties. Of all the known diagnostic methods, endoscopic examination not only allows you to correctly establish the diagnosis, but also makes it possible to conduct endoscopic hemostasis, the clinical effectiveness of which exceeds 85% [7].

The main reasons for the unsatisfactory results of endoscopic arrest of bleeding are the presence of intense arterial bleeding, which leads to difficulties in visualizing the source of bleeding, the presence of blood disorders, etc.

Material and methods: We analyzed 215 clinical cases with acute erosive-ulcerative bleeding, which were received by the emergency surgery department of the clinic of the Tashkent Medical Academy for the period from 2014 to 2021 yy. The age of patients ranged from 18 to 83 years. Of these, over 65 were over 50.0%. In 157 (73.0%) patients, the cause of bleeding was acute ulcers and erosion of the stomach (antrum and prepyloric part - 117 cases, the body of the stomach - 16, the cardial part- 7, the bottom of the stomach - 3 and the back wall of the body and a large curvature of the stomach - 14 cases) and 58 (27.0%) had an acute duodenal ulcer. It should be noted that the last location of stomach ulcers is not common, but there are technical difficulties in visualizing these zones of the stomach associated with the location of blood clots over this area during bleeding from the upper gastrointestinal tract. By the intensity of bleeding, all patients were distributed as follows: F-I-A - 7 (3.3%), F-I-B - 19 (8.9%), F-II-A - 34 (15.7%), F-II- B - 135 (62.8%) and F-II-C - 20 (9.3%) observations. (Table. No. 1.)

Table 1.

Distribution of patients by the intensity of bleeding

Stage	Characteristics	Patients	Rebreeding
F –I A	Jet arterial bleeding	7	3.3%
F-I-B	Oozing	19	8.9%
F-II-A	Visible Vessel	34	15.7%
F-II- B	Adherent clot	135	62.8%
F-II-C	Black spot in ulcer crater	20	9.3%

An analysis of the main causes of acute ulcers revealed that in 115 (53.5%) patients, the pathology developed due to uncontrolled administration of non-steroidal and steroidal anti-inflammatory drugs, 72 (33.5%) patients were associated with volume surgeries, car accidents and burns, the rest 28 (13.0%) patients were hospitalized for a long time, and the cause of gastrointestinal hemorrhage (GH) from acute ulcers was a complicated course of the underlying disease or its decompensation. Moreover, in most cases, preventive antiulcer therapy was not carried out.

Most often, acute ulcers were observed in the hospital, appearing against the background of decompensating of some acute and chronic diseases, often associated with multiple organ failure syndrome. Most ulcers in this group occurred with a combination of diseases of the cardiovascular, respiratory system and diabetes mellitus. When analyzing the nature of the concomitant pathology, a significant dependence of the appearance of acute ulcers with the number of systemic organ lesions was found. In 182 (84.5%) patients with concomitant pathology, a combination of two or more diseases was observed, the most frequent manifestations of coronary heart disease, chronic non-specific lung diseases and cerebrovascular disease. In addition, in this group there were 23 patients with decompensated cirrhosis and liver failure and 10 patients with chronic renal failure.

Thus, the risk factors for the development of complications from acute ulcers in this group include: 1. advanced age; 2. limited nutrition, leading to an imbalance in the acid-base balance in the stomach; 3. Uncontrolled intake of steroid and non-steroidal anti-inflammatory drugs; 4. 2-3 degree of organ dysfunction in assessing the severity of APACHE; 5. long bed rest.

Therefore, when these adverse factors are detected in patients, erosive and ulcerative lesions of the gastrointestinal tract should be prevented. Acute ulcers associated with taking medications are observed in 45–68% of elderly patients and recently account for a third of the causes of gastroduodenal bleeding. According to our data, this is the first frequency cause of complications of acute ulcers in inpatients.

For the most part, these ulcers appear after taking cyclooxygenase inhibitors. Among our patients, 115 (53.5%) were over 65 years old, took more than 3 drugs per day, usually disaggregants (analogues of acetylsalicylic acid), anticoagulants (warfarin), NSAIDs (diclofenac, voltaren, ibuprofen) and steroid preparations. Of these, 39 (18.1%) patients had systemic diseases and diabetes mellitus, and they regularly received steroid (prednisone, beclamethasone) and hypoglycemic drugs in combination with anti-inflammatory drugs and antiplatelet agents.

Acute ulcers in the early postoperative period develop in 2.5–24% of patients [8]. Under our supervision, there were 72 (33.5%) patients with acute ulcers in the postoperative period. All acute ulcers in this group manifested on the 4th – 9th day after surgery and were observed in the complicated course of the postoperative period and the progression of organ dysfunction.

According to the conclusion of the Russian Association of Surgical Infection Specialists, 2 variants of acute ulcers in the early postoperative period are distinguished: I - superficial diffuse erosion with a low risk of bleeding; II - deep localized ulcers with a high risk of hemorrhagic complications, the frequency of which in patients in ICU reaches 14%, and mortality in them is 64% [9]. Difficulties in diagnosing acute ulcers and erosion of the stomach are that 60% of patients do not have clinically significant symptoms of bleeding; the disease is hidden and is diagnosed only with the appearance of hemodynamic disorders.

The standard in the diagnosis of erosive and ulcerative lesions of the upper gastrointestinal tract is endoscopy. Usually, acute ulcers of small sizes 5–10 mm in diameter, the shape of the ulcers is round, the edges are smooth, the bottom is not deep, often with a hemorrhagic plaque (Fig. 1, 2). Their multiplicity is characteristic of acute ulcers, a combination of their localization in the stomach and in the duodenum is often observed.

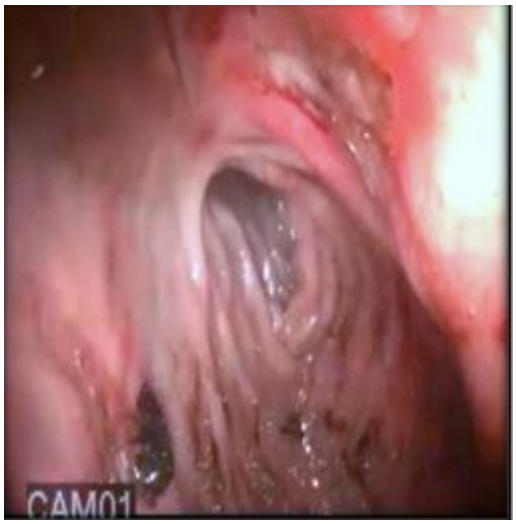

Fig. 1. Acute ulcers of the body of the stomach
(the ulcer of the posterior wall is covered with a

fresh thrombus)

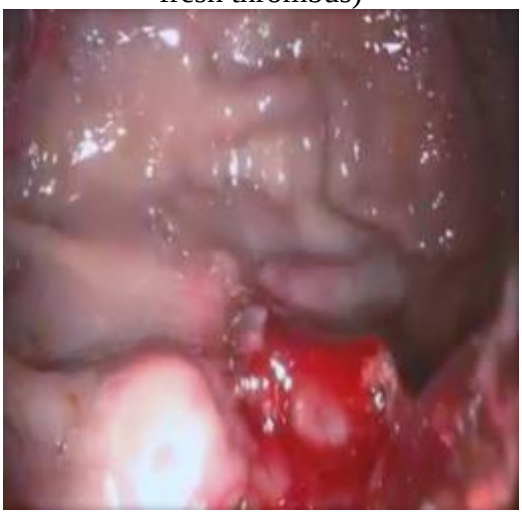

Fig. 2. Acute ulcer of large curvature of the stomach with signs of bleeding (F-I-B)

During an endoscopic examination, in addition to examining the gastroduodenal zone, a primary assessment of the intensity and nature of the bleeding is of particular importance. In order to achieve hemostasis, we used thermal (monopolar, bipolar electrocoagulation, hydrocoagulation, argon plasma coagulation), injection and mechanical (vessel clipping) hemostasis methods. The choice of hemostasis method depended on the intensity of ulcerative bleeding. With bleeding F-II-B and F-II-C, conservative therapy was performed in 155 (72.1%) patients. In 21 cases (9.7%), the edges of the ulcer were chipped, electrocoagulation was performed in 7 (3.3%), argon plasma coagulation in 12 (5.6%), and clipping in 9 (4.2%). In 11 (5.1%) cases, combined methods of endoscopic stopping of bleeding were used (Diagram. No. 1).

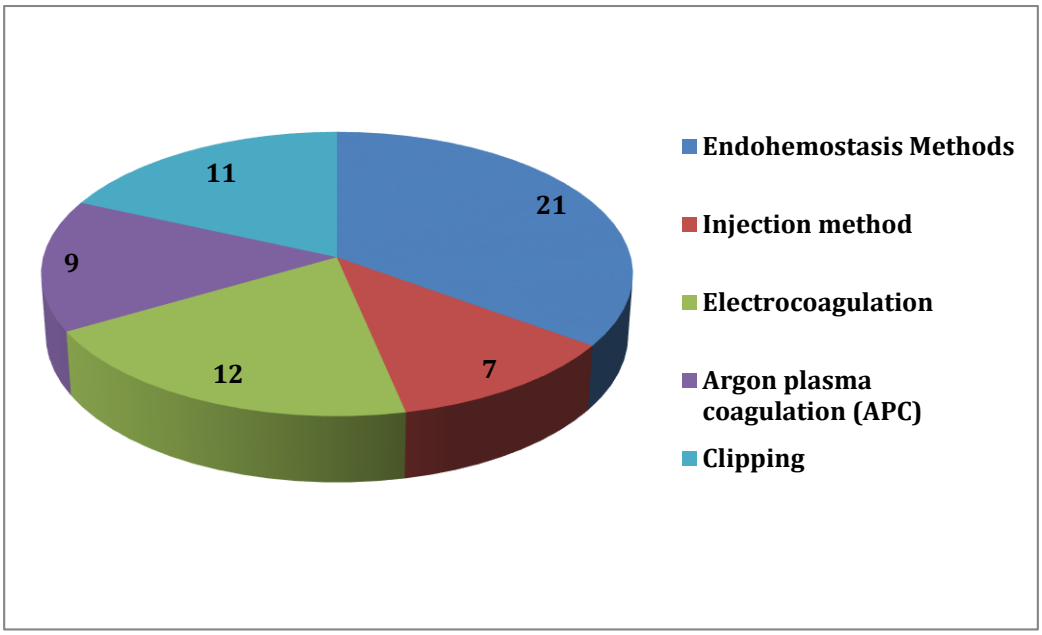

Diagram. No. 1. The applied methods of endoscopic hemostasis

It should be noted that in 14 (6.5%) cases, endoscopic hemostasis was performed for the first time in the position of the patient on the right side with bleeding ulcers of the posterior wall of the upper third of the body and large curvature of the stomach (Figs. 3).

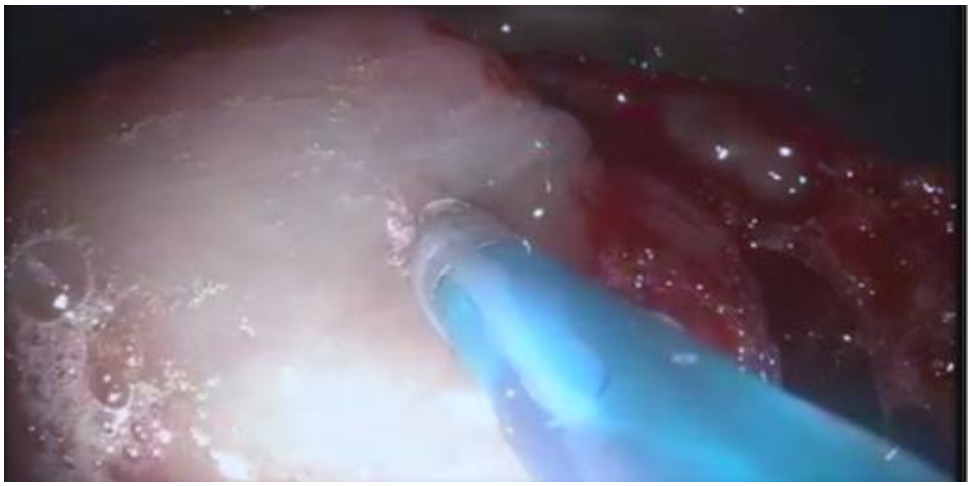

Fig. 3. Acute ulcer of large curvature of the stomach with signs of bleeding (F-I-B). Endoscopic retrograde hemostasis by injection in the "on the right side" position.

Clinical example No. 1. Patient K., 69 years old (IB No. 7822). Received (08/06/2019) in our clinic with signs of profuse bleeding from the gastrointestinal tract. From the anamnesis, the patient suffers from IHD, PICS, diabetes mellitus, type 2 and liver cirrhosis. The patient regularly takes antiplatelet agents, anti-inflammatory drugs.

On EGDS, the esophagus without features in the lumen of the stomach contains blood clots of about 300 ml, the duodenum, the antrum and the body of the stomach without pathology. Upon further retrograde examination, there is an acute ulcer in the upper third of the stomach body from the side of great curvature; however, it is not possible to visualize the size of the ulcer, the nature of the bleeding due to the presence of blood clots over this area. In order to visualize the latter, the patient's position on the right side was changed. After that, all blood clots moved to a small curvature. It was further revealed that there is an acute ulcer in the area of large curvature of the stomach, 10x12 mm in size with signs of active bleeding (Fig. 4.). Performed retrograde endoscopic chipping of the edges of the ulcer with a 33% ethanol solution. Bleeding was stopped. The patient in satisfactory condition was discharged on the 4th day.

After performing endoscopic hemostasis with active bleeding with acute ulcers, it is necessary to identify groups of high and low risk of recurrence according to the Forrest classification. To the groups of high endoscopic risk of

recurrence of bleeding from acute ulcers, we included patients with active bleeding from one or more acute ulcers at the time of primary endoscopy (F-I-A, F-I-B, F-II-A). In patients with bleeding F-II-B, F-II-C, F-III, with a clinical manifestation of bleeding, regardless of the severity of anemia, a low risk of bleeding recurrence was observed.

According to the results of primary gastroscopy in high-risk groups of recurrence of bleeding, a dynamic study is necessary to implement endoscopic prophylaxis of repeated hemorrhage. The term for performing repeated EGDFS depended on the reliability of the performed primary hemostasis and averaged 0.5–3 days from the moment of primary endoscopy. During dynamic EGDFS, the quality of hemostasis, the risk of recurrence of bleeding was reevaluated and its prevention was carried out with a continuing threat. With successful endoscopic hemostasis, further methods of prevention and treatment were intensive antiulcer therapy, normalization of the motor – evacuation function of the stomach, and symptomatic treatment.

Results and discussion: Among patients undergoing endoscopic manipulations, the final hemostasis was achieved in 53 (88.3%) cases. Recurrence bleeding was noted in 7 (11.7%) cases. After repeated endoscopic intervention in 3 cases, the bleeding was finally stopped. 4 (1.9%) patients, due to the inefficiency of endoscopic methods of hemostasis in an extremely serious condition, were taken for surgery ongoing bleeding. The overall mortality rate was 1.4% (3 observations). In the postoperative period, 2 patients died due to multiple organ failure. Another patient died in the early postoperative period due to the development of suture failure, peritonitis and DIC.

According to I.M. Gralnek [10], the use of endoscopic methods of hemostasis in combination with modern antisecretory therapy in most cases of bleeding from acute ulcers can prevent its recurrence and achieve adequate hemostasis without surgery. In general, the effectiveness of endoscopic hemostasis can reach 90–95%. In our observations, recurrence of bleeding in the low-risk group was not observed. In 7 (4.2%) patients at high risk, a recurrence of bleeding was noted. After repeated endoscopic intervention in 3 cases, final hemostasis was achieved.

According to P.W. Elroy [11], using the injection method with the use of a 33% ethanol solution, primary hemostasis was achieved in 90% of patients, the final hemostasis in 85% of patients, the rate of bleeding recurrence was 15%. However, often this method can lead to tissue destruction and massive necrosis of the organ wall with its subsequent perforation, which is the negative side of this method.

In his research E. Wedi [12] claims that the use of coagulation methods of hemostasis allows primary hemostasis to be achieved up to 91-94.0% of cases, final - in 85.0-88.0% of patients, reduces the number of urgent operations to 10.5%, mortality - to 3.0- 4.5%, recurrence of hemorrhage occurs in 8.0-9.5% of patients. In 21 cases, we used coagulation methods (diathermocoagulation - 7, argon-plasma coagulation - 12, combined method - 2). Relapse of hemorrhage was noted in 2 (9.5%) cases, which required surgical treatment.

In 1980, for the first time in Japan, Dr. Hung, together with the company "Olimpus", created a clipper and clips for endoscopic hemostasis. In his opinion, with the help of endoscopic clipping for ulcerative bleeding, hemostasis is achieved in 85-100% of cases, reducing the frequency of recurrence from 20% to 2% [13].

M.Venerito [14] in Italy, applying the endoclipping technique in 88 patients with active ulcerative bleeding from the upper gastrointestinal tract, obtained an excellent result. Relapse was observed in 5 (5.6%) cases, of which one patient was operated on. There were no fatal cases.

Many authors claim [15, 16] that using rotary clips in patients with active ulcerative bleeding can achieve final hemostasis in 95% of cases, recurrence decreased to 5.0% of cases. Moreover, the inefficiency of the method may be associated with technical difficulties in visualization and from the location of the bleeding source. We used endoscopic clipping in 12 patients, of which in 3 cases they were combined with other methods. Bleeding recurrence was noted in 2 (16.6%) cases, in one of them it was possible to stop bleeding endoscopically, in the other - surgical treatment was required.

A randomized study was published in the journal "Gastrointestinal endoscopy", which reported that the frequency of primary final hemostasis during endoclipping increased from 92 to 96%, and the number of bleeding recurrences decreased by almost 2 times (from 15 to 8.5%). However, a change in the method of endoscopic hemostasis did not affect mortality rates and open surgical interventions [17].

Such a considerable difference in indicators of persistent hemostasis or relapse of bleeding is mainly due to the "difficult" location of the source of bleeding and profuse arterial bleeding. Despite the advantage of modern endoscopic methods of hemostasis, further research is needed to develop more effective methods.

Conclusions

1. Endoscopic methods of hemostasis are effective for bleeding (especially F-I-A, F-I-B, F-II-A degrees) from acute ulcers and erosion of the upper gastrointestinal tract, with the frequency of final hemostasis up to 93.3%.

2. The use of combined methods and retrograde hemostasis in the position on the “right side” made it possible to stop bleeding in 90% of cases.

3. With the ineffectiveness of endoscopic methods, it is necessary to resort to open surgery.

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TREATMENT PROCEDURES FOR ANEMIA IN EXPERIMENTAL ANIMALS WITH LOCAL VEGETABLE PROTEIN PRODUCTS

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ABSTRACT

To model the anemia, 4 groups used 5 female rats without white offspring, the first group received an equivalent amount of distilled water for the control group, the second group was given a mash for experimental animals, the third was given a pea and the fourth was given a bean. On 10, 20 and 30 days of the experiment, blood was taken from 0,5 ml for analysis of the level of hemoglobin, hematocrit level and erythrocytes in animals. The experiment showed that hemoglobin in the blood after blood loss in animals was 72,16% of the results of 2 days of anemia compared to the background level of the control group, 65,28% in the mosh-given group, 68,66% in those who received beans, and 70,92% in those who consumed peas. On the 10th day of the experiment for the "control" group, the hemoglobin content was 10% lower than in the experimental group, and by 115959 g/L, by the 20th day of the experiment, this indicator mark even decreased-98,82 g/L, that is, the differences in the experimental group were on average 12% for mosh and peas, 10% for beans. On the 20 - th day of the experiment and 30-th day of the experiment, the amount of erythrocytes in the animals in the experimental group was compared with the initial signs.

Key words: experimental animals, anemia, beans, mosh, chickpea, hemoglobin, erythrocyte, hemochrite indicator.

INTRODUCTION

The urgency and necessity of the problem. Today, a number of authors are concerned about the restoration of health of various segments of the population, including the prevention of eating disorders, nutritional status disorders, i.e, iron deficiency anemia and iodine deficiency, osteoprosis, diseases of the gastrointestinal tract, diabetes mellitus. reflected [1,2,3,4,5,6,12,13,14]. Iron deficiency disease, changes in blood composition contribute to the development of

functional changes not only in patients with iron deficiency anemia, but also in other organs and systems [6,7,8,11]. In order to prevent anemia among different segments of the population, "Karotino" oil, flour products are enriched with vitamins and iron microelements, confectionery products [10,12,13,14,15,16], but the treatment of anemia with protein from local products is the most is one of the effective methods.

In this regard, a number of measures are being taken in our country. During the reform period, special attention is paid to the development of the medical sector in our country, the adaptation of the medical system to the requirements of world standards, including the diagnosis, treatment and prevention of complications of eating disorders caused by eating disorders. One of the tasks set in Strategy actions in five priority areas of the Republic of Uzbekistan in 2017-2021 years is «...implementation of comprehensive measures aimed at improving and strengthening the health of the population, reducing morbidity, preventing diseases related to nutrition, and increasing life expectancy...» [4].

Therefore, one of the current scientific directions is to provide the population with quality food and adherence to the criteria of healthy eating, prevention of food-related cases, the ability of the population to work, resistance to environmental factors, nutrition and micronutrient content in childhood to increase life expectancy. The daily prevalence of pathologies such as anemia among the population requires scientists to constantly seek a means to prevent this condition. In this case, a special place is given to alternative products from animals that feed on agricultural crops.In this regard, products such as mosh, beans and peas grown in local agriculture were offered.

The purpose of the study. Iron deficiency anemia is an evaluation of the efficacy of treatment using local protein-preserving products in an experimental animal model.

Research materials and methods.

White non-fertil female rats were used to modelling anemia. The animals were divided into 4 groups of 5 in each group. In the first group, the control group was assigned to the experimental animals in the second group; animals in the third group were given the mung beans and animals in the fourth group were given peas. Hygienic certificates are obtained in accordance with the established sanitary norms and regulations on the quality and safety of food consumed by animals. Before starting the experiment, the experimental animals were taken from 3 ml of blood under ether anesthesia for 2 days from animals in both groups until a clear appearance of anemia appeared. Hemoglobin, hematocrits concentration and erythrocyte count were analyzed. From day 5, the experimental group of animals

was sent into the stomach in the form of boiled, crushed aqueous porridge of mung beans (mosh) and peas in addition to the general vivarian diet. An equivalent amount of distilled water was administered to the control group animals. On days 10, 20, and 30 of the experiment, 0.5 ml of blood was taken from the animals for analysis of hemoglobin, hematocrit level, and erythrocyte count. The concentration of hemoglobin in the blood was determined using a standard method software (Cypress Diagnostics, Belgium) on a semi-automatic biochemical analyzer CYANSmart, hematocrit was determined in a centrifuge (Cypress Diagnostics, Belgium), and the amount of erythrocytes was determined in Goryaev's chamber. Statistical analysis of the obtained results was carried out using traditional variational statistical methods using Excel, a personal computer software package based on the Pentium-IV processor.

Analysis of the obtained results. The results of the analysis of blood hemolytic parameters in the experimental conditions determined for the purpose of scientific substantiation of the results obtained in the implementation of the goal show that the amount of hemoglobin concentration in the analysis of blood composition of experimental animals as a result of consumption of the studied products is determined in Table 1.

Table 1

Results of hemoglobin content of the product under study, g / l

Observation periods	Control	The main group		
		Mung bean	Beans	Peas
Fon	104,6±6,3	115,9±5,1	113,8±5,9	110,1±4,7
2 days (anemia)	75,5±5,2^	75, 7±3,4^	78,1±4,2^	78,1±3,3^
10 days	110,6±7,4**	121,6±5,7***	113,5±5,8***	115,0± 4,9***
20 days	98,8±5,3**	113,2±6,2***	109,7±5,5***	111,3±5,5***
30 days	113,9±6,5***	108,0±4,6***	116,0±6,1***	115,8±6,2***

Note: The difference between * -2 days is reliable (** - P <0.01; *** - P <0.001)
^ - the difference from the background is reliable (^ -P <0.001)

As can be seen from Table 1, the analysis of the amount of hemoglobin at 10, 20, and 30 days after the organization of the diet, consisting primarily of anemia, consists of the following. The analysis of hemoglobin in the blood of experimental animals after blood loss revealed that the results of anemia in 2 days compared to the background level of the control group was 72.16%, while the results of the experimental group were 65.28% in the group that consumed mung bean, 68.66% of those who ate beans and 70.92% of those who ate peas. The data obtained indicate evidence of severe posthemorrhagic anemia in animals. It should be noted

that in the diet of legumes evaluated during the study, it was noted that the morphological parameters in the blood of white rats are reliably restored relative to the initial symptoms.

The results in the control group were found to increase 1.46 times in 10 days compared to 2 days, 1.30 times in 20 days, and 1.50 times in 30 days. The analysis showed that the amount of hemoglobin in 20 days decreased by 0.16 times compared to 10 days and then increased again by 30 days. It can be seen that it is recommended to consume these results for 1 month or more. When consuming mosh, the following cases were found: an increase of 1.60 times, 1.49 times in 20 days, and 1.42 times in 30 days.

The performance of experimental animals consumed by mung bean products was as follows, increased by 1.45 times, 1.40 and 1.48 times, respectively. In experimental animals, the level of the above was as follows: in 10 days of the study, the number of peas increased by 1.47 times compared to 2 days, 1.42 times in 20 days and 1.48 times in 30 days. It should be noted that the experimental animals consumed by local mung bean, beans and peas, along with the assessment of the level of anemia, their main indicators show that after 30 days they show clear results. The role of not only animal proteins in the prevention of iron deficiency anemia, but also plant proteins in relation to the vegetarian diet, and the role of proteins, amino acids and vitamins and minerals in their structure is great. It should be noted that it is not the level of protein consumption, but the degree of their absorption in the body.

The results of hematocrit readings in the blood of experimental animals called iron deficiency anemia are presented in Table 2

Table 2

The amount of hematocrit in the blood under the experimental conditions,%

Observation periods	Control	The main group		
		Mung beans	Beans	Peas
Background	33,6±1,6	34,2±1,5	33,4±1,4	33,2±1,5
2 days (anemia)	27,3±1,2^^	27,2±1,1^^	28,7±1,2^	28,9±1,3^
10 days	34,9±1,7**	36, 8±1,8***	33,9±1,5*	32,3±1,5
20 days	31,4±1,5*	33,0±1,4**	32,4±1,3*	33,0±1,4*
30 days	34,1±1,3***	32,2±1,3*	33,1±1,2*	34,1±1,5*

Note: The difference between * -2 days is reliable (* -P <0.05; ** - P <0.01; *** - P <0.001); ^ - the difference in background values is reliable (^ -P <0.05; ^^ - P <0.01)

As shown in Table 2, the analysis of hematocrit in the blood of experimental animals revealed that the results of anemia in 2 days relative to the background level of the control group was 81.3%, their results in 10 days compared to 2 days were 127.79%, in 20 days 124 , 72%, and 124.72% in 30 days. In the group that consumed mung beans, it was 135.41% at 10 days, 121.57% at 20 days, and 118.55% at 30 days compared to 2 days. When taking mosh in 30 days, the figures decreased by 0.97 times compared to 20 days. It is advisable to analyze the research results in this regard. 117.96% of the analogous content in the experimental group consumed beans; 112, 95, and 115.11%, respectively, while those consuming peas accounted for 117.85%, 114.25%, and 117.85%, respectively.

Positive results were also obtained in hematocrit.

Another key indicator is the assessment of erythrocyte counts in the blood under experimental conditions, the results of which are presented in Table 3.

Table 3

Results of erythrocyte count in animal blood under experimental conditions, 10^{12} / l

Observation periods	Control	The main group		
		Mung beans	Beans	Peas
Background	6,8±0,24	7,0±0,31	6,8±0,28	6,7±0,27
2 days (anemia)	6,2±0,21^	6,1±0,23^	6,2±0,24	6,2±0,25
10 days	6,9±0,28*	7,1±0,32*	6,7±0,26	6,8±0,28
20 days	6,8±0,26	6,8±0,28*	6,6±0,25	6,7±0,25
30 days	6,9±0,29*	6,6±0,25*	6,8±0,27	6,8±0,30

Note: The difference in * -2 day values is reliable (* -P <0.05); ^ - the difference in background values is reliable (^ -P <0.05)

Table 3 shows that the analysis of erythrocyte counts in the experimental blood showed that the results of anemia in 2 days compared to the background level of the control group were 91.4%, their results in 10 days compared to 2 days were 111.81%, and in 20 days 109 , 22%, and 111.48% in 30 days compared to 20 days.

In the experimental group, mung beans was consumed 1.15 times in 10 days, 1.11 times in 20 days, and 1.07 times in 30 days compared to 2 days. In the experimental group, which consumed beans, it was 108.57%; 107, 28 and

109.20%, respectively.It should be noted that the changes in the blood when consuming beans relative to mosh are partially low. The results of the changes in the blood of the experimental group consuming peas were as follows: the results in the background group were 92.3%. The results were 109.53% on day 10, 108.88% on day 20, and 109.20% on day 30 after anemia was diagnosed. From the results of the experiment, it should be noted that when anemia was called, it decreased in 20 days compared to 10 days in all products and increased again in 30 days. At the same time, a special intensity was observed in the first 10 days. The performance of the animals of the “control” group was characterized by a slower recovery of activity compared to similar animals with added moss, beans and peas in the diet. This information is confirmed by the presence of reliable differences between the morphological parameters of white rat blood in the "Control" and "experimental" groups. For the control group, on the 10th day of the experiment, the hemoglobin level was 10% lower than in the experimental group and amounted to 110.59 g/l, and on the 20th day of the experiment, this indicator even decreased to 98.82 g/l., i.e., the differences relative to the experimental group were on average 12% lower for mosh and peas and 10% lower for beans. On days 20 and 30 of the experiment, the erythrocyte count in the animals in the experimental group was comparable to the initial indicators. The sign of hematocrit was characterized by a tendency to normalize in all observed animals, but the control group had a statistically reliable decrease of an average of 10% by the 20th day of observations. Evaluating the hematocrit parameters of the experimental group compared with the control group, it can be determined that the experimental group that consumed mung bean had a tendency to recover all blood parameters more rapidly, but the recovery of hemoglobin concentration, hematocrit and erythrocyte count was the same in all.

Thus, the results obtained show that mung beans, beans and peas have a stimulating effect on erythropoiesis, while the effectiveness of the use of moss is several times higher than that of beans and peas.Statistical analysis of the nutritional and biological value of these local products shows that they are rich in enough protein and are active in increasing the energy value of the organism, with its structural unit.

CONCLUSIONS

1. The analysis of hemoglobin in the blood of experimental animals after blood loss revealed that the results of anemia in 2 days compared to the background level of the control group was 72.16%, while the results of the experimental group were as follows, i.e 65.28% in the mung beans consuming group. 68.66% of those who ate beans and 70.92% of those who ate peas.

2. The experiment showed that the hematocrit in the blood of animals showed that the results of the control group in the background of 2 days of anemia were 81.3%, the results of 10 days were 127.79%, 20 days - 124.72%, 30 days - 124.72. %. In the group that consumed mung beans, it was 135.41% at 10 days, 121.57% at 20 days, and 118.55% at 30 days compared to 2 days. 117.96% of the analogous content in the experimental group consumed beans; 112, 95, and 115.11%, respectively, while those consuming peas accounted for 117.85%, 114.25%, and 117.85%, respectively.

3. The amount of erythrocytes in the blood increased 1.15 times in 10 days, 1.11 times in 20 days and 1.07 times in 30 days compared to 2 days in the group consuming mung beans, 108.57% in the experimental group consuming beans in a similar order; 107, 28 and 109.20%, the experimental group consuming peas accounted for 109.53% on day 10, 108.88% on day 20, and 109.20% on day 30.

4. Mung beans is the most active local product rich in plant protein, but given the allergenic properties of mung beans, it is advisable to periodically add mung beans, beans and peas to children's diets.

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NURSES' ROLE IN CARRYING OUT REHABILITATION ACTIVITIES IN HYPERTENSIVE PATIENTS

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ABSTRACT

The medical field is developing rapidly. In the latter years, we can observe that the disease of hypertension has been occuring more not depending on age and sex. Among the population, the incidence of stroke diseases is in previous places, the cause of which is mainly smoking and alcohol consumption.Scientists thought much more about hypertension and its consequences. We can see that for such patients need to organize rehabilitation. According to research, it leads to a change in the quality of life. It is possible to restore damaged functions, with rehabilitation measures it is carried out. Timely rehabilitation can be achieved so that the disease does not escalate and the complications are reduced, and after the treatment, most patients are able to conduct their own work activities.

Key words: hypertension, blood pressure, alcohol, rehabilitation.

INTRODUCTION

Hypertension is a very common disease among diseases of the cardiovascular system, accounting for 80-85% of all arterial hypertension, symptomatic (secondary) hypertension is 15-20%. Women and men suffer from this disease equally. The list of terms used abroad has been adopted the term "arterial hypertension" in coexistence with the symptoms of diagnosis of syndromes and verification; it reflects the high degree of arterial pressure and evidence in itself. Therefore, it differs from primary (essential) and (symptomatic) arterial hypertension.

Hypertensive disease (HD) is a chronic pathological condition of the body, has a genetic origin, is important in the development of long-term systolic hypertension, is a disease that leads to dysfunction of the central nervous neuroendocrine system and membrane receptor pathology, disorders of the structure of vessels, heart, liver. The degree of consequences of HD is high, and it is dangerous with stroke, infarct, heart failure, chronic renal failure, as well as with a lethal outcome. In addition, increased blood pressure is associated with the development of atherosclerosis, ischemic heart diseases. The increased risk of disease progression is higher in men than in women, taking into account the presence of harmful habits, various stresses, the transition from generation to generation, and in women-more menopause. Another factor to increase the risk of cholesterol, the suppression of the effects of insulin to glucose in diabetes mikroalbuminuriya, obesity, little mobility, an increase in the level of fibrinogen, tissue activators declining, plazminogen the exogenous 1-type inhibitors increased aminoprotein concentration, the high cost of coagulation factor, gomosistein, 01–dimer C-reactive protein, focusing esterogen failure, cardiovascular failure, chronic immune system in the presence of the process, its clear stirring in the presence of software for technical, socio-economic status of low profile, ethnic layer, living in the endemic geographic region, the specific features of the disease (latent aggressiveness, airy "A-appearance behavior") cause an increase in blood pressure, mainly a violation of the blood circulation balance and an increase in peripheral resistance of the vessels. The minute volume increase in blood circulation also affects the heart. It, in turn, leads to a decrease in the myocardium and an increase in blood circulation. Peripheral resistance of the vessels depends on the degree of resistance of the arterial tone and the degree of vascular remodeling (narrowing of the vessels as a result of mediointimal complex hypertrophy and an increase in the rigidity of the vascular wall). Violations of hemodynamics in HD are due to changes in the cardiovascular system and kidneys, as well as a violation of the physiology of the pressur and depressur mexanizms rhythm. The increase in arterial pressure in HD leads to changes in the blood circulation of the Central and sympathetic nervous system, which is closely related to endocrine hardware activity, kidney function and microcirculation. At present, the structure of the initial factors of arterial hypertension is the detection of predisposition to genetic diseases, it appears in the violation of the spread of the ion transport system. The result of this is a decrease in the level of silcysi exchange, hormonal cellular connection, the appearance of hypothalamic-pituitary renal activity, renin-angiotensin-aldosterone, insular system, etc. Saturation of cells to calcium increases strengths the contraction of smooth muscle vessels increases the

peripheral resistance of functional components. The resulting myocardial hypertrophy and high contraction, the rupture of the wall and narrowing of the vessels determine the high level of arterial pressure. As a result, arterial hypertension is the result of a violation of baroreceptor communication with the center of the brain, sympathetic nerves, resistive and capacitive vessels, renin-giotensive activity of the heart muscle, increased aldosterone secretion and, ultimately, increased consumption (termination) of depressor mexanizm, (prostoglandin F2, kallikrin, bradykinin), vessels 12 prostaglandin or prostocyclin, calcareine kinin and the dopaminergic system is considered to be the relaxation factor of the tension of the endothelial muscles) and the heart (the front of the ventricles factor). Pathogenetics of Arterial hypertension is that insulin resistance in tissues (due to sodium reabsorption, increased activity of the sympathetic nervous system, protoonkogen expression and relaxation of vasodilating stimuli), increased thickness of the vascular pathway receptor and myocardium, its adrenergic cortisone secretion, increased sensitivity to adrenergic effects and thyroid hormones, changes in the main biological rhythm of the nervous system and, at the same time, the rhythm of the vascular system is a regularity. Endortel dysfunction in the pathogenesis of hypertonic diseases is associated with an increase in the synthesis of endothelin, and the decrease in the synthesis of oxide-nitrogen is the main role. Reconstruction of the heart and vessels, a prolonged course of hypertension, a violation of blood circulation as a result of work in severe conditions, leads to a violation of relaxation, and myocardial contraction, cerebral, coronary, complication peripheral hemodynamics lead to stroke, infarction, heart and kidney failure.

The main syndrome of HD is cardialgia, cephalgia, arterial hypertension. Neurogumoral is dysregulation, membrane receptor pathology, kidney dysfunction.The main goal in the treatment of HD is to restore the uniformity or norm between the regurgitation of the pressor and depressor mechanisms of the ABP. The main drugs in the treatment of Arterial hypertension are neurotopoeuvres. These means include the antagonist renin angiotensive system of smooth muscle elements of the vessels, diuretic agents. Physiotherapeutic treatment of HD is aimed at strengthening MAT (sedative method) braking process, correction of arterial hypertension (hypotensive method), reduction of sympathoadrenal system activity, vegetocorrection method, reduction of activity of renin angiotensin-aldosterone (RAAS), and the mechanism of ABP regulation is directed to renal volume correction.

Objective: Coverage, study and improvement of the axity of rehabilitation programs of physical exercises in the rehabilitation of patients with hypertension.

Research materials: For the study and analysis of the theoretical material on the topic of the study 58 patients from cardiorheabilitation Department of 1st Clinic of the Tashkent Medical Academy and 58 patients from cardiology department were involved in the survey.

Research methods: The following research methods were used to obtain the results: theoretical and statistical, questionnaire survey.

Obtained results: The study shows that in order to improve the rehabilitation work of the Department of the Tashkent Medical Academy, rehabilitation programs were presented for patients undergoing treatment, and the patient's condition was regularly monitored, a survey was conducted by patients before discharge, analyzed, as a result, it was noted that the condition of patients participating in the program improved. The main tasks of rehabilitation in Arterial hypertension are: normalization of arterial blood pressure, reduction of body weight, refusal of harmful habits (tobacco smoking and alcohol), improvement of lipid profile, regulation of physical exertion, improvement of the psycho-emotional state, Prevention of lesions and clinical signs of target organs, maintenance of patient social status in the family and society, restoration of the ability to work

The modern approach of patient rehabilitation includes, on average, the 3-5-week hospital phase of restorative treatment.

In this program, patients are prescribed treatment gymnastics as a physical exercise. The main goal of therapeutic physical education at the stationary stage is the activation of the extracardial factor of blood circulation, the elimination of hypodynamia, the preparation of patients for household physical exertion.

The entire hospital stage is conditionally divided into 4 activity steps. Bunda is assigned to each patient an individual step and gradually increased.

In the 1-activity step, the patient is prescribed a bed regimen. Exercises are performed in a lying position in bed. Between exercises, breathing exercises are performed. The duration of the training is 10-12 minutes. During the training period and in the first three minutes after completion puls 20 beats, number of breaths 6-9 times, SABP 20-40 μg/L, DABP 10-12 μg/L the increase is an indication that the stresses are being carried out correctly. When the organism reacts adequately to complex therapeutic gymnastics, it goes to step 2, when angina pectoris attacks disappear, when there is a negative dynamics on the ECG.

In the 2-activity step, the patient is allowed to sit at the table, eat at the table, walk around the bed and in the ward. Complex's main tasks: to engage the cardiorespirator system, prepare the patient for a walk in the corridor and for a free fall on the stairs. Treatment № 2 Gymnastics complex is performed in lying - sitting - lying cases. Gradually, the number of exercises to sit down and perform is

increased. Treatment №2 performing gymnastics complex is recommended to patients in the form of morning hygienic gymnastics. The duration of the training is 10-15 minutes. Exercise complex, which calls for ST - segment depression, disrupts the rhythm or causes the development of tachycardia more than 100 times a minute, is excluded from the program, or more gentle exercises are added. Indications for the transfer of the patient to the 3-activity Step are adekvat reaction of the pulse and ABP, orthostatic test, the formation of a T-coronary tooth.

In the 3-activity step frequent violations of the paroksizmal rhythm with repeated angina attacks, symptoms of a lack of blood circulation and severe hemodynamic changes, as contraindications of the patient. The 3-step of activity begins when the patient leaves the corridor and continues until he leaves for the street.

The patient is allowed to walk in small steps in the corridor from 50 to 200 meters (up to 70 steps per minute). The main tasks of treatment gymnastics in Step 3-activity: preparation of the patient for full self-service, free walking on the street, dosed walking. Treatment gymnastics is performed in the sitting and standing position. Gradually №3 treatment is carried out increasing the size of the strain on the border of gymnastics. The pace of the exercise is accelerated by a slow start, the total duration of the exercise is 20 minutes. Patients are recommended to perform treatment №1 gymnastics in the form of morning hygienic gymnastics or in the second half of the day. The first exit to the corridor and the first exit to the stairs are recommended to be conducted under the supervision of a telemonitor. In adequate reactions to the strain, it is allowed to travel in the corridor without time and distance restrictions. By this time, patients begin to completely self-disorders, they are allowed to take a shower.

4-Activity step (the last step of the hospital stage) involves increasing physical activity at the border of the free regime in patients. The patient is allowed to go outside and take 500-900 steps at a distance of 70-80 m. In Step 4, patients are prescribed treatment № 4 gymnastics. The task of treatment gymnastics in Step 4 is to prepare the patient for the transition to the 2-stage of rehabilitation or to respond to home under the supervision of a local therapeutist. In the process of performing exercises, it is considered normal that the number of heartbeats increases by an average of 110 times for 3-6 minutes. The pace of walking can range from 70-80 steps per minute to 80-100 steps, and the distance can range from 500-600 meters to 2-3 km. It is allowed to take a walk 2 times a day. Therapeutic nutrition in hypertensive disease is formed on the basis of the main pathogenetics mechanisms in the development of the disease, depending on the severity of complications. Calories of the diet should correspond to the energy expenditure of the body, calories of the diet

should be low when atherosclerosis develops and especially when the concomitant disease is obesity. In ration, the amount of precipitation, mainly saturated fats and animal fats, should be reduced. They are partially replaced by vegetable oils (corn, sunflower, soybean, olive, etc.), because they are rich in high unsaturated fatty acids (linoleic, linolenic, arachidonic acids) and lecithin. Restriction of fat will depend not only on the presence of concomitant atherosclerosis in the diet, but also on the purpose of stopping the excitation processes in the cerebral cortex again. Because I.P.In experimental observations of I.P.Razenkov has proved that fatty nutrition leads to an increase in the processes of reflection in the cortex of the Cerebral Hemispheres.The amount of protein in the ration should correspond to the norms of healthy exteriors (that is, 1kg per 1.2-1.5 g of body weight per day); of course in the ration there should be a sufficient amount of full-fledged proteins. The lack of protein in food leads to a slowing of reflexive processes. When the disease is complicated by nephroangiosclerosis, the amount of protein in the diet should be limited. The amount of carbohydrates is not limited in ration, carbohydrate nutrition, according to experimental data, reduces the excitation processes in the cerebral cortex. Especially rapidly reducing the consumption of digestible carbohydrates (sugar, honey, jam, porridge and rice dishes, confectionary products, etc.) should consume a lot of products rich in vegetable dietary fiber (sour fruits, vegetables, peanuts). It is necessary to limit the intake of light digestible carbohydrates in the development of hidden functional insufficiency of the insular apparatus, hypercholesterinemia and atherosclerosis, vegetable dietary fiber allows to reduce the calorie content of food for a while, without damaging the saturation index, without changing the volume of ration in combination with the outflow of cholesterol (in the case of coprosterin). The richness of fruits, vegetables and ground fruits with potassium, magnesium and vitamins corresponds to the general direction of therapeutic nutrition in hypertension. Restriction of salt in the ration is associated with an increase in the mineralocorticoid function of the adrenal gland (excessive production of aldosterone), since this condition leads to the retention of sodium and fluid in the body. Restriction of salt in the diet contributes to a decrease in the opacity of the central nervous system. Salt is 4-6 gr per day. Salt-free diet when hypertension is complicated by severe and prolonged circulatory insufficiency leads to an increase in diuresis, a decrease in the volume of blood plasma. In addition, salt restriction helps to increase the activity of lipoprotein lipase and reduce cholesterol in the blood, prevent the development of atherosclerosis. Therefore, a lot of salt preservatives can not be salted, marinated products and clupea. It is not recommended to consume salt for a long time, since hypochloremia leads to the accumulation of nitrogen residues in the blood. When the disease is complicated by nephroangiosclerosis, nitrogen residues can be caught in the

body and become a compensatory polyuria, salt can not be very limited in the diet when there is an excessive loss of sodium in the body. Its amount depends on the Daily excretion of sodium with urine (up to 8-12 g per day). It is impossible to limit the liquid when there is no lack of blood circulation, because against the background of nephroangiosclerosis, nitrogen residues accumulated in compensatory ravishdaorganism in polyuria are excreted. The diet should be enriched with vitamins (vitamin R, nicotinic acid, ascorbic acid, riboflavin, pyridoxine), because they support the vital functions of the body for life. Ascorbic acid has a positive effect on oxidation – recovery processes. Reduces the amount of cholesterol in the blood and inhibits the lipoid infiltration of blood vessels. Nicotinic acid blood vessels. Depressor effect, improves blood circulation in the brain, heart and kidneys of the head. Riboflavin and nicotinic acid needed for tissue respiration and synthesis of ATP. Riboflavin is necessary to reduce the activity of catecholamines and to exert a pressure effect. Pyridoxine needed to convert linolenic acid into arachidonic acid, thereby providing the lipotropic effect of choline increased and cholesterol discharge from the body. Vitamin R also reduces vascular permeability in part to cholesterol and improves hemodynamics in the capillaries. It is necessary to introduce a sufficient amount of cyanocobalamin into the body. It improves the indicator of lecithin-cholesterin and helps to save choline. At the same time, limiting the intake of Vitamin D prevents the development of atherosclerosis. The diet should be enriched with potassium, magnesium and iodine. Potassium is a physiologic antagonist of and has a direct depressive effect sodium strengthens on the blood vessel wall. It is recommended in case of a lack of blood circulation, since it contributes to the contraction function of the myocardium. Ration should be enriched with potassium salts, because in a hyponatric diet it quickly leaves the body. Magnesium strengthens the braking processes in the cerebral cortex reduces spasm of smooth muscles of the vessels thanks to this lowers arterial pressure through. Magnesium ions have a hypocholesterinemic effect, preventing the development of atherosclerosis. Beans, soybeans, green peas, raisins, figs, lentils, corn, prunes are rich in magnesium. A special" magnesium " diet has been developed and is now used.

CONCLUSION

In the early detection of the disease, the implementation of a wide range of preventive medical examinations, the more Organization of the activities of rehabilitation centers, at the same time, the further strengthening of the promotion of understanding among the population. Within the framework of a multi-faceted approach to the implementation of therapeutic and rehabilitation measures, the importance of nursing care is emphasized in the works of many authors, both local and foreign. In this regard, studies aimed at improving the methods of nursing care, rehabilitation therapy and blood circulation profilactics in the head brain, using

modern printing techniques and evidence-based nursing practice of quality management of medical services, are now gaining scientific and practical significance.

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EFFECT OF PLANT PHOTOSENSITIZER PSORALEN ON MITOCHONDRIAL STRUCTURES IN INFLAMMATORY PROCESSES

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ABSTRACT

The effects of the plant photosensitizer psoralen in various combinations on experimental chronic inflammatory conditions and its mitochondrial structures in the liver have been demonstrated in this paper. Liver mitochondrial suffocation in chronically inflamed rats was found to be 140.0 ± 6.5% higher than in healthy rats. Under conditions of chronic inflammation, high permeability pores of hepatic mitochondria were found to inhibit increased permeability of mPTP by 35.7 ± 2.5% and psoralen by 22.6 ± 1.5% compared with those of chronically inflamed rats. However, under similar conditions, it can be seen that the complex effect of UV-irradiation and psoralen reliably inhibits hepatic mitochondrial suffocation by 50.0 ± 4.5% and maintains the homeostasis of calcium ions in the matrix. Decreased ATP synthesis under the influence of various disorders in the mitochondria alters the cycle of potassium ions in the membrane. Examination of the activity of K+ ATP-channels of isolated liver mitochondria revealed the following results. Experimental chronic inflammation was found to be 21.1 ± 1.2% more active when the K+ ATP-duct permeability of their liver mitochondria was exposed to UV-irradiation than in rats with chronic inflammation. Specific administration of psoralen has been shown to increase mitoK+ ATP -channel activity by 13.1 ± 0.3% compared with rats with chronic inflammation. The complex effect of psoralen and UV-irradiation led to the activation of mitochondrial K+ ATP-channel activity by 30.2 ± 2.4% compared with those of chronically inflamed rats. From the results obtained, it can be concluded that the complex effect of psoralen and UV-radiation showed the highest effect on the structures in the mitochondrial membrane under experimental chronic inflammatory conditions.

Key words: mitochondria, mitochondrial pore, mitoK+ ATP-channel, psoralen, photodynamic therapy.

INTRODUCTION

The functional activity of the mitochondria determines the vital activity of cells and the whole organism. Experimental studies have shown that mitochondrial dysfunction plays an important role in the development of various pathological conditions. The view of the mitochondria as the main organelles that control energy metabolism is now complemented by the view that they are organelles that contain the factors that determine the fate of its cell.

Mitochondria play an important role in various aspects of cell physiology [2]. One of the main features of mitochondria is the formation of transmembrane potential in its inner membrane and its use in ATP synthesis and cation transport. Changes in the permeability of the mitochondrial membrane lead to a decrease in the membrane potential and a sufficient change in its fluorescence and light transmittance using ion-selective electrodes [16,6].

Animal cell mitochondria are the most suitable model for studying the mechanism of action of biologically active substances. On the other hand, mitochondria and structures localized in them, primarily high-permeability pores of the respiratory chain and mitochondrial membrane (permeability transition pore, PTP, megapora, Ca^{2+} -bound megacanal) are the target for exposure to biologically active substances [9,19]. Currently, the role of mitochondrial PTP in cell vital activity and physiological processes, as well as in the development of various pathologies is being actively discussed. It is known that mitochondrial megaporas - mPTP play a key role in the development of various cell pathologies, as well as cell death - necrosis and apoptosis. The formation of reactive oxygen species in the cell and the over-activation of free radical oxidation processes are considered as a universal mechanism for the development of various pathologies [22]. It is also known that mitochondria are the main source of reactive oxygen species in the respiratory chain [10].

It is known that many physiological processes of mitochondria and cells are controlled at the level of mitochondrial megaporas (mPTP) [3,7]. Impairment of mitochondrial function leads to the development of various pathologies: the formation of reactive oxygen species (ROS), dysfunction of ion channels, lipid peroxid activation, oxidation of membrane thiol groups, etc. [4,18]. In this regard, modern research pays special attention to the effect of mPTP management mechanisms on potential drugs.

Photodynamic therapy (PDT) is a photochemical therapy in which oxygen interacts with a photosensitizer (PS) and light of a certain wavelength to form singlet oxygen, which in turn reacts very rapidly with cellular structures, damaging them and even killing them. leads to Photodynamic therapy has a wide range of effects, both directly, at the cellular level, and indirectly - the effects of

pathological tissue on vascular injury and immunomodulation are known [8]. By studying the mechanisms of PDT, it is possible to increase the effectiveness of its application in clinical practice.

Research conducted by the Institute of Plant Chemistry of the Academy of Sciences of Uzbekistan has shown that a number of plants of the local flora are a source of natural compounds with photodynamic properties. One of the plants with similar photosensitizing properties is fig. Scientists have found that fig leaves contain a certain amount of the two most active furanocoumarins - psoralen and bergapten [23]. Under the influence of light of a certain wavelength, psoralen can modify biological molecules in two ways: as a result of oxygen-independent photobiotic reactions and as a result of oxidative photoreactions [11].

Furanocoumarins have an effective effect on the membrane processes of mitochondria. Furanocoumarins have a protective effect on mitochondrial membranes by stimulating membrane potential [5]. The protective and restorative properties of furanocoumarins have been observed in tumors of the breast, lungs, kidneys, liver, colon, cervix, ovaries and prostate gland [1]. Apoptosis, autophagy, participation in the antioxidant cell cycle, effective in activating V-cells have been reported in the literature [1]. In this study, we conducted experiments showing the role of furanocoumarins in the treatment of chronic inflammation. The effects of radiation and psoralen on rats in chronic inflammatory conditions have been studied at the level of hepatic mitochondria.

The purpose of the study

To study the effect of the use of psoralen in different combinations (with UV-irradiation and separately) on the structures of the liver mitochondria in experimental chronic inflammatory conditions.

Materials and Methods

The experiments were initially performed on mature white male rats weighing 180–220 g, quarantined under standard vivarium conditions for 14 days. The “cotton plate” method was used to study anti-inflammatory activity [15]. Clinically healthy rats with clean skin were divided into 5 groups for the study.

The initial radiation dose was determined by determining the minimum erythemal dose (MED). This was found to be 2 minutes. We administered psoralen at a dose of 10 mg / kg. One day after the last administration of the drug (on the eighth day), the animals were removed from the experiment by decapitation under light ether anesthesia. The cotton balls were separated along with the granulation tissue formed around them, weighed on an electronic scale (SINKO, Japan) and dried at 60° C for 3 days until they reached a constant weight. The degree of proliferative stage was assessed by the difference between the mass of the dried

granule and the initial mass of the balloon. The exudative reaction was evaluated by the difference between the masses of the wet and dried bubbles [21].

Table 1

Scheme of experiments in rats using the method of "cotton plate"

Animal group	The scheme used	UV radiation transmission time and exposure distance			Psoralen insertion path and transmission frequency
		First day, the day of surgery	4th day	7th day	
1-group	healthy	-	-	-	-
2-group	untreated	UV-irradiated			Psoralen was not sent
3-group	UV radiation	2 minutes at a distance of 50 cm	2 minutes 30 seconds 50 cm away	3 minutes at a distance of 50 cm	Psoralen was not sent
4-group	Psoralen	UV-irradiated			The drug was administered to the stomach once every 3 days for 7 days
5-group	Psoralen + UV radiation	2 minutes at a distance of 50 cm	2 minutes 30 seconds 50 cm away	3 minutes at a distance of 50 cm	The drug was administered to the stomach once every 3 days for 7 days

The experiments were carried out in accordance with the “Rules for the Use of Experimental Animals” as well as the provisions of the European Convention

for the Protection of Animals Used for Experimental Research or Other Scientific Purposes (ETs № 123, Strasbourg, 03/18/1986).

Mitochondria were isolated from rat liver using the W.C.Schneider [17] method of differential centrifugation. Separation medium composition: 250 mM sucrose, 10 mM tris-chloride, 1 mM EDTA, pH 7.4.

Determination of mitochondrial PTP permeability. Mitochondrial swelling (swelling) kinetics (0.3–0.4 mg / ml) was determined by varying the optical density of the mitochondrial suspension at 26 ° C in an open cell (volume 3 ml) at 540 nm. The following incubation medium (IM) was used to determine the permeability of PTP in mitochondria: 200 mM sucrose, 20 μM EDTA, 5 mM succinate, 2 μM rotenone, 1 μg / ml oligomycin, 20 mM tris, 20 mM HEPES, and 1 mM KH_2PO_4, pH 7.4 [7].

Determination of mitochondrial ATP-dependent potassium channel activity. MitoK^+_{ATP} -channel conductivity (0.3–0.4 mg / ml) was determined by varying the optical density at a wavelength of 540 nm in 3 ml cells. IM were as follows: 125 mM KCl, 10 mM Hepes, 5 mM succinate, 1 mM $MgCl_2$, 2.5 mM K_2HPO_4, 2.5 mM KH_2PO_4, 0.005 mM rotenone, and 0.001 mM oligomycin, pH 7.4 [20,12].

Statistical processing of the obtained results was carried out using computer software OriginPro 7.0 (Microsoft, USA). In the experiments, the kinetics of hepatic mitochondrial suffocation were performed as a percentage of the maximum, by calculating the arithmetic mean of 4 different experiments. The difference between the values obtained from the control and the experiment was calculated on the t-test. In this case, the values of $P<0.05$ and $P<0.01$ represent statistical reliability.

Results and Discussion

In evaluating the anti-inflammatory activity, it can be seen that all the treatment combinations performed stopped the development of the granule. When psoralen was used without UV irradiation, the mass of dry granulation-fibrous tissue was 48.66 ± 5.57 mg, and group II-chronic inflammation was 44.2% lower than in the untreated group. Similarly, the exudate mass was 288.8 ± 24 mg, which was 17.6% lower than that of group II animals (Table 2). When used in combination with psoralen + UV-irradiation, the mass of dry granulation-fibrous tissue was 33.4 ± 3.1 mg, and the mass of exudate was 178.4 ± 14.71 mg, which was 61.5% and 49.2% lower than in the control group, respectively. This means that psoralen was more effective when used with UV radiation than psoralen itself. When exposed to UV radiation itself, the mass of dry granulation-fibrous tissue

was 48.33 ± 3.8 mg, and the mass of exudate was 269 ± 22.37 mg, which is 44.5% and 23.3% higher than in group II, respectively.(Table 2).

Table 2

Effect of psoralen, UV and psoralen + UV treatment regimens on inflammatory stages in rats, n = 6 (M ± m)

Observation groups	Dry granulation-fibrous tissue mass, gr	Exudate mass, gr
Control	87,58±24,1	351,8±36,43
UV radiation	48,33±3,8	269±22,37
Psoralen	48,66±5,57	288,8±24
Psoralen + UV radiation	33,4±3,1	178,4±14,71

P <0.05 relative to the control.

Initially, experiments studied the effects of UV radiation and psoralen on rat liver mitochondrial megaporas (mPTP) in chronic inflammatory conditions. Pathophysiological changes at the level of these mitochondrial membranes can be regulated or corrected using pharmacological agents and plant active substances. The psoralen compound can also pharmacologically modulate molecular changes that occur in liver structures during chronic inflammation.

In experiments, a 20 μM concentration of $CaCl_2$ was used as an inducer to activate high-conductivity pores in the mitochondrial membrane of the liver. According to the results, in the presence of a concentration of 20 μM of $CaCl_2$ in the incubation medium, the rate of suffocation in the presence of mitochondrial Ca^{2+} ions isolated from the liver of healthy group I rats was 0.35 DE540 / 10 min (Fig. 1).

Hepatic mitochondrial obstruction of chronically inflamed group II rats was found to be 0.84 DE540 / 10 min, an increase of 140.0 ± 6.5% compared to the healthy group. This suggests that stress developed in group II rats and that it affected permeability at the mitochondrial membrane level. It is known from the literature that Ca^{2+} ions increase the conductivity of mPTP and transfer it to the open state, matrix swelling is observed [13,14,7].

In experimental group III rats, when exposed to UV radiation for chronic inflammation, their mPTP permeability in the liver mitochondria was found to be 0.54 DE540 / 10 min, inhibiting 35.7 ± 2.5% compared to group II rats (Fig. 1). UV radiation has been shown to partially inhibit the function of the highly

permeable pores of the liver mitochondria resulting from chronic inflammation in rats.

In experimental group IV rats, chronic inflammation was induced and they were injected orally with a 10 mg / kg dose of psoralen on days 1, 4, and 7, respectively. Mitochondria were then isolated from the rats' livers. Their suffocation under the influence of Ca^{2+} ions was recorded as 0.65 DE540 / 10 min, inhibiting 22.6 ± 1.5% compared to group II. From this result, it was found that hepatic mitochondrial mPTP permeability was inhibited by psoralen and manifested by partial recovery in chronic inflammation.

Continuing the experiments, group V rats with chronic inflammation were exposed to UV radiation and on days 1, 4, and 7, 10 mg / kg of psoralen was administered orally through a probe. After that, mitochondria were isolated from the liver of group B rats. The results showed that rats exposed to chronic inflammation were exposed to UV-radiation in a complex way and that the delivery of psoralen reliably inhibited the suffocation of their hepatic mitochondria in the presence of Ca^{2+} ions. The liver mitochondrial permeability of this group of rats was 0.42 DE540 / 10 min and inhibited by 50.0 ± 4.5% compared to group II.

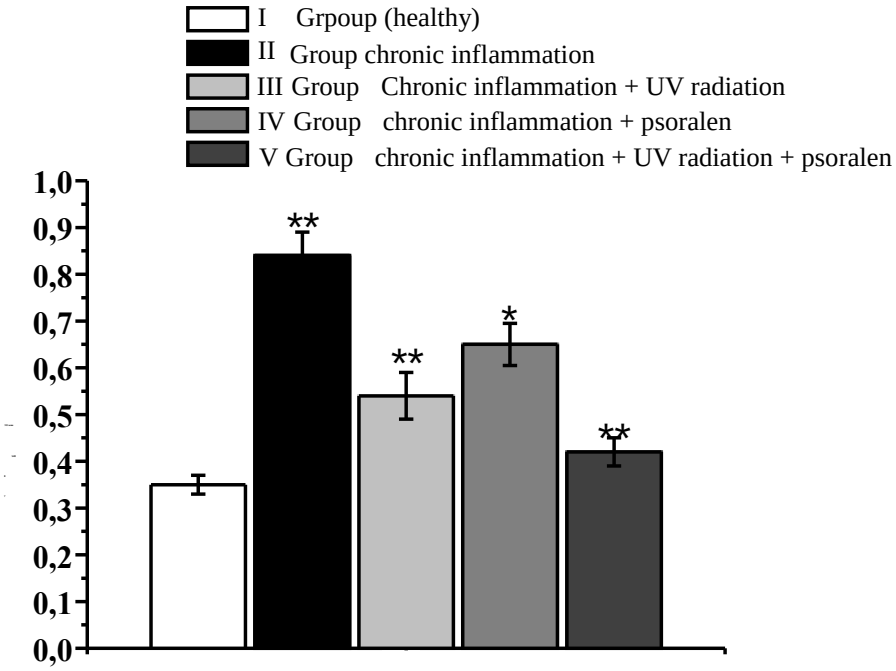

Figure 1. psoralen, UV-irradiation and their complex effects on the highly conductive pores of rat liver mitochondria under conditions of chronic inflammation (* P <0.05; ** P: <0.01; n = 6).

Such changes in the permeability of the mitochondrial membrane that occur in chronic inflammatory processes may also affect other ion-transport systems located in them. Another such ion-transport system located in the mitochondrial membrane is ATP-dependent potassium channels, which can exhibit their functional activity under conditions of physiological concentration of ATP. Decreased ATP synthesis as a result of disruption of electron transport in the respiratory chain and separation of oxidative phosphorylation processes caused by various disorders in the mitochondria alters the cycle of potassium ions in the membrane.

At present, there are no data on changes in the functional activity of K^+_{ATP} - channels of rat liver mitochondria in chronic inflammatory conditions and in cases of UV radiation and psoralen delivery. For this purpose, in our next experiment, rats with chronic inflammation were exposed to UV radiation and psoralen, and their liver mitochondria were isolated. Examination of the activity of K^+_{ATP} - channels of isolated liver mitochondria revealed the following results (Fig. 2). We know that a concentration of 200 μM of ATP in isolated mitochondria leads to a partial inhibition of its functional activity.

The results showed that the activity of K^+_{ATP} -channel of liver mitochondria of group II rats with chronic inflammation caused by inhibition of ATP at a concentration of 200 μM in the incubation medium was inhibited by 45.7 ± 3.4% compared to control (Fig. 2). Hence, the mitochondrial mitochondrial mitoK^+_{ATP} - channel activity of rats may reduce the cycle of potassium ions under the influence of inflammation.

In experimental group III rats, when exposed to chronic inflammation under the influence of UV radiation, it was found that their liver mitoK^+_{ATP} -channel permeability is 21.1 ± 1.2% more active than in group II (Fig. 2). UV radiation has been shown to partially increase liver mitoK^+_{ATP} -channel activity, which results from chronic inflammation in rats.

In experimental group IV rats, chronic inflammation was induced and they were injected orally with a 10 mg / kg dose of psoralen on days 1, 4, and 7, respectively. After that, mitochondria were isolated from the liver of rats and their mitoK^+_{ATP}-channel activity was found to be 13.1 ± 0.3% more active than in group II (Fig. 2).

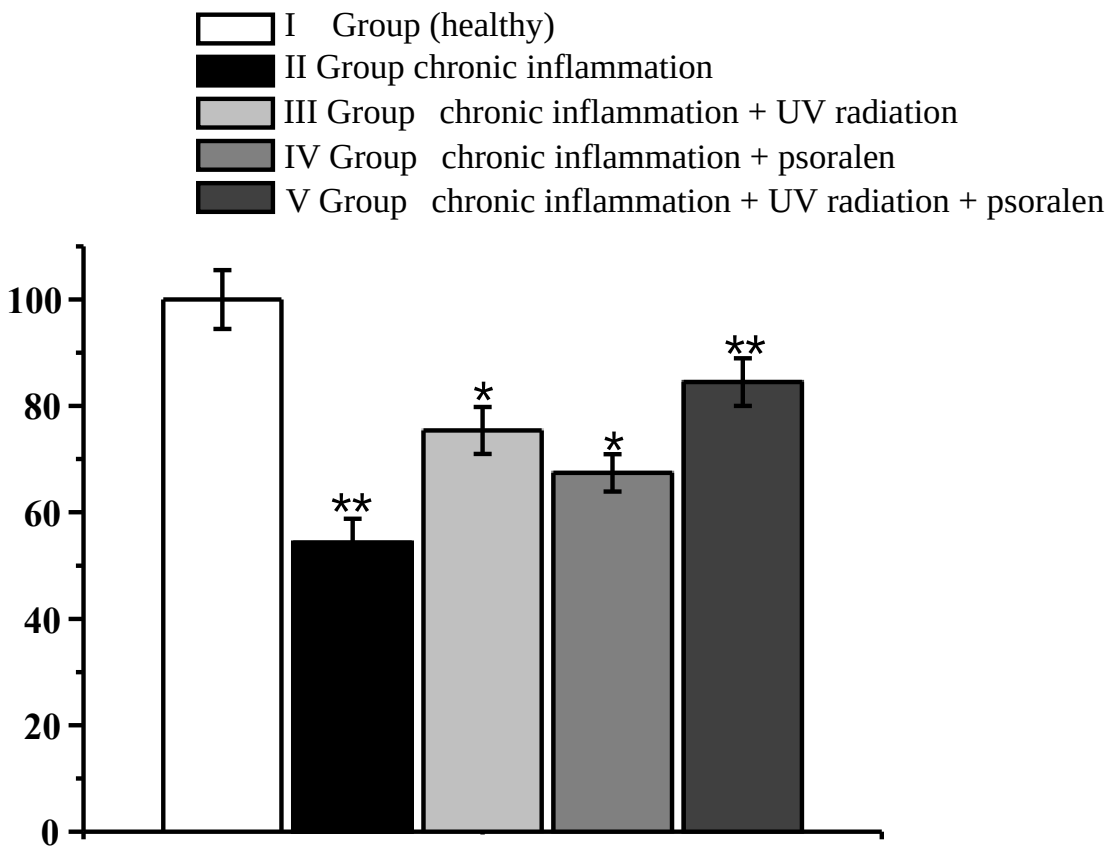

Figure 2. The effect of psoralen, UV-irradiation and their complex on the K^+_{ATP}-channel activity of rat liver mitochondria in chronic inflammatory conditions (* P <0.05; ** P <0.01; n = 6).

Continuing the experiments, group V rats with chronic inflammation were exposed to UV radiation, and on days 1, 4, and 7, 10 mg / kg of psoralen was administered orally through a probe and mitochondria were isolated from the liver. Rats exposed to chronic inflammation were exposed to UV radiation, and the administration of psoralen resulted in their activation of liver mitoK^+_{ATP}-channel activity by 30.2 ± 2.4% compared to group II indicators.

CONCLUSION

1. Mitochondria are the first and most responsive structure within the cell structures in inflammatory processes.

2. In chronic inflammatory conditions, when UV-radiation and psoralen are used separately, the permeability of the liver mitochondrial megaporas - mPTP is partially reduced. However, under the same conditions, the complex effect of UV-radiation and psoralen reliably inhibits this conductivity, allowing water and ions to enter the matrix and reduce its swelling. As a result, damage to the outer membrane of the mitochondria and the release of cytochrome C and proapoptosis

proteins from the matrix to the cytosol and the occurrence of cell apoptosis are prevented.

3. The complex effect of UV-irradiation and psoralen in the conditions of our experimental chronic inflammation activated the permeability of the mitoK^{+} $_{ATP}$-channel in the membrane of the hepatic mitochondria. This is the initial stage of the adaptation process under conditions of cellular hypoxia.

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Central Asian Journal of Medicine

COMPARATIVE ANALYSIS OF TREATMENT RESULTS IN PATIENTS WITH DAMAGE TO DUENUM IN DIFFERENT SURGICAL TACTICS

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ABSTRACT

The analysis of the results of surgical treatment and complications in the early postoperative period in 82 patients with duodenal lesions was carried out. The most frequent and formidable complication in the early postoperative period is the failure of the sutures of the duodenal wound with the development of peritonitis or the formation of an external fistula. The immediate complication leading to a fatal outcome is most often the failure of the sutures of the anastomoses to be applied, retroperitoneal phlegmon, which leads to septic infection and systemic multiple organ failure (SPON).

Key words: Damage to the duodenum, diagnosis, surgical treatment, complications.

INTRODUCTION

The relevance of the research. According to the analysis of home and foreign literature, mechanical damage to the duodenum is an insufficiently studied problem. At the same time, the quality of diagnosis and the results of surgical treatment of patients with duodenal injury still remain at a rather low level, which is explained by the lack of a unified approach to diagnosis and unified surgical tactics for various types of damage to the duodenal wall [1, 3, 9]. The most frequent and severe complication in the early postoperative period is the failure of the sutures of the duodenal wound with the development of peritonitis or the formation of an external fistula [5, 7, 11]. High postoperative mortality occurs mainly due to late hospitalization and diagnosis, ranging from 11.8 to 30.5% with isolated duodenal injuries, and from 46.6 to 80% with combined ones. With the development of retroperitoneal phlegmon, mortality can reach 100% [2, 6, 9].

The direct complication leading to death is most often the failure of the sutures of the applied anastomoses, which result in septic infection and systemic multiple organ insufficiency (MOI) [4, 10, 12]. Also in the literature there are indications of the causes of death: pneumonia, severe toxicosis due to progressive peritonitis and retroperitoneal phlegmon, unrecognized damage to the abdominal organs, sepsis, progressive exhaustion, purulent complications of traumatic pancreatitis, shock, necrosis of the intestinal wall after gunshot woundin, severe concomitant injury [11, 12], multiple organ failure that developed against the background of pancreatitis, disseminated intravascular coagulation syndrome [6, 8, 13]. These problems are the subject of our scientific work.

Purpose of the study. Comparative analysis of treatment results in patients with damage to the duodenum with various surgical tactics.

Material and research methods. The work is based on the analysis of studies carried out in 82 patients with various mechanical injuries of the duodenum who were examined and treated in Samarkand, Surkhandarya, Kashkadarya, Navoi, Jizzakh branch of the Republican Scientific Center for Emergency Medical Care for the period from 2000 to 2020. In most cases, patients of young and middle age were operated on - 63 (76.8%) patients in all, there were 3 times more men than women. There were 64 (78.1%) men and 18 (21.9%) women among the affected patients.

Damage to the duodenum in 5 (6.1%) cases was the result of a fall from a height (catatrauma); the vast majority of duodenal injuries were in 63 (77%) cases due to road accidents; in 4 (4.9%) cases - industrial injuries, and suicide attempts - in 2 (2.4%) observations, iatrogenic damage occurred in 3 (3.6%) observations, beating - in 5 (6.1%) patients. Most of the damage to the duodenum was due to a road accident.

In the conditions of the regions of the Republic of Uzbekistan, it is possible to relatively quickly deliver the victim to a hospital for rendering of qualified specialized medical care. For most cases, this time was 45.3 + 14.5 minutes. However, 17 (20.7%) patients appealed for medical aid more than 6 hours after getting injury. Mostly these are patients with closed abdominal trauma. First of all, the late treatment was associated with patients inadequate assessment of their condition. In the first 6 hours after getting injury, 55 (67%) of 82 victims were admitted to the hospital. In the period from 6 to 24 hours, 17 (20.7%) victims were hospitalized. 24 hours later 10 (12.2%) victims were hospitalized.

Damages to the descending part of the duodenum were revealed in 54 (66%) cases, to the lower horizontal part - in 11 (13.4%) cases, to the upper horizontal part of the duodenum - in 17 (20.7%) cases.

Table 1.

Localization of damage to the duodenum

Localization of damage to the duodenum	*Number of patients*	
	Abs	Abs
Upper -horizontal part	17	20,7%
Descending part	54	65,9%
Lower-horizontal part	11	13,4%
Total	82	100%

An isolated injury appeared in 27 (32.9%) cases. The share of combined and multiple injuries accounted for 55 (67.1%), which were more often revealed in duodenal injuries, that influenced the severity degree of this type of injury. Damage to the duodenum was combined with injury to the pancreas 28 (34.1%), liver - 11 (13.4%), gallbladder - 4 (4.9%), large intestine 4 (4.9%), small intestine - 3 (3.6%) and stomach - 3 (3.6%), portal vein 2 (2.4%). There were no significant differences when comparing the clinical symptoms of patients with isolated and combined closed duodenal injury ($p>0.05$).

The combination of damage to the duodenum with other organs and anatomical areas is presented in Table 2.

Table 2.

Organ damage	*Number of patients*	
	Abs	%
Pancreas	28	34.1%
Liver	11	13.4%
Portal vein	2	2.4%
Gallbladder	4	4.9%
Stomach	3	3.7%
Small intestine	3	3.7%
Colon	4	4.9%
Total	55	67.1%

Depending on the goal and objectives of the study, all the studied patients were divided into two groups.

I (control) group consisted of 34 (41.4%) patients who were treated with the traditional method of treatment, according to the protocol developed in the clinic, designed for placing of a primary suture on the damage to the duodenum with drainage of the abdominal cavity.

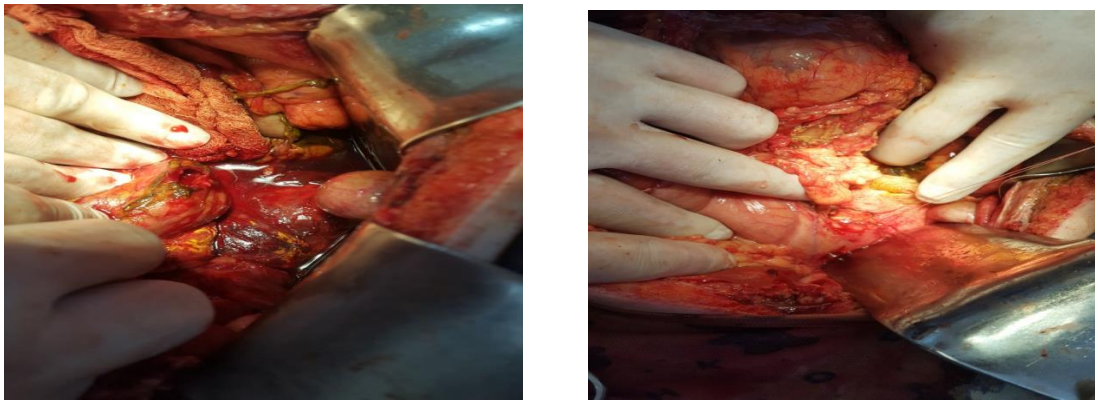

Fig.1. Placing of a primary suture on the damage to the duodenum.

II (main) group consisted of 48 (58.6%) patients, in whom the primary suture of the duodenal wound was supplemented with nasogastroduodenal decompression and passage of a feeding tube, with damage to more than 1/2 of the duodenum circumference, the primary suture was supplemented with a gastric draining operation, diverticulization of the duodenum, antrumectomy, gastrojejunostomy, duodenostomy, drainage of the common bile duct.

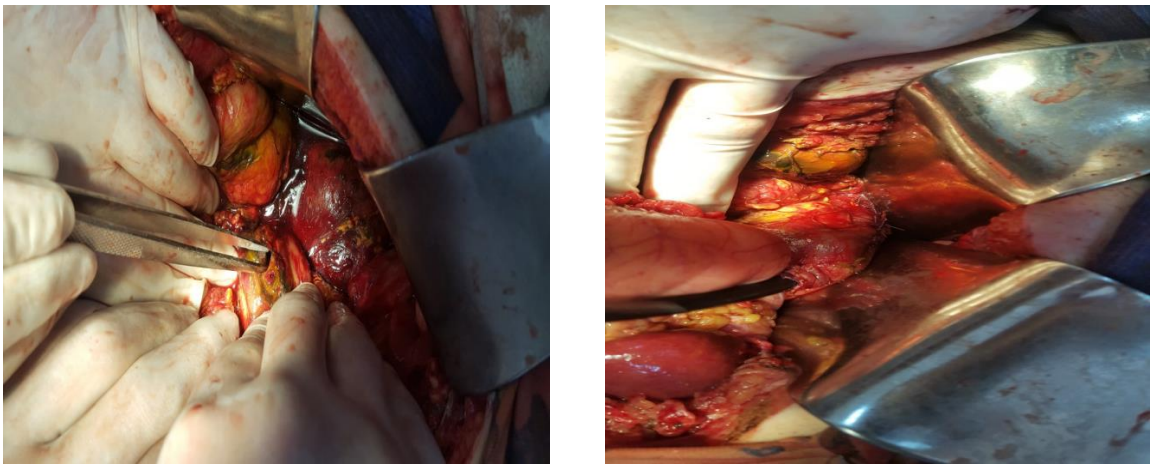

Fig.2. Closure of the duodenal wound, diverticulization of the duodenum, duodenostomy.

All patients underwent clinical and biochemical blood tests, X-ray examinations, ECG, ultrasound of the abdominal cavity and retroperitoneal space, and diagnostic laparoscopy, and, if necessary, computed or multispiral computerized tomography. Due to the organizational measures taken and the provision of modern equipment and qualified personnel, it has made it possible to significantly expand diagnostic capabilities and reduce the time for examination of patients admitted for emergency indications with closed injuries and wounds of the abdomen and acute surgical pathology. In the majority of patients with injuries and wounds of the abdomen, the examination was performed directly in the operating room against the background of anti-shock measures.

Research results. As a result of the analysis of surgical treatment of patients with duodenal injuries, the following data were obtained:

In the postoperative period on the 1st and 3rd day in both groups there were signs of intoxication: tachycardia, subfebrile fever, moderate increase in LII. On the 6th and 9th days, all indicators in group II were lower than in group I (table 3). Analysis of the data obtained shows that in group II after surgical treatment of duodenal injuries, symptoms of intoxication and improvement in the well-being of patients occur faster than in group I. Consequently, the ongoing treatment in group II contributes to a favorable course of the postoperative period.

Table 3.

Dynamics of body temperature, heart rate and LII in the postoperative period

Indicator	*1st day*		*3rd day*		*6th day*		*9th day*	
	1 gr	2 gr	1 gr	2 gr	1 gr	2 gr	1 gr	2 gr
body temperature (°C)	38,7± 0,5	37,7± 0,3	37,8± 0,4	37,3± 0,5	37,7± 0,4	36,9± 0,3	37,2± 0,4	36,7± 0,5
heart rate (per min)	118±5	114±4	116±5	108±5	98±4	91±3	88±4	77±3
LII (unit)	2,5±0,2	2,3±0,3	4,5±0,4	4,1±0,3	3,5±0,3	2,1±0,3	3,1±0,2	1,8±0,2

Analysis of the data obtained shows that in group II, after surgical treatment of duodenal injuries, symptoms of intoxication and improvement in the well-being of patients occur faster than in group I. Therefore, the ongoing treatment in group II contributes to the favorable course of the postoperative period.

Taking into account the high percentage of complications and mortality in both the main and control groups, a small number of observations, an assessment of the reliability of an unfavorable outcome was carried out.

In order to carry a dynamic analysis of the condition of patients from the moment of admission to the hospital to discharge, taking into account physiological and clinical data, the following systems of scales Ranson, MIP (Mannheim Peritoneal Index), APACHE II were used. In the group of patients with developed peritoneal phlegmon on the background of duodenal injuries the indices of Ranson and MIP scales were notoriously high and remained high despite treatment. Table 4.

Table 4.

Evaluation of the severity of the condition of patients with duodenal injuries in dynamics in the main and control groups

Group, points	Main Group п=15	Control Group n=21
PIM on the 1st day	19 points	19 points
PIM on the 10 days	11 points	11 points
Ranson on the 1st day	3 points	3 points
Ranson after 48 hours	1 points	4 points
APACHE II 1 day	8 points	9 points
APACHE II 10 th day 3	3 points	5 points

The APACHE II score reflected the positive dynamics of the treatment in the main group. According to the results of the study of clinical and biochemical analyzes, control of the contents of the retroperitoneal space, a dynamic study of the Ranson and MIP criteria, positive dynamics was noted in the main group.

The greatest number of postoperative complications was noted in the group of patients with combined injuries of the liver, pancreas, and intestines. It should be noted that in the postoperative period in 56 (68.3%) patients with closed duodenal injuries, 76 complications were observed (average 1.3 per 1 victim). Rupture of the duodenum due to a closed injury of the abdomen is very often accompanied by post-traumatic pancreatitis, which manifests itself only in the early postoperative period. Against this background, the likelihood of failure of duodenal sutures increases.

Table 5.

Complications of duodenal injury treatment

Type of complication	Control group (n-34)	The main group (n-48)
Pancreatitis	14 (41.2%)	12 (25%)
Pancreatic necrosis	5 (14.7%)	7 (14.6%)
Suture failure	11 (32.3 %)	7 (14.5%)
Retroperitoneal phlegmon	5 (14.7%)	6 (12.5%)
Duodenal fistula	8 (23.5%)	5 (10.4%)
Sepsis	5 (14.7%)	4 (8.3%)
Arrosive bleeding	4 (11.7%)	6 (12.5%)

In group I, after surgical treatment, complications occurred in 24 (70.6%) patients, and in group II - in 16 (33.3%) patients ($p<0.05$). The analysis of complications after surgical treatment shows that in group I more common complications such as pancreatitis in 11 patients (32.3%), pancreatic necrosis in 4 patients (11.7%) than in group II (25% and 12.5% respectively) occured. The incidence of arrosive bleeding in group I was 11.7% (in 4 patients), and in group II

-12.5% (in 6 patients). Also in group I, there were complications such as failure of duodenal sutures (32.3% in 11 patients), retroperitoneal phlegmon (14.7%, in 5 patients), in group II (14.5% and 12.5%, respectively) in group I -duodenal fistula (23.5% in 8 patients), in group II (10.4% in 5 patients), in group I - sepsis (14.7%, in 5 patients), in group II (8.3% in 4 patients respectively).

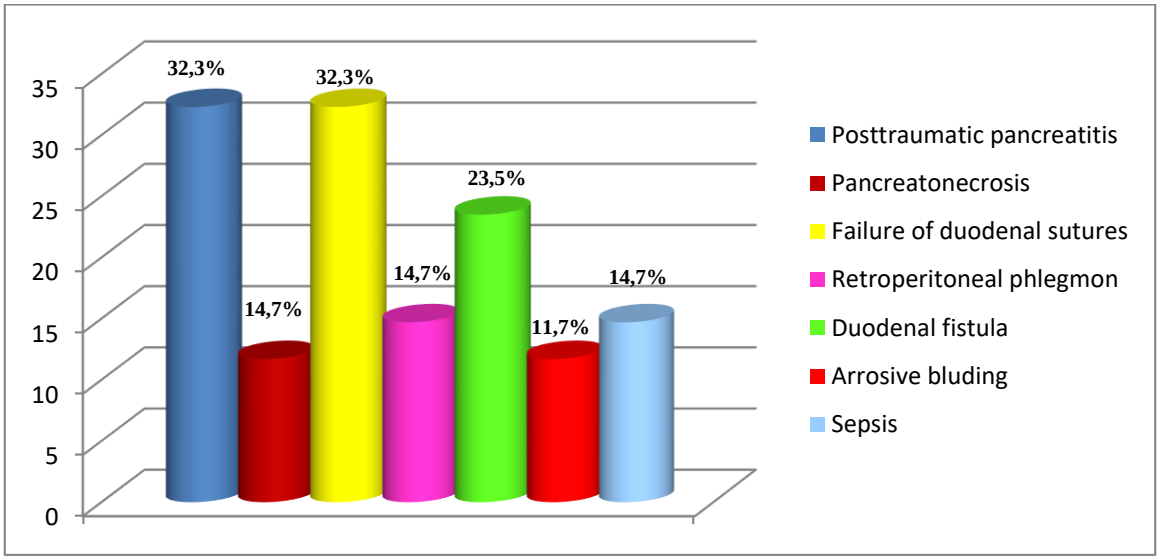

Fig. 3. Complications in the control group after surgical treatment.

As a result of the analysis of the surgical treatment of duodenal wounds, it was found that the likelihood of failure of duodenal sutures increases with the development of complications such as acute pancreatitis and retroperitoneal phlegmon. The most typical were subphrenic, interintestinal and retroperitoneal abscesses, sepsis, retroperitoneal phlegmon, post-traumatic pancreatitis complicated by pancreatic necrosis.

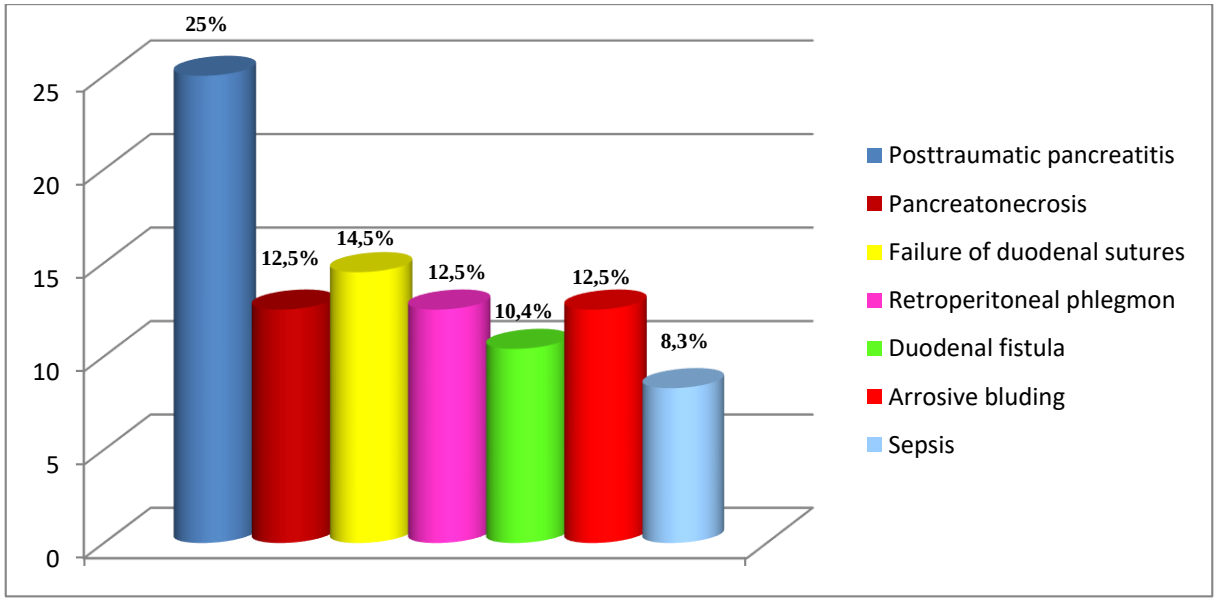

Fig. 4. Complications in the main group after surgical treatment.

The most highly lethal complication was: retroperitoneal phlegmon - 15 (18.3%) cases, of which the largest number was revealed with a closed injury. Lethality depending on the degree of damage is presented in Table 6.

Table 6.

Mortality in duodenal injury depending on the degree of damage

Degree of damage	Number of patients	Mortality	
		abs.h	**%**
Grade I	19	1	5,2
Grade II	36	6	16,6
Degree W	16	4	25
Grade IV	7	3	42,8
Grade V	3	3	100

Mortality among patients with damage to the duodenum of I degree was 1 (5.2%) case, with II degree - 6 (16.6%) cases. The highest mortality was observed among patients with damage to the duodenum of the III degree - 4 (25%) cases. 3 (42.8%) patients died in IV degree of duodenal damage, combined damages to the biliary tract, pancreas, small intestine, transverse colon, and 3 (100%) patients with damage to the duodenum of V degree. With IV and V degrees of damage, the death of patients occurred in the first hours and a week after hospitalization, which was due to the extensiveness of the injury received, a large number of lesions of vital organs.

Lethal outcomes after operations for damage to the duodenum were observed in the following periods: In the first 1-6 days after operations, 7 (8.5%) patients died. The cause of death was associated with the extremely serious condition of the victims before the operation and the progression of multiple organ failure in the postoperative period. Of these, 6 patients were admitted to the hospital in a condition of IV degree traumatic shock and in a condition of endotoxic shock due to retroperitoneal phlegmon. In 10 patients who died from 6 to 10 days after surgery, late purulent-septic complications were noted: arrosive bleeding - in 2 (the source of bleeding was the vessels of the pancreatic head bed - 2); fistulas of the gastrointestinal tract in 2 (duodenal fistula - 2), in 6 victims the cause of death was intoxication caused by retroperitoneal phlegmon and sepsis.

With developed retroperitoneal phlegmon, 5 (55.5%) patients died in the control group, and 4 (66.6%) patients died in the main group.

The treatment performed in the main group made it possible to reduce the risk of an unfavorable outcome, i.e. to reduce mortality to 18.7%. Mortality in the control group, among victims with duodenal injury, was 23.5% (8 patients). In the main group, 9 victims died, while mortality was 18.7% ($p<0.05$).

The average hospital stay of patients with closed duodenal injury was 17.6±11.8 days in the main group and 22.2±13.4 days in the control group ($p>0.05$).

Discussion. Thus, the technique of duodenal injury treatment used in the main group reduces the incidence of complications. Characteristically, the frequency of complications increases with an increase in the degree of damage, and also reaches a maximum value with damage to the descending part of the duodenum.

The proposed treatment and diagnostic program for choosing the method of surgical intervention and management of the postoperative period, depending on the degree of damage to the duodenum with the use of surgical sonation of the retroperitoneal space, will significantly reduce the number of complications, postoperative mortality and improve the results of treatment.

CONCLUSIONS

1. The final decision on the scope of the operation must be taken directly during the operation, taking into account many factors, such as the severity of the patient's condition, the volume and degree of damage to other organs, and the possible need for programmed sanitation.

2. In the early stages after the injury, the imposition of duodenojejunostomy, in our opinion, is the best.

3. In the later stages after the injury, the imposition of duodenostomy on the stretch with disabling the duodenum and with draining operations on the stomach gave good results.

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MONITORING OF WATER POLLUTION IN HOT CLIMATES

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ABSTRACT

It has long been noticed the tendency of mankind to hang catchy labels on everything that comes to hand, especially on any epoch-making events. So the twentieth century, which has sunk into the past, was called - oil and nylon, nuclear and space, information and computer. The coming age from its very threshold is often called the water age, and inveterate pessimists do - the age of water wars. Meanwhile, scientists have long calculated that approximately 1366 million cubic kilometers of water have accumulated on our small planet, or more than two hundred million tons per average earthling. But for a completely comfortable existence, hundreds of tons of water per year are more than enough for an earthling, if we focus on reasonable standards for domestic water supply. And each of these tons, obeying the inexorable world cycle, sooner or later returns to the bosom of nature, so why sound the alarm? However, there is more than enough reason for concern. 97.5% of the planet's water resources located in the seas, oceans and depths of the earth are not yet suitable for consumption due to excessive mineralization.

Key words: Wastewater, sewerage, open reservoirs, health, aerotank, treatment facilities, disinfection, sources of drinking water supply

INTRODUCTION

Water is an invaluable gift of nature. Water is of great importance in the existing manufacturing sector and in the national economy. Everyone knows the living conditions of the population, the need for water for flora and fauna. Water is a natural habitat for many species of living things. Freshwater scarcity is one of the major challenges facing the world today. The growing demand for water in the manufacturing sector and agriculture makes it difficult for the whole world to find

different sources of solutions to this problem [3]. The expansion of cities, the rapid development of production, the steady growth of agriculture, the significant expansion of irrigated fields, the improvement of cultural and living conditions, and a number of other factors are further complicating water supply problems. The following areas of water use remain relevant at the present stage; these include more rational use of water resources and expanding the recovery of freshwater resources; development of new technological processes that will prevent pollution of water resources. When water bodies of economic and cultural significance are considered polluted, the composition and properties of water at the point of use must be directly or indirectly affected by economic activities, domestic use and be found to be partially or completely unfit for use [1].

In many industrialized countries, the sanitary protection of water bodies is one of the most important tasks in connection with the growing demand for water for the domestic needs of the population [2].Water is necessary for all forms of life, as well as for most types of human activity. Water is extremely sensitive to changes in the natural environment associated with human activities, and this poses acute and persistent challenges to humanity. This delicate and unstable mechanism of interaction between man and water has existed since the emergence of mankind, and is now in a critical state as a result of the rapid development of industry and population growth. So, for example: 250 tons of water for the production of 1 ton of paper, -60-210 m^3 for the production of 1 ton of yarn, -1 ton for the production of fabrics - 250 m^3, for the production of 1 ton of soap -50m^3, 1 ton of glue 240 m^3 for production, -130m^3 for the production of 1 ton of pipes, -25m^3 for the production of 1 ton of oil, 385m^3 for the production of cellulose, -84 m^3 for the production of margarine, -30m^3 for the production of 1 ton of metal structures (.....) water is consumed. According to G.G. Onishenko, water consumption in developed countries (2016) has increased 15 times over the past 20 years, and water consumption for domestic purposes amounted to 500 million m^3 per day. The economic and domestic activities of modern society are so closely connected with the use of natural waters that daily knowledge of the condition of water bodies and early detection of changes in their regime has become a priority. Along with the increase in water supply, the amount of wastewater discharged into water bodies is also increasing. According to Drachev S.M. [2019], the amount of wastewater in the United States in 2019 increased 4.6 times compared to 2012-2014. The increase in wastewater is accompanied by an increase in water pollution in a number of countries [7]. A number of scientists have shown in their work that aggressive pollution of water bodies in industrialized countries [Key A, B; Klein L., Pescroix P., Filg O., Petrilli F.L., Porges R 2015]. This condition has not

stopped to date [Hillis P., Padley M.B., Powell N.I., Gallagher P.M. Effects of backwash conditions on out-to-in membrane microfiltration, Desalination, 118, 197-204, 2019.]. At present, the problem of protection of natural waters from pollution has covered almost all economically developed countries.

Especially the water basins of the Netherlands, Italy, Sweden, England, Japan are heavily polluted with various chemical and biological substances. For example, the production of 24 million tons of polluted water from the Rhine annually leads to the discharge of industrial wastewater into the sea.The Danube River, more than a hundred kilometers from the city of Krems to the Slovak border, has become a biologically dead basin in its composition [4]. Various chemicals, including highly toxic dioxins, enter the water basin with wastewater [I.A. Kryatov, E.A. Mojaev, 1998; Marsalen J.K., 1998; W.Pettenkoven, 1999; S.Marapoul et.el 1999; M.Nutten, C.Symon, 2000; H.H. Dieter, 2000]. Water contaminated with wastewater not only becomes unusable or less usable, but it also causes significant, often irreparable damage to the entire natural environment it affects. In polluted water, fish die, and other members of the plant and animal world become extinct. The solution to the problem of protecting water resources is mainly to protect them from wastewater pollution. Domestic wastewater retains about 60% of organic matter, which is especially important for sanitation. Pollutants entering wastewater can be conditionally divided into several groups. Hence, insoluble, colloidal and soluble additives are separated according to their physical composition. Typically, mineral contaminants are manifested in the form of sand, clay mixtures, metal particles, mineral salts, soluble acids, alkalis and other substances. Organic pollutants are divided into plant, animal and bacterial species according to their origin [1]. According to G.I. Sidorenko (2001), pathogenic bacteria and viruses are isolated from municipal wastewater, the excretion fund of which (in the central part of Russia) is up to 80%. It has been established that the duration of retention of pathogenic bacteria depends directly on the initial contamination dose. This means that at an initial concentration of 10 microbial cells in 1 ml of river water, Flexner’s diarrhea bacteria survive for 9 days at a temperature of 19-24^{0}C for 3 days, at a dose of 10,000 per ml.

Studies conducted by I.V. Khanigin revealed that typhoid fever, enteroviruses: poliomyelitis, coxsackie V-3; V-4, ECHOs were detected when the wastewater in Irkutsk was poured into the Angar River after mechanical treatment. In this case, the wastewater is less effective for 30 minutes of contact with a large dose of chlorine (residual chlorp content - 0.5 mg/l). Discharge of wastewater containing large amounts of organic matter and various trace elements into an open water body can lead to the general development of bacteria, algae, fungi,

contamination of river water with toxic substances, which can be a source of poisoning for fish, humans and pets. possible [G.Vogler, 1967; E.J.Curtis, C.R.Curgs, T.G.Kokoliya, 1971; A.N.Leventsev, 1990]. The rapid development of separate species of plankton and bectos in rivers often leads to deterioration of water quality [9]. Some algae and aquatic fungi give the water an unpleasant odor, saturating it with toxins, making it unsuitable for drinking and recreational purposes [7]. In addition, the coverage of rivers with biologically simple organisms can lead to an increase in the lifespan of pathogenic microflora entering the watershed or, conversely, to the destruction of pathogenic microorganisms [10]. It has been established that for some species of viruses, blue-green algae is a nutrient medium that is a good source of growth [11]. Discharge of wastewater containing large amounts of organic matter into an open body of water often results in the flooding of water bodies with Leptomitus Lacteus (hereinafter leptolitus). Many rivers are affected by this fungus: Volga, Kama, Yauz, Neva, Oka, Iya, Biryus. As soon as their colonies reach a certain size, they are cut off from the bottom of the water and from various objects in the water, and the water flows downstream for miles. As a result of slowing of water flow in deep places, biomass sinks to the bottom, accumulates, decomposes and secondaryly pollutes rivers with organic matter, which leads to a sharp decrease in dissolved oxygen in the cold season and creates unfavorable conditions for the development of others [11].

One of the main sources of water pollution is car wash points.Technological analysis of the car wash process allowed to determine the average amount of water used to wash one car a year in a public survey of car owners, which is estimated at 4.34 million m^3 of water used for car washing in Tashkent, and they are unfortunately not enough unfortunately the cannot be cleaned enough. 734 kg of suspended solids, 446 kg of petroleum products and 127 grams of UFMs enter the sewage system from one car wash. These substances disrupt the biological treatment process when they enter the municipal sewage system [3,4]. Currently, there are more than 125 car washes in Tashkent. One station uses 10,621.5 m^3 of fresh water per year. The resulting wastewater is mainly discharged into the sewer system without treatment or through sewers and without the necessary treatment. The water consumption for cars at the officially registered car washes in Tashkent is 1.33 million m^3. If we take into account that the number of cars in Tashkent (according to official statistics 417,646) consumes 200 liters of water for one wash and the car is washed once a week, the figure is 4.34 million m^3.

This does not include trucks, buses and special vehicles (Resolution of the Cabinet of Ministers of the Republic of Uzbekistan "On measures to implement national goals and objectives in the field of sustainable development until 2030").

In the analysis conducted by Uzhydromet, the amount of pollutants in the Chirchik River (petroleum products, EKBBE, phosphates, iron), in the Karasu canal (nitrogen ammonium, nitrogen nitrite, phosphates, iron), Bozsu canal (nitrogen ammonium, phosphates, chlorides, petroleum products), In the Salor canal (sulfates, phosphates, iron, ammonium nitrogen) it was noted that it is higher than sanitary and hygienic standards. The major anthropogenic impact on Uzbekistan's water resources has been the drying up of the Aral Sea and the reduction of water saturation in the Amudarya delta. By 2005, the river had lost 5 to 4 parts of its volume, the water surface had shrunk by a third, and the water level had dropped to 22 m (Regional Action Plan to take measures against Desertification of the Aral Sea Basin (CRAPCD), 2000 (GTZ. Taking measures against Desertification). UN Convention on the Law of the Sea). Pollution of open water bodies is widespread and even leads to significant contamination of groundwater, including drilled wells. Water pollution of this group plays an important role in the growth of diseases (kidney, oncological and acute infectious diseases), mortality, including children. leads to an increase in mortality.

Anthropogenic impacts also lead to soil pollution (salinity, toxic substances, pesticides, fertilizer residues, heavy metal poisoning) and impact on public health (National Report on the of Water Reuse). Currently, the country's water resources remain unsatisfactory. The highest levels of mineralization and pollution are more common in the lower and middle reaches of the river. This poses a serious threat to the life and health of the population and resists the preservation of natural habitats. Sources of pollution are: agricultural irrigated lands (78%), manufacturing enterprises (18%) and the municipal sector (4%). Agricultural wastewater is the main source of pollution of open and groundwater (90%). Although industrial effluents are small in size, they are more harmful and dangerous in terms of their toxicity. According to the Water Pollution Index (WPI), there are seven classes of water quality from I (very clean water, WPI <0.3) to VII (extreme polluted SII> 10). Excessive use of agricultural chemicals (nitriates, phosphates, pesticides) leads to rapid pollution of agricultural lands and water sources, contaminated water from irrigated lands enters the collector-drainage system. This, in turn, leads to the contamination of open water bodies through collectors.

CONCLUSION

Water is the most important irreplaceable natural factor on earth. Its availability and quality depend on human health, the level of sanitary-epidemiological well-being, the comfort of living, and as a result, the social stability of society. The development of science and technology, the chemical

industry and industry in general, the favorable living conditions of people lead to the pollution of water resources from year to year with different amounts and contents of wastewater. This will have a negative impact not only on the level of pollution of all types of open water bodies in the Republic of Uzbekistan, but also in the Central Asian region.

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COMPLEX TREATMENT OF SPINAL TUBERCULOSIS IN FUNCTIONAL DISORDERS OF THE GASTROINTESTINAL SYSTEM

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ABSTRACT

Complicated forms of tuberculous spondylitis occur in 70% of adults and 100% of children. Recovery from the disease is recorded in 36.5-69.5% of cases, and disability because of complications of the disease - in 67.0-88.8%. Functional changes in the gastrointestinal tract were detected in 44.0% of patients with complicated spinal tuberculosis. Carrying out therapeutic measures for identified diseases has a positive effect on the effectiveness of surgical treatment. [1,2,3,4,5,6].

Key words: tuberculous spondylitis, gastrointestinal tract, expansion, extrapulmonary tuberculosis.

INTRODUCTION

To study the effectiveness of complex treatment of motor-motor dysfunction of the gastrointestinal tract in complicated spinal tuberculosis. Materials and methods: 100 patients with complicated tuberculous spondylitis, of which 60 (60.0%) patients with tuberculous spondylitis and functional disorders of the gastrointestinal tract (group 1), group 2 40 (40.0%) people with tuberculosis spondylitis and no functional disorders of the gastrointestinal tract.

As a comparative group, 20 healthy individuals formed the 3rd group. Patients aged 18 to 20 years accounted for 20.0%, 21-40 years - 35.0%, 41-60 years - 30.0% and over 60 years - 15.0%. The mean age ratio was 37.2 ± 1.2 years. Of the patients examined, 31 were in group 1 (51.6%) and 21 (52.5%) in group 2;

In the 1st group there were 29 women (48.3%), in the 2nd group there were 19 people (47.5%). 56.0% of patients, including 27 (45.0%) in group 1, 19 (47.5%) in group 2, low hemoglobin, 35 (58.3%) leukocytes in group 1, 26 in group 2 (65.0%), in a total of 61 (61.0%) cases 18.3 ± 1.4 * 109 / l. in terms of volume, the ESR was 61 (61.0%), of which 31 (51.6%) in group 1 and 30 (75.0%) in group 2 ranged from 24.8 ± 2.8 mm / s. In both cases, 46.0% in group 1 and 49.0% in group 2, the tuberculosis process was characterized by signs of poisoning, deterioration of clinical laboratory and radiographic findings. In 10.0% of patients with tuberculosis, surgery was performed on the spine affected by tuberculosis in the neck, 27.0% of the chest, 40.0% of the lumbar and 23.0% of the lumbar spine, ie on the basis of an orthopedic regimen for up to one month (Table) №1).

Table 1.

Complications of spinal tuberculosis

Group	Anterior, lateral abscesses of the spine		Spinal dysfunction	Instability in the spinal segment
	One-sided	Two-sided		
1	48 (80,0%)	51 (85,0%)	39(65,0%)	41(68,3%)
2	29 (72,5%)	30(75,0%)	33(82,5%)	35(87,5%)
Total	77 (77,0%)	81(81,0%)	72 (72,0%)	76(76,0%)

Complaints on clinical examination in group 1 patients include pain in the epigastric region of the gastrointestinal tract, strong and marked pain, burning in the stomach, discomfort in the stomach after a meal, feeling of fullness in the stomach, less pain in the epigastric region, feeling of fullness in the stomach after a meal, functional abdominal pain after defecation, recurrent pain during the day and recurrent throughout the day. It is known that since all functions of the gastrointestinal tract are closely related to motor-motor function, motor-motor function in patients is divided into two types: - starvation peristalsis and digestive peristalsis, ie the state of food mass after entering the gastrointestinal tract. The motor-motor function of the gastrointestinal tract was studied in a real-time mode by the F.Tympner method on a 3.5-5 MHz linear sensor ultrasound machine Interskan-250 (Germany).

The norm of motor-motor function of the gastrointestinal tract was determined at 8.0 <= T /2<=21.5 relative to fluid. The significance of the half-life in the case of slowing gastrointestinal motor-motor function is 30 +/- 10.2 minutes, accelerated motor-motor function - 6.2 +/- 1.8 minutes, motor-mmovement function -12. 1 + / 8.9 min rated. The severity of neurological complications is based on the conclusion of a neuropathologist, Frankel H.L. and co-authors., 1969y., and extended Mushkin A.Yu. and co-authors., 1989, rated at 5 levels.

Diagnosis of gastrointestinal motor dysfunction in patients with complicated tuberculosis spondylitis and risk factors for motor and motor dysfunction in patients with spinal cord dysfunction in the preoperative and postoperative period, depending on the location of the tuberculosis process in the tuberculosis-affected spinal segment.

Based on the purpose and function of the study, functional anamnestic and clinical course of the gastrointestinal system in patients with complicated spinal tuberculosis in the preoperative and postoperative period was assessed in 4 rounds (Table №2). The first type (mild) is abdominal pain (range of 2-8 points), long-lasting (rapid recurrent or persistent), persistent (blunt, simmering), diffuse (without clear boundaries), not localized in the last 6 months. The main criterion for this option is that abdominal pain has long been observed in patients. The second option (less developed) is less pain observed in the abdomen (between 6 and 8 points), periodic in nature, with no clear boundaries and diffuse. The third type (advanced) - strong (range of 9 - 13 points), the first appearing periodic in nature, occupying several areas of the anterior wall of the abdomen, not widespread. The fourth type (strongly developed) abdominal pain syndrome (14 - 17 point range) is observed in the first emerging aggressive appearance, diffuse, abdominal asymmetry.

Table 2.

Types of functional disorders in patients with OIT

Group	**Types of OIT functional disorders**			
	1- type	**2- type**	**3- type**	**4- type**
1- group	12 (20,0%)	8 (13,3%)	13 (21,6%)	13(21,6%)
2- group	10 (25,0%)	13(32,5%)	12(30,0%)	11 (27,5%)
total, %	22 (22,0%)	21(21,0%)	19(19,0%)	30(30,0%)

Clinical radiological examination revealed 66.0% of patients in both groups in the active stage of spinal tuberculosis, 34.0% in active torpedoes and in 3 (6.0%) patients in the same category with pulmonary tuberculosis, inactive. Clinically, tuberculosis of the spine in the active phase began with an acute onset of the disease, an increase in body temperature to 37.0-38.0 C, general weakness, loss of appetite and a significant decrease in body weight. It was noted that in patients with active torpedo spinal tuberculosis, the general symptoms of tuberculosis poisoning are less developed. In the EFGDS Olympus (Japan) study in group 2 patients, the disease was detected in 17 (42.5%) patients. In patients with chronic gastritis 5 (12.5%), ulcer disease 2 (5.0%), gastric atrophy 4 (10.0%), gastric hyperplasia 6 (15.0%) were detected. In the treatment of diseases diagnosed in

patients, broad-spectrum antibacterial, antacid and proton pump inhibitors were prescribed after consultation with a gastroenterologist.

All data were statistically analyzed based on the Student's t-test.Pharmacological drugs prokinetics in order to increase the propulsive activity of the gastrointestinal tract and normalize the bite in the hollow organ under various exposures in the digestive system: domperidone 10 mg, procerin 0.05% - 1.0 m / o, metoclopramide 10 mg 2.0 m / o, which directly stimulates the release of acetylcholine and has a central and peripheral antidopaminergic effect.

CONCLUSIONS AND DISCUSSION

It is known that regenerative, energy-consuming nutrients enter the gastrointestinal tract, and the stages of digestion, absorption and utilization are provided by the motor-motor function of the gastrointestinal tract. In patients with spinal tuberculosis is associated not only with functional disorders of the gastrointestinal tract, but also with temporary dysfunction, dysfunction of the liver, biliary tract and pancreas. The condition is important, as well as the functional status of the internal organs, including the functional status of the gastrointestinal tract. No significant difference in peripheral blood analysis was observed in both groups of patients.

The values of alanine aminotransferase and aspartate aminotransferase in group 1 were (0.97 ± 0.02) and (0.69 ± 0.03) μmol / l, in group 2 (0.58 ± 0.03) and (0.38 ± 0, 02) mkmol / l., Formed. Anti-tuberculosis drugs were administered based on the basic rules, based on the susceptibility of tuberculosis mycobacteria. Patients examined in the complex treatment of the underlying disease received complex treatment procedures in an strictly orthopedic regimen. Tuberculosis isoniazid 10 mg / kg (600 mg per day), rifampicin 8-12 mg / kg (600 mg per day), ethambutol 15–25 mg / kg, pyrazinamide 15-25 mg / kg, tuberculosis mycobacteria sensitivity was determined based on 3 to 6 months of antipsychotic drug sensitivity. Based on patients, stol 5 tables were ordered.

In both groups of patients, the prevalence of inflammatory processes in the spine, anterior and lateral spinal abscesses, accompanied by various degrees of neurological complications, 12.0% in group 1, 9.0% in group 2 due to allergic reactions to antibacterial drugs, isoniazid 10% -5 , 0 + Vit V6-5% -2.0 administers №30 intravenously and rifampicin 450 mg + glucose 5% -250.0 intravenously. However, in this category of patients, side effects when taking antibacterial drugs against tuberculosis were observed by 6.0% more than in group 2. Despite the complex treatment interventions, 24% of cases in group 1 and 31% in group 2 had worsening neurological complications, so early diagnosis of the underlying disease was considered an indication for surgery.

In both groups of patients, a reconstructive type of spinal cord injury was performed. In the postoperative period in group 1, functional complaints of the gastrointestinal tract improved clinically, pain in the epigastric region decreased by 36.5%, severe pain and burning sensation in the gastrointestinal tract were not observed, and a significant decrease in pain sensation was observed by 49.0%. no feeling of fullness was observed. Few pains in the epigastric area and a feeling of fullness in the stomach area after a meal were not noted. Abdominal pain decreased by 51.0% after functional stools, and no recurrent pain was observed during the day and in one day. Within 2-3 months after surgery, 46 (65.5 ± 1.7) of the 1st group had a decrease in the activity of the spinal cord, 76 (88.5 ± 2.5) of the patients of both groups had tuberculosis. In the segment, local pain disappeared in 91 (92.7 ± 0.7) patients. X-ray obscure abscess shadows were observed in unilateral 44 (84.0 ± 0.7) cases, bilateral bilateral abscesses in 97 (98.2 ± 0.3) cases, loss of tuberculosis activity in the spine in 76 (82.3 ± 1.0) cases .On the sixth postoperative day, 1 patient with confirmed pulmonary tuberculosis showed worsening of blood circulation in the coronary posterior wall of the spine, and during the 1st month, serous pleurisy was observed on the operated side of the chest, 2 of them had changes in liver enzymes (increased transaminase) and allergic dermatitis. X-ray spinal abscess was preserved in 3 patients, of which 1 patient developed a body temperature of 37.0-37.5 C for 2 months, and 2 developed toxic hepatitis. Detected changes in the patients ’cardiovascular system, lungs, and liver were terminated with targeted pathogenetic treatments. Thus, functional disorders of the gastrointestinal tract complicate the clinical course of complicated spinal tuberculosis and reduce the severity of complex treatment. As a result of complex treatment of functional disorders of the gastrointestinal tract in patients with tuberculosis increases the effectiveness of etiological and surgical treatment, improves the general condition of patients, early disappearance of tuberculosis, stabilization of the tuberculosis process.

CONCLUSIONS

1. Functional disorders of the gastrointestinal tract in spinal tuberculosis aggravate the clinical course of the underlying disease.

2. Impaired motor function of the gastrointestinal tract in spinal tuberculosis complicates the complex treatment of the underlying disease.

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RESULTS OF ATMOSPHERIC AIR POLLUTION MONITORING

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ABSTRACT

Sanitary protection of atmospheric air, which is the most important factor of the external environment, ensuring its quality indicators in accordance with environmental standards is one of the current global problems. While global emissions are declining at this rate, global warming and climate change are having unpredictable consequences. Currently, one of the most dangerous sources for human health is toxic gases emitted by vehicles, in particular, the exhaust gases from vehicles enter the body through the respiratory tract and combine with hemoglobin in red blood cells to form carboxyhemoglobin. In samples that did not meet hygienic requirements, sulfur dioxide was found to be in the second place after dusting. In the analysis of atmospheric air pollution with formaldehyde, it was found that all samples met the hygienic requirements.

Key words: atmospheric air, motor transport, nitric oxide, disease, work gas, pollution, dust.

INTRODUCTION

High levels of pollutants are constantly detected in the air of large cities, which have a negative impact on the environment and public health. Sanitary protection of atmospheric air, which is the most important factor of the external environment, ensuring its quality indicators in accordance with environmental standards is one of the current global problems. According to the United Nations,

nine out of ten people in the world breathe polluted air. 91% of the world's population lives in air-polluted areas. In 2018, 7 million people die each year as a result of excessive air pollution. In particular, the countries of Asia and Africa rank high in this indicator. Twenty-five percent of heart disease, 24 percent of paralysis, and 43 percent of lung diseases and lung cancers in humans are caused by breathing polluted air. At the same time, greenhouse gases emitted into the atmosphere are causing global warming and climate change. If global emissions go at this rate, global warming and climate change could have unpredictable consequences. In this regard, the Republic of Uzbekistan has a strong legislation, in particular, Article 1 of the Law of the Republic of Uzbekistan "On Protection of Atmospheric Air" states that atmospheric air as a component of natural resources is a national asset and protected by the state. At the same time, the main objectives of the legislation are: to preserve the natural composition of atmospheric air; to prevent and reduce harmful chemical, physical, biological and other effects on the atmosphere. One of the most dangerous sources of human health today is toxic gases from vehicles. In addition to polluting the atmosphere with various toxic gases, cars use 3-4 times more oxygen than the oxygen that the world's population needs to breathe. A car engine in a year consumes breathing oxygen of 20-30 people. Each year, 1 car removes an average of 4 tons of oxygen from the air, releasing 800 kg of carbon monoxide, 40 kg of nitrogen oxides and about 200 kg of various toxins, including hydrocarbons. Taking into account that there are now more than 500 million cars in the world one can imagine the amount of pollutants emitted into the atmospheric air which is very large. Vehicles pollute the atmosphere with 45.7% nitrogen oxides and 42% hydrocarbons. Of the almost 100 million tons of carbon dioxide emissions per year in the world, 75.5 million tons or 78% come from cars. 60% of urban air pollution is caused by vehicles. Exhaust gas from vehicles is a colorless toxic gas formed by the incomplete combustion of motor fuels. It is carbon dioxide that enters the body through the respiratory tract and combines with hemoglobin in red blood cells to form carboxyhemoglobin. This substance cannot bind oxygen, resulting in a lack of oxygen in tissues and cells, primarily nerve cells. It leads to dysfunction of all organs and all systems of tissues and cells. A single car can emit up to a kilogram of lead into the air throughout the year. The toxic amount of lead in human blood is 0.8 parts per million, which means that if a person takes 40 mg of lead a day with food, the amount of lead in his blood will increase from one million to 0.4 parts per day. The increase in the number of vehicles, the creation and widespread use of powerful mechanisms have a negative impact on the generous nature, including atmospheric air, leading to its degradation. Cars are one of the main causes of urban air

pollution today. As a result of the growing number of car fleets in the world, the share of vehicles in air pollution is increasing. The data show that in the United States and Japan, motor vehicles are among the main leading sources of air pollution. Among the gases that pollute the air of foreign countries, carbon monoxide, hydrocarbons, as well as nitrogen oxides make up 60% of all aggressive gases, while in our country they make up 14%. Cars, locomotives, airplanes, and tractors emit large amounts of O_2 into the atmosphere, releasing 260 million tons of carbon monoxide. t, volatile hydrocarbons - 40 mln. t, nitrogen oxide - 20 mln. t and releases harmful compounds of lead. The increase in the number of cars is leading to an increase in the amount of emissions into the atmosphere. The average car used for 6 years emits 9 tons of SO_2, 0.9 tons of CO_2 and 80 kg of hydrocarbons into the atmosphere. The country has more than 3.5 thousand industrial enterprises with 99.5 thousand stationary sources of pollution and more than 2.816 million mobile sources of pollution, i.e. vehicles. From 2010 to 2018, the amount of pollutants emitted into the atmosphere increased almost 1.3 times and in 2018 amounted to 2.442 mln. tons. Of this, 65% or 1 mln. 560,000 tons are motor vehicles. In particular, due to the growing number of private cars and the growing population, vehicles are the main source of air pollution in Tashkent. In Tashkent, the figure is 80%. According to the data, Tashkent's air is polluted with 395 tons of toxic gases annually. 90% of the emissions are due to vehicle emissions. There are more than 2 million registered vehicles in the country, of which 450,000 are in Tashkent.

About 50,000 cars enter the city every year from other regions and countries. About 75% of the capital's vehicles run on gasoline and diesel fuel, and 25% on gas. The number of cars per capita in Uzbekistan is growing sharply. This figure has increased by 14.5% over the past year. As of January 1, 2021, the number of vehicles owned by individuals in the Republic of Uzbekistan amounted to 2,955,295.

Research methods

The situation is further complicated by the fact that the number of cars in the capital has more than doubled in the last 10 years, public transport networks were built in the 80s of the last century, but not yet completely revised, resulting in serious problems in the urban public transport system. Atmospheric air pollution has always been a concern due to its harmful effects on human health. Air pollution has a negative impact on human health and is one of the leading causes of allergies and respiratory diseases. That is why the quality of the air we breathe is so important. Almost every major city has high levels of pollutants in their atmosphere, which have a negative impact on ecosystems and public health.

Atmospheric air quality monitoring programs include five major pollutants: dust (solid suspended particles), sulfur dioxide, carbon monoxide (carbon monoxide), nitrogen dioxide, and nitric oxide. Other substances (ammonia, phenol, formaldehyde, ozone, chlorine, solid fluorides, hydrogen fluoride, heavy metals) are added to the program measurements depending on the composition of the industrial separations and the characteristics of nearby cities and adjacent areas. *The increase in emissions of air pollutants can be attributed to the increase in the number of manufacturing enterprises and vehicles in the process of rapid economic development.* Based on the above, we aimed to retrospectively analyze the ecological and hygienic condition of the atmospheric air in residential areas in the dynamics of the years. The object of inspection is atmospheric air and its content of nitrogen oxides, carbon dioxide, formaldehyde, lead, dust at gas stations, intersections and car washes located in residential areas.

In carrying out the work, the legal normative document SanQ and M "REK list of pollutants in the air of residential areas of the Republic of Uzbekistan" was used. The monitored population is the largest district in the southern part of Tashkent, with a total area of 5.6 thousand hectares by 2020, and a population of 167.6 thousand people. Chirchiq and Karasu rivers, Salar and Jun canals run through the territory of the district. 50% (2800 hectares) of the district is planted with greenery. There are 174 streets in the district, the main ones are Tashkent Ring Road, Yangi Sergeli, Choshtepa Anna Akhmatova and Kipchak Streets. There are 4 and 12 bus parks in the district, RAF car park and Tashkent International Airport.

There are Sergeli industrial zone, 2097 organizations and enterprises, 12 large industrial enterprises, 300 industrial enterprises, 1748 micro-firms in the district, the largest of which are the air repair plant and Novatr plants.

We made a retrospective analysis of the ecological and hygienic condition of the atmospheric air of the settlements of this district in the dynamics of 2017-2020 and obtained the following results:

The total number of samples taken in 2017 - 1902 (100%), of which - 263 (13.8%), the total number of samples taken in 2018 - 1950 (100%), of which -323 (16.5%), The total number of samples taken in 2019 - 1677 (100%), of which - 198 (11.8%), the total number of samples taken in 2020 - 973 (100%), of which - 130 (13.3%) hygienic did not meet the requirements (Figure 1).

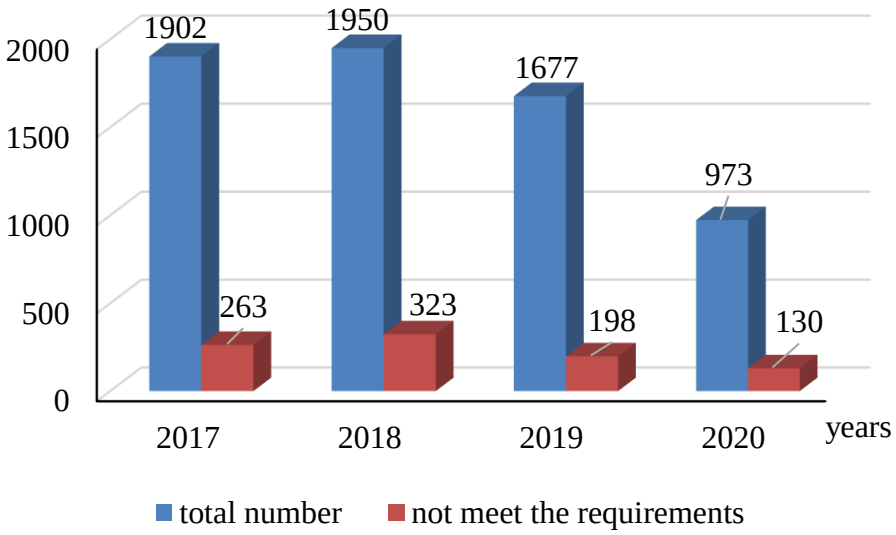

Figure 1. Atmospheric air is the number of samples that do not meet the hygienic requirements in the dynamics of the sample over the years

The analysis of the tested samples in terms of pollutants: in 2017, a total of 416 samples were taken for dust, of which 115 - 27.5%, in 2018 - a total of 404 samples for dust, of which - 141 - 34.9%, In 2019, a total of 370 samples of dust were taken, of which 83 - 22.4%, in 2020 - a total of 290 samples of dust, of which 55 (18.9%) did not meet hygienic standards. Of the 416 samples of sulfur gas in 2017 - 75 (18.0%), in 2018 - 436 samples - 89 (20.4%), in 2019 - 330 samples - 62 of them (18.7%), and in 2020 - out of 196 samples taken - 32 (16.3%) did not meet the hygienic requirements (Figure 2).

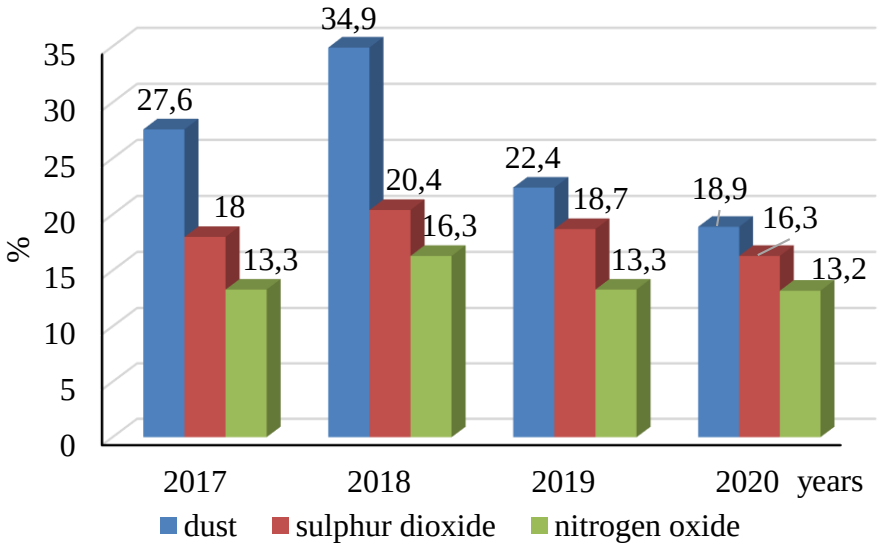

Figure 2. Non-standard samples of air pollutants, %

In samples that did not meet hygienic requirements, sulfur dioxide was found to be in the second place after dusting. In the analysis of air pollution with

formaldehyde, it was found that all samples taken in 2019-2020 met the hygienic requirements.

Conclusion

Based on the above, it is expedient to expand green areas along the roads and further improve the quality of fuels and increase the number of environmentally friendly vehicles, as well as to constantly monitor the level of pollution in the sanitary protection of residential areas from air pollution.

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THE INCIDENCE AND MORPHOLOGICAL FEATURES OF THROMBOCYTOPENIA IN PREGNANCY

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ABSTRACT

The research has focused onthe frequency, causes and consequences of thrombocytopenia acquired at all stages of pregnancy. The purpose of which was identification of the frequency and characteristics of thrombocytopenia at different stages of pregnancy. Clinical material for the study was obtained from 30 pregnant women aged 18-35 years who were treated from January 2021 to March 2022 in the department of pathology of pregnant women of the Tashkent Medical Clinic of the Ministry of Health of the Republic of Uzbekistan.

Key words: pregnancy, thrombocytopathy, adhesion and aggregation, bleeding.

INTRODUCTION

Concerns and study of medico-socialproblems of the health status of women of reproductive age is the is a major challenge of the state and public health. These problems need to be addressed on a national scale, but at the same time, specific tasks to improve their health should be determined and solved within each region, taking into account the real situation on the ground. The increase in morbidity among women of reproductive age, in particular during pregnancy, in recent years is of particular concern, as this leads to an increase in the number of various diseases and severe complications in both the mother and the child to be born [7]. A huge number of studies conducted both in Uzbekistan and abroad are devoted to the study of issues related to the characteristics of hemostasis during pregnancy, which is primarily due to the increased risk of maternal and perinatal death and

disability in the group of patients with certain deviations from the norm in the system regulation of the aggregate state of blood [8].

Important cause of maternalmortality, hemorrhages are at the leading place throughout the world, ranging from 13 to 25%. Despite the fact that the dynamics of maternal mortality in Uzbekistan has a clear downward trend [1,7], the structure of causes is identical to that in developing countries: bleeding, septic complications. The decrease in the level of maternal mortality occurs mainly due to a decrease in the number of deaths after complications of childbirth, while the decrease in the frequency of obstetric bleeding in the structure of maternal mortality is extremely slow [5,2]. In recent years, violations of hemostasis have become of particular relevance, due to the increase in their occurrence and aggravation of the course under the influence of various pathological processes and environmental factors [4,3]. The causes of hemostasis disorders are quite diverse, platelet pathology is not the last among them, which is the cause of bleeding in almost 80% of cases [6]. During pregnancy, a woman's body undergoes physiological changes in the hemostasis system associated with the appearance of the uteroplacental circulation. As the gestation period progresses, changes occur in all parts of the blood coagulation system aimed at preparing a woman for possible complications during pregnancy, childbirth and the early postpartum period [2].

Literature data seen that there has been the clinical manifestations of thrombocytopenia in 70-90% of cases are single, and only in 10-30% of patients they recur under various conditions. In some patients, they can recur under the influence of various factors at regular intervals. During pregnancy, as you know, there are significant changes in the systems of the body, an increase in psycho-emotional stress. This, in turn, causes the emergence, aggravation and aggravation of the course of immune thrombocytopenia in pregnant women [7].

World literature testifies to the combination of thrombocytopenia and pregnancy as a serious and severe condition, often ending in a sad outcome for the fetus and mother, who dies from heavy bleeding during abortion or childbirth. According to the literature of the 1920s, infant mortality was approximately 50%, and maternal mortality was almost 100% (from uterine bleeding) [3].

The increase in the number of various diseases in pregnant women, as a result of which there is a progressive degradation of their health, has contributed to the study of many of them. However, studies on the study of platelet pathology in pregnant women (clinical and laboratory features) and the development of algorithms for managing patients during pregnancy and childbirth have not been developed enough. Therefore, the problem of protecting and improving the health

of pregnant women with platelet pathology is one of the topical areas of medicine of national importance.

Purpose. Explore the detection rate and characteristics of thrombocytopenia in women at different stages of pregnancy.

Scientific novelty of the study.

1. By the method of retrospective analysis in pregnant women with hemorrhagic symptoms, the cause of bleeding associated with platelet pathology will be studied.

2. The morphological picture of platelets and the course of pregnancy in thrombocytopenia and thrombocytopathy will be studied.

MATERIALS AND METHODS.

The clinical material for the study was 60 pregnant women with thrombocytopenia, aged 18 to 35 years old, who were registered at the gynecological consultative clinic of the Tashkent Medical Clinic of the Ministry of Health of the Republic of Uzbekistan in the period from 2020-2021.

RESULTS AND DISCUSSIONS.

Studies were conducted in 60 pregnant women with thrombocytopenia who were under constant observation in the gynecological consultative clinic of the Tashkent Medical Clinic. The mean age of the patients was 26.5±8.5 years. The duration of the disease ranged from 1.5 to 2 years. All 60 patients included in the study at the time of conception were in the stage of clinical and hematological remission. The study of anamnestic factors that preceded and contributed to the onset of the disease during pregnancy revealed that in 31.7% (19) of cases, the onset of the disease was associated with acute colds; 15% (9) of patients indicated that bleeding first appeared on the background of psycho-emotional and physical stress; in 30% (18) - the presence of foci of chronic infection was found, and in 23.3% (14) of the examined, the disease was detected against the background of pregnancy itself (Table 1).

Table 1.

Factors preceding the exacerbation of the disease

	Preceding Factors	Number of group pregnant women with thrombocytopenia, n=60	
		Absolute	%
	Colds	19	31,7
	Psycho-emotional and physical stress	9	15
	Chronic infection foci (tonsillitis, sinusitis)	18	30
	Pregnancy	14	23,3
	TOTAL	n=60	100%

It should be noted that in the first trimester the proportion of exacerbation of thrombocytopenia was 48% of all cases, in the second trimester - 37%, in the third trimester an exacerbation of the disease was observed in 15% of patients (diagram 1). Such differences in the exacerbation of thrombocytopenia during pregnancy may be due to the fact that in the II and III trimesters of pregnancy, the amount of corticosteroid hormones and the duration of their circulation in the maternal body during this period of gestation increase due to a slowdown in the metabolism of corticosteroids and the beginning of the functioning of the fetal adrenal glands (Diagram 1).

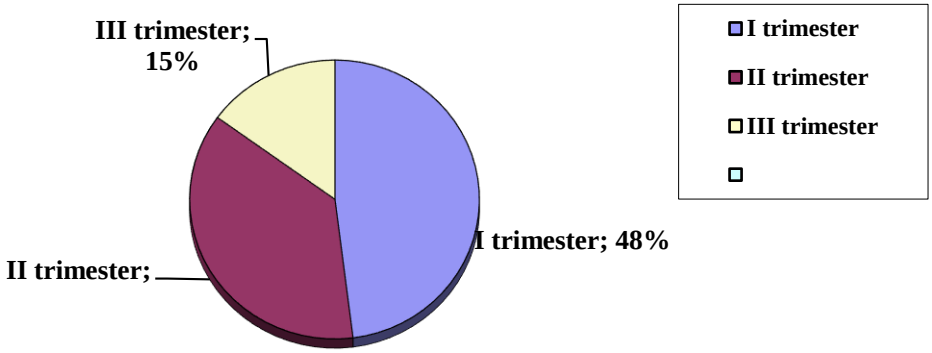

Diagram 1. Thrombocytopenia recurrence during pregnancy.

From the data shown in Diagram 2, it follows that in pregnant women with chronic thrombocytopenia included in the study, the number of patients with moderate and severe severity of the disease prevailed.

The number of platelets in the group of pregnant women with thrombocytopenia was 7.6±3.05x10^9/l (Diagram 2).

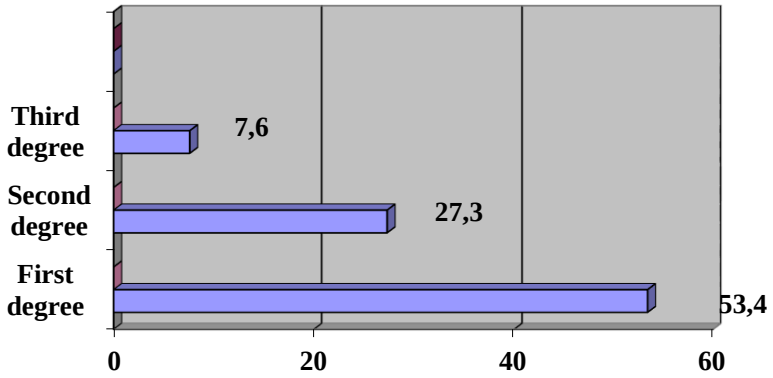

Diagram 2. The number of platelets (X109 / l) according to the severity of thrombocytopenia.

During the analysis of the dynamics of the course of pregnancy in women with immune thrombocytopenia, the following complications were identified, which are presented in Diagram 3.

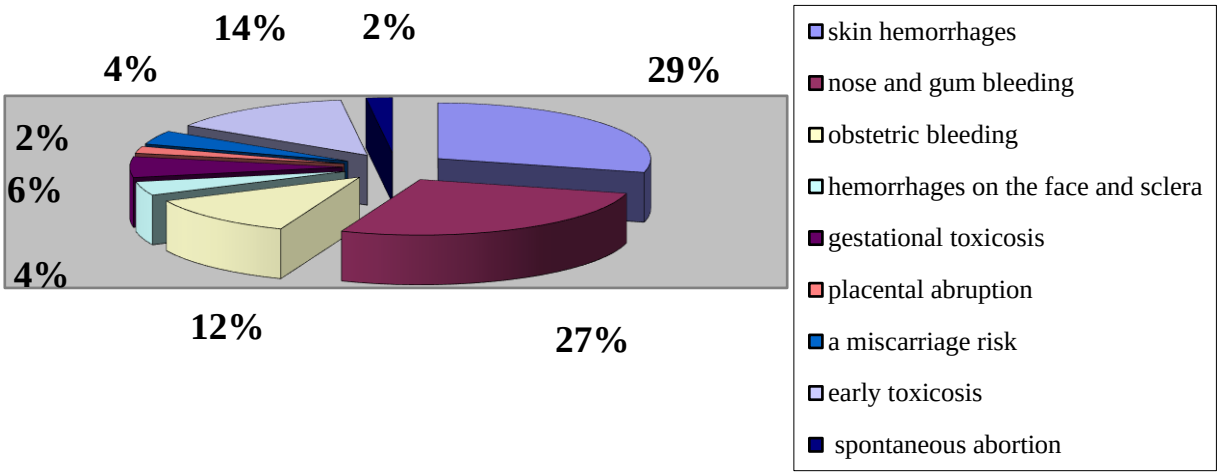

Diagram 4. The frequency of complications in pregnant women with thrombocytopenia.

The complications shown in Diagram 4 were observed in the group of pregnant women with thrombocytopenia with moderate and severe severity. From the above data, it can be seen that complications are characterized by a variety of manifestations, which were detected in the form of skin hemorrhages in 29%, nasal and gingival bleeding in 27%, obstetric bleeding in 12%, hemorrhages on the face and in the sclera in 4%, preeclampsia in 6%, threats of abortion in 4%, placental abruption in 2%, early toxicosis in 14% and miscarriages in 2% of the examined patients in the group of pregnant women with thrombocytopenia.

Thus, based on the above data, we can conclude that a dynamic clinical examination of patients with thrombocytopenia showed that the course of thrombocytopenia during pregnancy, the risk and severity of its exacerbations are determined by the stage of the disease at conception and the severity of its course, and above all, depends on the severity of the disease.

CONCLUSIONS

1. Pregnant women with thrombocytopenia are at risk for the development of hemorrhagic complications of varying severity during pregnancy, childbirth and the postpartum period;

2. Pregnancy that occurred against the background of clinical and hematological remission of thrombocytopenia in 66.3% does not lead to a significant deterioration in the course of the disease throughout pregnancy and after childbirth. Timely delivery through the natural birth canal was observed in 75% of pregnant women with mild to moderate thrombocytopenia, in 3.3% of pregnant women with severe thrombocytopenia in the 1st trimester of pregnancy, spontaneous miscarriage was observed, in 16.6% - abortion due to uterine bleeding;

3. The use of GCS at a dose of 0.5-1.0 mg/kg in 57.9% of cases led to complete clinical and hematological remission, 42.1% of patients needed to continue maintenance from 4 to 6 months at doses of 5-10 mg per day; maintenance therapy was ineffective in 9.1% of patients, who underwent premature operative delivery due to aggravated thrombocytopenia.

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EFFICACY IN ASSESSING THE NUTRITIONAL AND BIOLOGICAL VALUE OF GINGER GELATIN CAPSULES IN PATIENTS WITH COVID-19

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ABSTRACT

The purpose of the study: To study the nutritional, biological value and effectiveness of a new food supplement of ginger in a gelatin shell in patients with COVID-19.

Research methods and materials. A new ginger food product in a hard gelatin shell, developed by SHANAZ LLC; coronovirus patients, case histories.

Results: ginger in a gelatin capsule, developed in collaboration with SHANAZ LLC (Uzbekistan), which contains sufficient nutrients, minerals, vitamins and dietary fibers. The study of effectiveness in patients with COVID-19 showed a decrease in body weight, ensuring the function of the digestive organs, the exclusion of metabolic products, and the normalization of metabolic processes.

Conclusion. Ginger in a gelatin capsule contains proteins (g) 1.8±0.104, fats (g) 0.8±0.076, carbohydrates (g) 15.8±0.55; dietary fiber (g) 2±0.275, total calorie (kcal) - 80±1.445. The composition contains vitamins and mineral elements that play a primary and secondary role in strengthening the immune system.

Key words: ginger in soft and hard gelatin capsules, patients with COVID-19, blood biochemical parameters.

INTRODUCTION

Nutrition is a factor that determines the immune status of the body, and the main cause of immunodeficiency in the world is malnutrition. [3,4,9,10,11].

«Your food should be your medicine and your medicine should be your food» – This point of view of Hippocrates, as in the rest of the world, has established restrictions on the movement and communication of people in our country, associated with an increase in the incidence of severe acute respiratory infection COVID-19 (Coronavirus disease 2019), etiologically associated with the new coronavirus SARS-CoV-2. Experts from the World Health Organization (WHO) have described the situation with the spread of COVID-19 less than three months after the onset of the disease as a pandemic [7,8,9,10,11]. WHO and PHEIC (Public health emergency of international concern) have declared the 2019-2020 coronavirus epidemic. emergency of international concern [17,18,19]. With the onset of the COVID-19 pandemic, the World Health Organization (WHO) has identified nutrition as one of the key factors in protecting public health during quarantine. The WHO European Office for the Prevention and Control of Noncommunicable Diseases has developed a number of the most needed regulations. It is known that nutrition plays a key role not only in various diseases, but also in the prevention of health disorders in quarantine [13].

Objective: to study the nutritional, biological value and efficacy of the ginger gelatin capsule (ginger) fresh dietary supplement in patients with COVID-19.

Research methods and materials. The materials for the study are a new food product from ginger in a hard gelatin capsule, developed by "SHANAZ" LLC, obtained by pressing with the addition of mineral, vitamin and plant extracts enriched with OMEGA-3, OMEGA-6 fatty acids and the medical history of patients with coronavirus infection.

In the process of scientific research, a complex of organoleptic, physicochemical, clinical, biochemical, calculation and statistical methods was used, depending on the following tasks.

Scientific research was carried out in: at the Department of Children, Adolescents and Nutritional Hygiene of the Tashkent Medical Academy (TTA), in the 1st and 2nd infectious dispensaries of the Zangiata district of the Tashkent region, in the testing center of the Institute of Plant Raw Materials named after. Academician S.A. Yunusov. The following properties of a new food product made from ginger (ginger) in a hard gelatin capsule were studied. [9]:

- humidity, acidity, gluten (15113.4-91, 15113.5-91, 202239-91).
- According to the Keldahl method - crude protein (State Standard 0846-91);
- According to the Rushkovsky method - total lipids in the (State Standard 0846-91) Soxhlet apparatus;
- after firing in a muffle furnace - application (A.P.Yermakov, 1972).

The effectiveness of a new food product from ginger (ginger) in a hard gelatin capsule was carried out in the 1st and 2nd infectious dispensaries of the Zangiata district of the Tashkent region. The main group included 31 patients with COVID-19 infection in the main group and 30 patients in the control group. In patients, the body mass index, biochemical parameters of blood were studied.

In cooperation with the team of "SHANAZ" LLC, a new nutrient has been developed - a hard gelatin capsule of ginger (ginger), which is obtained by pressing with the addition of minerals, vitamins, plant extracts, as well as other substances that are mixed and then obtained from them in the form of soft and hard capsules.

The study of nutritional value and organoleptic indicators of soft and hard gelatin capsules "Ginger" revealed that the form of release of gelatin capsules is hard and soft, the predominant color and smell of raw materials and oils have the characteristics of this product. During this period, body weight, BMI, waist and hip area were assessed. In the hospital, in agreement with the doctors, clinical and outpatient blood tests were carried out: hemoglobin (Hb), erythrocytes (RBC), lymphocytes (WBS), glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), protein, total urea, creatinine). The study was conducted at the beginning and end of diet therapy and its effectiveness was evaluated. The data obtained during the study were performed on a personal computer using Microsoft Office Excel-2013 software packages.

Research results and discussion. In cooperation with "SHANAZ" LLC, we have developed a mixture of minerals, vitamins, plant extracts and other substances and other additives made from oil, gelatin capsules - ginger, as well as in the form of soft and hard capsules.

Gelatin capsule - while studying the organoleptic characteristics and nutritional value of ginger food supplement, the distinctive features of this type of food supplement were studied. The study shows that the content of the raw material of the gelatin capsule - the oil has its own specific color and smell.

A nutritional study showed that the ginger gelatin capsule contains 1.8±0.104 (g) protein, 0.8±0.076 (g) fat, 15.8±0.55 (g) carbohydrates; dietary fiber 2±0.275 (g), total energy consumption 80±1.445 (kcal). Contains individual vitamins (B1, C, D, E, K) and minerals (zinc, iron, selenium, magnesium, copper, etc.).

100 g of the product contains the following vitamins: vitamin B1, thiamine (mg) - 0.25±0.001; vitamin S (mg) 5±0.001; vitamin E 0.26±0.025; Vitamin K (µg) 0.1±0.01; vit. PP-0.75±0.01.

In addition, the food supplement retains the following minerals: potassium (mg) - 415±2.717; calcium (mg) -16±0.466; magnesium (mg) - 43±0.768; sodium (mg) - 13±0.505; phosphorus (mg) - 34±0.529; iron (mg) - 0.602±0.036; selenium (mcg) - 0.7±0.037; zinc (mg) - 0.34±0.037.

This product was developed by the Ministry of Health of the Republic of Uzbekistan and the State Standard of the Republic of Uzbekistan "Technological guidelines for drinking soft and hard gelatin capsules", approved under the number TC (technical condition) 202224500-14:2019 [1,2].

The next stage of the biomedical evaluation of a new food product with gelatin capsules was aimed at the most objective assessment of the effectiveness of its clinical trial in patients with coronovirus. At the first stage, patients digested a new food product (allergy, nausea, vomiting, dyspepsia and other indications for 3 days). After the completion of this phase of the study, a second phase of in-depth study of the effect of the new product on metabolic processes in patients with coronavirus was carried out. Patients with coronavirus under our supervision received a standard diet No. 11 in the clinic. Purpose of appointment: to provide good nutrition, moderate stimulation of the secretory function of the digestive tract, normalization of motor function.

Products are allowed in varying degrees: ground and heat-treated - boiled, steamed, refined, fried without a hard glaze (fried with flour or stale breadcrumbs on top). Products from chopped vegetables rich in connective tissue, or fiber. It is forbidden to give the following foods: long and difficult to digest, affecting the gastric mucosa, very cold and hot foods. Chemical composition: proteins 100-120 g (60% animal proteins), fats 90-100 g (25% vegetable), carbohydrates 400-420 g; energy value 11.7-12.6 MJ "(2800-3000 kcal); sodium chloride - up to 15 g, free liquid 2.5 liters. Diet: 5-6 times a day in small portions.

The study group included 31 patients with COVID-19 infection in the main group and 30 patients in the control group at their own discretion. The main age group ranged from 17 to 64 years with an average age of 50.4 ± 1.5 years (31 patients, including 16 men and 15 women), in addition to the main treatment, “ginger” hard gelatin capsules were taken with meals 3 times a day. day. The course of treatment was 60 days, it should be noted that the patients were discharged at home (within 10 days) after discharge from the hospital, on their own initiative, with the introduction of the above products, a new therapeutic diet was prescribed. Patients received ginger in gelatin capsules free of charge. The study was carried out for three months.

Clinical examination of patients in our study revealed the following: weakness, fatigue, headache, dizziness, fever, shortness of breath, fatigue, some diarrhea, severe psychoemotional disorders.

According to the literature, obese patients are more prone to infection [3.8]. Their immune system is trying to fight excess body fat, so they are unable to fight viruses. Research scientists show that the age of patients and comorbidities such as

obesity, cardiovascular, pulmonary, diabetes, are the strongest predictors of their hospitalization. According to the World Obesity Federation (WOF), obesity significantly worsens the course of coronavirus infection (COVID-19). Individuals with a BMI of 30 and above are advised to take extra care, and for obese individuals, prevention of infection is paramount. The WHO Centers for Disease Prevention and Control reports that people with heart disease and diabetes are at higher risk of complications from COVID-19 [11,12,13,15]. Obese patients with disease and requiring intensive care have problems in patient management, since intubation of obese patients is difficult, it is also more difficult to obtain diagnostic imaging of the pathology (due to weight limitations in imaging devices) [4,5,6]. Thus, weight control is an important factor not only for health, but also for preventing the severe course of COVID-19. Numerous sociological studies show that the most effective for this purpose is the use of a diet that reduces calories [2,3]. According to the literature, obese patients are more prone to infection [11]. Their immune system is trying to fight excess body fat, so they are unable to fight viruses. The following diseases were observed in patients aged 18 to 69 years who participated in our study: obesity, cardiovascular diseases, diabetes mellitus, overweight and obesity of I, II and III degrees. I and II degrees of obesity were observed in patients older than 60 years (38.05%). The results of treatment showed that over a three-month period, the body weight of the subjects in the main group significantly decreased by 3-4.3 kg, in the control group by 1-1.3 kg (Table 1).

Table 1

Body mass index in patients with coronavirus

№	Parameters	Control group		Main group	
		Before treatment	After treatment	Before treatment	After treatment
1	Age	53,2±0,98		50,7±0,39	
2	Height (sm)	168,6±1,75		167,3±1,73	
3	Weight (kg)	73,5±1,49	72,2 ±1,13*	72,6±1,46	68,3±1,08**
4	BMI (kg/sq.m^2)	25,8±3,87	25,4±3,9*	25,94±2,73	24,41±0,61*

Note: * - the differences are significant relative to the indicators of the group of physiological norms (* - R<0.05, ** - R<0.01).

Intoxication is not only a disease-specific condition, but also a consequence of taking highly toxic drugs during treatment, prolonged stay of patients in an isolated environment, low mobility, etc. Symptoms of poisoning, such as weakness,

chronic fatigue, loss of taste, hearing, vision, muscle pain, in many cases psycho-emotional disorders, exacerbation of the pathology of the gastrointestinal tract (GIT) for a long time after discharge from the hospital, it is known that in addition to the respiratory system is also a "gateway" for the entry of coronavirus into the body [3,11,13,14].

An analysis of the literature shows that the use of specialized dietary preventive products during the period of detoxification and quarantine and self-isolation in patients with coronavirus is more effective [2,3]. All this requires intensive research, as well as rehabilitation measures not only after illness, but also after clinical recovery and even after the patient is discharged from the hospital. The results of a clinical study of the effectiveness of the use of gelatin capsules - ginger, showed a decrease in body weight in the study of patients with coronavirus for three months; loss of appetite; reducing the load on the digestive organs; exchange and release of other toxic products; normalization of metabolism; normalization of the gastrointestinal tract; improvement of the functional state of the liver and gallbladder, kidneys, skin; it was also noted that vitamins and trace elements are in balance.

After taking a specialized preparation - a gelatin capsule for 2-3 months, patients notice a significant improvement in their condition, a decrease in pain, discomfort, and an increase in the quality of life.

Laboratory studies in patients with coronavirus revealed detoxification properties, improvement in the function of the main organs and systems, the participation of products in the metabolism of xenobiotics and endotoxins, which manifested themselves after taking the “ginger” gelatin capsule. This is confirmed by the hepatoprotective, antioxidant, hypocholesterolemic effects that appear in large-scale clinical studies identified in laboratory studies.

The data in tables 2 and 3 reflect the results of a biochemical blood test before and after taking "ginger" in patients with coronavirus. In the main group, there was a significant increase in hemoglobin up to 13%, in the control group - up to 6.47%. The most pronounced reductions were observed in small groups of patients with reduced concentrations of ECG and CRP, with changes in the original group in the original group (8.03 ± 1.067) and in the control group (10.89 ± 1.6), respectively. Studies in the main group revealed a statistically significant decrease in glucose concentration from the initial concentration to 29.8%, and in the control group to 15.9%.

Table 2

Hematological parameters of erythrocytes in patients observed before and after treatment, M±m

№	Indicators	Norm	Control group		Main group	
			Before treatment	After treatment	Before treatment	After treatment
1	Hb (hemoglobin)	Э; 130,0-160,0 g/l A;120,0-140,0 g/l	109,6±6,96	116,7±8,01**	108,4±8,767	122,6±9,309***
2	(ESR)	Э; 2-10mm/hour A; 2-15mm/hour	15,67±3,57	10,89±1,6	14,7±1,358	8,03±1,067***
3	WBS (leukocyte)	4,0-9,0 10^9 g/l	6,81±0,69	10,73±3,27*	5,8033±0,99	8,56±0,787**
4	Lymph (lymphocyte)	19-37 %	26,68±5,37	28,89±4,87	30,42±7,5	28,9±2,45

Note: * - differences are significant in relation to the indicators of the group of physiological norms (* - R<0.05, ** - R<0.01, *** - R<0.001)

Table 3

Indicators of ALT, AST and total bilirubin in the dynamics of complex therapy in patients with chronic hepatitis

№	Indicators	Norm	Control group		Main group	
			Before treatment	After treatment	Before treatment	After treatment
1	ALT, U/l	<40	39,17±10,32	28,67±6,12***	38,46±8,03	18,98±3,07***
2	AST, U/l	<30	41,52±9,64	23,09±3,52***	29,76±5,01	18,76±1,07***
3	Glucose, mmol/l	3,2-6,1	6,98±0,64	5,87±0,43	6,82±0,49	4,79±0,42
4	Urea, mmol/l	2,5-8,3	4,72±0,53	4,58±0,34**	5,64±0,43	4,89±0,61*
5	Total protein, g/l	46-70	71,03±1,94	70,18±1,24	71,64±1,81	67,2±2,84***
6	Creatinine µmol/l	Э: 44-115 A: 44-97	76,21±5,01	74,75±6,83	69,71±5,12	61,3±5,61

Note: * - differences are significant in terms of the group of physiological norms (* - R<0.05, ** - R<0.01, *** - R<0.001).

Consumption of a gelatin capsule "ginger" product led to a significant decrease in the concentration of urea in the blood (4.89±0.61) by 8.73% and creatinine (61.3±5.61) by 12.06%, which is formed in the body toxins allows us to

talk about the rapid excretion of metabolic products. We also studied the decrease in the concentration of key enzymes in the blood, which characterize the detoxification activity of the liver. The levels of aminotransferases (18.98±3.07) and aspartaminotransferases (18.76±1.07), as well as the content of total protein in the main group (67.2±2.84) and in the control group (70.18±1 ,24) at the level of the norm, i.e. change significantly (Table 3).

There was a normalization of metabolic processes, a significant improvement in lipid and carbohydrate metabolism. The diet formed with the introduction of detoxification products provides a decrease in the amount of primary and secondary peroxidation products (diene conjugates, ketodienes and carbonyls) against the background of an increase in total antioxidant activity, which suggests a decrease in antioxidant activity and resistance to the adverse effects of exogenous and endogenous factors.

The results of a clinical study showed a decrease in body weight when examining patients with coronavirus for three months; loss of appetite; reducing the load on the digestive organs; exchange and release of other toxic products; normalization of metabolism; normalization of the gastrointestinal tract; improvement of the functional state of the liver and gallbladder, kidneys, skin; it was also noted that vitamins and trace elements are in balance.

According to laboratory studies, the detoxification properties of the product were revealed after taking a specialized product of the gelatin capsule "ginger" in patients with coronavirus, the functions of the main organs and systems improved, and the participation of the product in the metabolism of xenobiotics and endotoxins was established. marked. This is confirmed by extensive, well-established hepatoprotective, antioxidant, hypocholesterolemic clinical efficacy studies that have been identified as a result of laboratory studies.

Therefore, it is recommended for the following cases created by “SHANAZ”, designed to detoxify the body:

- during self-isolation and quarantine in order to prevent poisoning and overweight;
- chronic diseases and their exacerbations; with a general deterioration in the state of the body, accompanied by a decrease in immunity, appetite, chronic fatigue and weakness;
- after drug treatment (antibiotic therapy, hormone therapy, and other drugs);
- in the presence of bad habits (smoking, drinking alcohol).

CONCLUSION

Gelatin capsule - protein (g) in ginger (ginger) 1.8±0.104, fat (g) 0.8±0.076, carbohydrates (g) 15.8±0.55; dietary fiber (g) 2 ± 0.275, total calories (kcal) 80 ± 1.445. Vitamins contain B1, C, D, E, K and mineral elements (zinc, iron, selenium,

magnesium, copper, etc.), which play the main and additional role in strengthening the immune system.

Decrease in body weight up to 3-4.3 kg according to the results of clinical examination; loss of appetite; reducing the load on the digestive organs; exchange and release of other toxic products; normalization of metabolism; normalization of the gastrointestinal tract; improved metabolism; improvement of the functional state of the liver and gallbladder; improvement of the functional state of the kidneys; improvement of the functional state of the skin; as well as maintaining the balance of vitamins and trace elements.

Improvement in hematological parameters, a decrease in the blood plasma of liver enzymes (AST, ALT and GGT), as well as total bilirubin, with a decrease in the concentration of liver enzymes (AST, ALT) in the blood plasma, which characterizes the detoxification activity of the liver, as it turned out, falls.

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SIMULTANEOUS SURGERIES IN CHRONIC IMMUNE THROMBOCYTOPENIA

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ABSTRACT

Background and objectives: Basic information about the essence of simultaneous surgeries and the possibilities of their performance in diseases of different organs and spleen in modern surgical practice is presented.

Design and methods: We retrospectively analyzed the data on 127 patients (56 males, 71 females) with chronic immune thrombocytopenia between 2015 and 2019 in the Research Institute of Hematology of Republic of Uzbekistan.

Results: The analysis of the results of the use of simultaneous surgeries in 17 (13.3%) of 127 patients with chronic immune thrombocytopenia was carried out. Taking into account the specifics of hematological pathology, the indications were determined for the most optimal options for such surgeries.

Interpretation and conclusions: Simultaneous surgeries are a promising method for the treatment of several surgical diseases in hematological practice.

Key words: blood diseases, splenectomy, simultaneous surgeries.

INTRODUCTION

Simultaneous surgical interventions in surgical practice have been known for a very long time. For the first time, A. Claudius reported such a surgery in 1735: the patient underwent appendectomy in combination with hernioplasty [19,18,20]. Currently, simultaneous surgeries are understood as a surgical intervention simultaneously performed on two or more organs for etiological unrelated diseases [9,16,18,20,22]. Interest in simultaneous surgeries is natural and due to the fact that combined surgical pathology, according to the WHO 20], occurs in 20-30% of surgical patients [20]. For instance, combined pathology occurs in every third patient in a surgical profile, however, paradoxically, the percentage of simultaneous surgeries is no more than 6% of all possible interventions.

According to the WHO data, in 30% of patients with abdominal pathology in a surgical profile, there are not two, but more combined diseases that require surgical treatment [18.20].

In the last two decades of the twentieth century, the number of publications on the possibility of performing simultaneous surgical interventions increased considerably to 500-700 publications per year (according to the results of the MEDLINE, EMBASE).

The advantages of simultaneous surgeries present not only in the fact that they cure the patient from several diseases at once, but also in the fact that they save the patient from the increasing risk associated with repeated surgical interventions, repeated anesthesia and, accordingly, with complications of the surgical and anesthetic profile [2,4,6]. It is important to remember that by agreeing to the simultaneous treatment of numerous surgical disorders, the patient eliminates the suffering decision for his mental condition for repeated surgical operations in the future..

According to several publications', simultaneously treatment of patients with combined surgical pathology rather than systematic, can decrease the consumption of medicines, the duration of the patient's hospitalisation and their general temporary disability. In addition, it can reduce the cost of treatment [6,9,17,19,23]. Due to the increase in the life expectancy of people and the improvement of diagnostic technologies, there has been a tendency in an increase in the number of patients with two or three combined surgical diseases, including in hematological patients. According to the World Health Organization (WHO) data, the frequency of combined surgical and hematological diseases in many patients is 15-20%, that poses a challenge for surgeons and hematologists about the possibility of simultaneous correction of such a pathology [3,17]. An increase in the

effectiveness of treatment of hematological patients requiring surgical intervention in the presence of combined surgical pathology is achieved by performing simultaneous surgeries.

However, in the scientific literature, evidence-based studies regarding to this problem are rare, although in practice many surgeons and hematologists note the need to perform such surgeries [3,23,26].

To decide the sequence of procedures, it is first required to determine the underlying condition, and the intervention should also be directed by asepsis, the importance of the stage of the operation, and the desire to reduce intervention time, albeit each case should be resolved individually.

Some patients with hematological diseases, including those with immune thrombocytopenia (IT), are currently undergoing splenectomy (SE).

Immune thrombocytopenia (IT) is one of the most common forms of hemorrhagic diathesis. According to V.G. Vogralik (1961), the proportion of this pathology is 43.1% of all forms of hemorrhagic diathesis. The pathogenesis of IT is based on the autoimmune process (Kafo A., 2003), when, for various reasons, the human body synthesizes antiplatelet autoantibodies, which also have an anti-megakaryocyte orientation (Donush E.K. etc, 1997; B Abdulkadirov K.M. 2004; Vorobev A.I. 2005; Kafo A. 2003; McMillan R. 2007).

It is vital to resolve the problem of planned splenectomy in patients with chronic PI (CIT) or frequent exacerbations with bleeding from the mucosal membranes. At the same time, clinical and laboratory remission is achieved in 70-90% of patients. The bulk of antiplatelet antibodies are synthesized in the spleen, after removal of which the antibody titer is significantly reduced and not detected. Splenectomy is a major surgery and the risk of post-splenectomy sepsis outweighs the risk of serious bleeding. Therefore, splenectomy should be performed no earlier than 12 months after diagnosis. The accepted age for splenectomy is five years and older, which is associated with the maturation of the immune system by this age. Indications for planned splenectomy are: frequent exacerbations with bleeding from the mucous membranes with a platelet count of less than 30,000. Moreover, in 12% -15% of cases, splenectomy is combined with other surgical interventions (Romashov F.N, 1989).

Before performing simultaneous procedures on patients with anemia and defective hemostasis, a thorough assessment and particular preparation is required, which influences the surgery's result.

Advances in anesthesia, hematology, and transfusion medicine, as well as improvements in surgical methods, reasonable preoperative planning, and

postoperative patient management, have made simultaneous surgeries in hematological patients more feasible.

The study focuses on the technical aspects of the splenectomy (SE), including a discussion of the numerous parameters that influence the trauma and success of the procedure. The goal of the study was to identify indications and contraindications for the use of simultaneous surgeries (SS), determine the most optimal choices for combining different surgeries, introduce them into clinical practice, and analyse the results of their usage in hematological pathology patients.

Materials and methods

The study analyzed 127 patients data with IT and other surgical pathologies who were assessed and treated in the surgical departments of the Republic of Uzbekistan's Research Center of Hematology between 2015 and 2019.

Among the 127 patients there were 56 (44%) were men, 71 (56%) were women. The duration of the disease ranges from 1 to 20 years. Patients received on average two or more different glucocorticoid drugs. All patients underwent inpatient and outpatient treatment from two to five r more times with temporary improvement.

The following tests were performed on the patients: general blood and urine analysis, biochemistry, coagulation tests with coagulation time and length of blood bleeding, serum iron, hepatitis markers, circulating immune complexes, and myelogram were all determined. Depending on the nature of the concomitant pathology, ultrasound of the abdominal organs, fibro gastroduodenoscopy, X-ray examination of the chest, contrast fluoroscopy of the gastrointestinal tract, ECG, magnetic resonance and X-ray computer tomography, spirography were additionally used.

All patients were admitted from single to 10 x 10^9 g / l platelets and with hemorrhagic syndrome. In most cases, ecchymosis and petechiae were accompanied by bleeding of the mucous membranes. Of these, 33 (26%) were admitted with epistaxis, 19 (15%) - with gingival bleeding, 17 (25%) women had hyperpolymenorrhea together with other types of hemorrhagic syndrome, 1 (1.4%) patient had hematuria and other stabbing manifestations. 54 (43%) have post-hemorrhagic anemia of varying degrees.

Of these, 19 (15%) patients were diagnosed with various surgical pathologies, including an umbilical hernia in 6 patients: of them 5 women, 1 man, 5 men have an inguinal hernia, 3 women have chronic calculous cholecystitis, 3 patient have chronic hemorrhoids - 2 of them are women, 2 are men, lipomas of various sizes in 2 men.

As a pathogenetic therapy, glucocorticoids (GCS) were prescribed 1-1.5 mg / kg for chronic IT, in the form of tablets. 10 patients with gastritis prescribed hormones in the form of inhalation. Inhalation was carried out on a «Boreal» nebulizer inhaler (made in Italy) at a dose of 1-2.0 mg / kg. In addition, the patients received inhibitors of fibrinolysis, vascular wall protectors, stabilizers of biological membranes, and local treatment for nasal and gingival bleeding. Patients with severe anemia received erythrocyte mass transfusion.

If conservative therapy was ineffective, splenectomy was recommended. To perform splenectomy, 2-3 days before the operation, the dose of hormones was increased 2-3 times to prevent adrenal insufficiency. Indications for splenectomy were: cases of IT refractory to hormone therapy, with frequent relapses.

According to indications, 127 patients with CIT underwent splenectomy with the upper median incision. Simultaneously, 17 patients with various concomitant surgical pathologies underwent simultaneous surgeries in the form of hernia excision (9), cholecystectomy (3), hemorrhoidectomy (3), lipoma removal (2). Two patients with umbilical and inguinal hernia after conservative treatment, the number of platelets, remained isolated, due to severe bleeding during the surgery, only splenectomy was performed.

Results and discussion

In 5 patients aged 18 to 51 years with CIT and umbilical hernia, after preparation for surgery, the number of platelets increased from 17000 to 28000. No signs of bleeding were taken for surgery. Splenectomy was performed using the traditional approach, accepted in the clinic, with minimal blood loss of about 50-70 ml and with careful hemostasis, subsequently, hernia repair was performed using the method according to Sapezhko and Mayo with minimal blood loss, about 15-20 ml. In the post-operative period, two patients developed a subcutaneous hematoma, which was drained on day 2. On the 2nd day after surgery, in these patients, the platelet count increased from 70,000 to 164,000.

Out of 4 patients aged 43 to 50 years with CIT and inguinal hernia, two of them had cutaneous ecchymosis and minor petechiae on the extremities, in these patients, after preparation for surgery, the number of platelets rose from 22,000 to 32,000. No signs of bleeding were taken for surgery and a splenectomy was performed with a blood loss of about 80 to 120 ml. Further, with careful hemostasis, a hernia repair was performed using the Girard-Spasokukotsky method with Kimbarovsky sutures, with a minimum blood loss of about 25-30 ml. In the postoperative period, one patient developed a subcutaneous hematoma, which was drained on day 2. On the 2nd day after the operation, the platelet count rose from 54,000 to 98,000.

In 3 patients aged 27 to 35 years with CIT with frequent exacerbations without signs of bleeding and chronic calculous cholecystitis, after preparation for surgery, the number of platelets rose from 35,000 to 42,000. splenectomy removed the gallbladder from the bottom with blood loss up to 50 ml. 60 ml of hemorrhagic fluid was discharged from the drainage tube in the subhepatic region in 2 days. On day 3, the drainage tube is clean and removed. On the 2nd day after the operation, the platelet count increased from 67,000 to 73,000 and on the 3rd-4th day from 124,000 to 180,000.

In 3 patients aged 23 to 32 years with CIT and external hemorrhoids (a history of frequent bleeding), two of them had skin ecchymosis. After preparation for the operation, the number of platelets rose from 24,000 to 33,000. No signs of bleeding were taken for surgery and splenectomy was performed with minimal blood loss of about 40-50 ml and hemorrhoidectomy by the Millegan-Morgapi method. On day 1 after the operation, the number of platelets rose from 54,000 to 86,000 and on days 2-4 from 154,000 to 210,000.

Simultaneous surgeries (SS) were performed in two stages. The surgery on the spleen was performed in the first stage, and in the second, intervention on another organ. All patients were discharged in a satisfactory state of healing per prima.

Discussion of results

All surgeries were carried out in a scheduled manner, with the operational risk factored in.. In these patients, the postoperative period had some peculiarities (the need for prescribing narcotic painkillers persisted for 2-3 days, the duration of bed rest was 5-8 days, given that patients with IT receive hormonal drugs for a long time). In three cases, a postoperative wound hematoma was discovered.

When performing SS it is advisable to perform the surgery on the spleen as the first stage. The second stage of surgical treatment is preferably performed for concomitant surgical pathology. Early physical activity helps to avoid postoperative pneumonia and thromboembolic complications.

Conducting surgeries on patients with severe post-hemorrhagic syndrome is not recommended since it raises the risk of surgical interventions and affects the course of the postoperative period. During and after surgery, problems increase.

The fact that SS in spleen pathology are formed using two separate surgical methods can make the postoperative period more difficult due to the intensity of the pain syndrome. Simultaneously, by carefully selecting patients and selecting an appropriate anesthetic option, potential negative effects were minimized in the majority of cases. No lethal outcomes were observed.

Conclusions

Considering the foregoing, it is reasonable to infer that SS in the spleen and other organs is a potential way of simultaneous surgical treatment of several diseases in the provision of specialized surgical planned care.e. One of the important principles of performing SS in the spleen is the simultaneous use of two surgeries using acceptable methods of surgical treatment. Simultaneous surgeries are justified in circumstances where refusing to undertake many surgical procedures at once can result in substantial consequences that worsen the underlying disease's progress. SS should be performed on the spleen in specialized departments and clinics that have the ability to adequately examine and with sufficient experience of surgeons operating in this field.

Advantages of simultaneous surgeries in hematological practice:

- Reducing the number of hours under general anesthesia;
- Possibility of simultaneous treatment of surgical pathology;
- Saving time;
- Simultaneous surgeries allow the patient to reduce the total time hospitalisation;
- Cost savings;
- Psychological comfort;
- For the patient, a simultaneous surgery is perceived as one surgical intervention, which significantly reduces the stress and anxiety levels before and after the surgery.

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RETROSPECTIVE ASSESSMENT OF JOINT SYNDROME AND JOINT STRUCTURE DISORDERS IN OSTEOARTHRITIS

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ABSTRACT

The purpose of the study: Retrospective assessment of clinical signs and course of the disease in patients with osteoarthritis in the ratio of gender.

This research study conducted a retrospective analysis of 300 patients hospitalized at the City Clinical Hospital No.3 from 2015 to 2019 on the basis of medical records and emphasized the analysis of the clinical course and consequences of the disease. On the basis of the obtained documents, the joint syndrome and disorders of the joint structure observed in patients with osteoarthritis (OA) were assessed by radiological images. It was noted that in patients with OA, joint syndrome was different and gender differences were identified.

Key words: osteoarthritis, joint, radiological images, X-ray.

INTRODUCTION

Today, many researchers describe the pathogenesis of osteoarthritis (OA) as a disease with a predominance of degenerative-destructive processes in the connective tissue of the joint, as well as other structures (subchondral bone, synovial membrane, muscle lengths) and polyetiologically. In modern rheumatology, there is a sufficient understanding of the prevention of possible consequences and complications in OA through the use of early and rational non-pharmacological and pharmacological measures [1,4]. In addition, the treatments achieved allow the patient to reduce chronic pain syndrome, synovitis, joint

deformities and defigurations, reduce the need for endoprosthesis practice, psychiatric and sleep disorders, coordinate depression, and improve patient quality of life. However, at the same time, the increasing incidence and prevalence of OA in the population, its predisposition to chronic disease, the persistence of problems such as irreversible joint disorders and the formation of ankylosis, determine not only the medical but also the socio-economic significance of the disease. One of the non-modifiable risk factors for the development of osteoarthritis is the gender of the patient [2,5]. On this account, the opinions of scientists are ambiguous. Some researchers argue that women not only suffer from OA more often, but may also have more severe forms of it. Being female increases the risk of knee and hand OA [3]. At the same time, men are more likely to suffer from OA of the hip joints. Other authors argue that OA of the hip joint progresses more intensively in women in the absence of a gender effect on the course and risk of developing OA of the knee and joints of the hands [6]. According to the General Practice Research Database, in 2005 in the UK, the risk of total hip and knee replacement at the age of 50 for women was higher than for men: 11.6 and 10.8%, respectively; 7.1 and 8.1%. Russian reviews present data showing the absence of significant gender differences in the development of OA of the hip joint [7].

MATERIALS AND RESEARCH METHODS

In our research, we conducted a retrospective analysis of 300 patients with OA based on medical records, and studied the clinical course of the disease by gender. In addition, we analyzed X-ray of 156 patients with OA, with a total mean age of 53.1 ± 11.2 years and an average duration of disease of 4.5 ± 1.9 years.

RESULTS AND DISCUSSION

In this case, monoosteoarthritis, as shown in Table 1, occurred in the same condition in both sexes. However, oligoostearthritis differed almost 1.5 times from men with a predominance in women ($p < 0.05$). In contrast, polyosteoarthritis was 2.5 times more prevalent in men than in women ($p < 0.05$). Alternatively, reactive synovitis in women came with a significant difference ($p < 0.05$).

In turn, differences were also identified when attention was paid to the localization of joint damage in patients with OA. As shown in Figure 1, knee joint damage (gonarthrosis) was almost 2 times more common in women ($p < 0.05$), while pelvic joint damage (coxarthrosis) was more prevalent in men ($p<0.05$). Alternatively, the functional activity of the joints changed based on the joint injury.

Table 1

Articular syndrome in patients with OA

Clinic signs	women (n=211)		men(n=89)		P
	Absolute	%	absolute	%	
Monoosteoarthritis	55	26,1	21	23,6	>0,05
Oligoosteoarthritis	123	58,3	29	32,6	<0,05
Polyosteoarthritis	33	15,6	39	43,8	<0,05
Sinovit	56	26,5	11	12,4	<0,05

Note: *p* – is the degree of reliability of the statistical results, calculated by the ratio of the sexes.

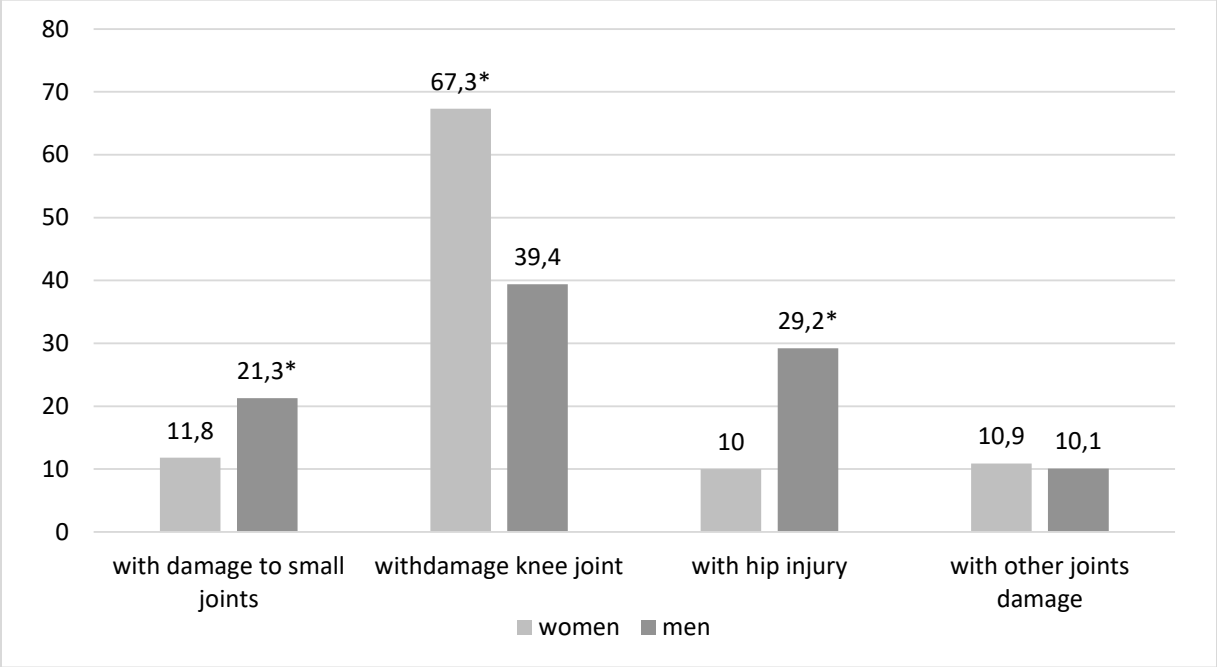

Figure 1. Distribution of joint damage by localization (%) in patients diagnosed with OA; * - the degree of reliability of statistical results, calculated in the ratio of gender.

At the same time, changes in joint function of different functional classes (FC) were observed, as shown in Figure 2, mainly I FC was the most common in both sex groups and no statistically significant difference (p> 0.05) was detected between them on the surface of FC II.However, III FC was 2 times more common (p <0.05) in women than in men.

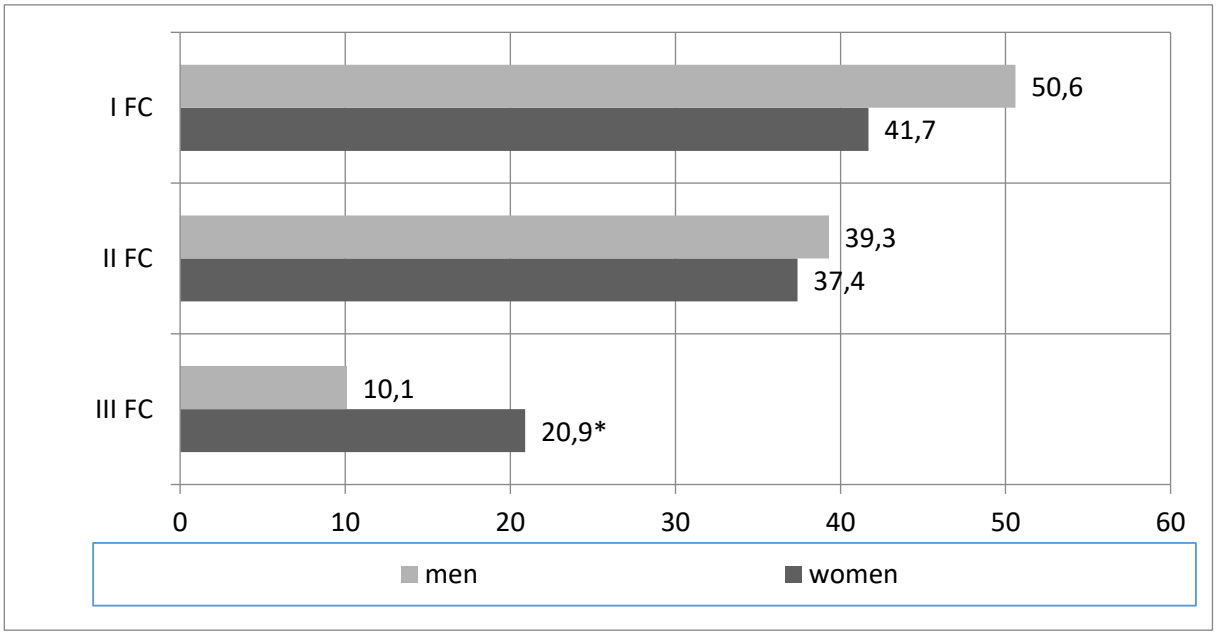

Figure 2. Possibilities of joint activity in patients diagnosed with OA. FC – functional class (%). * - level of reliability of statistical results, calculated in the ratio of gender.

It should be noted that inflammatory markers, as shown in Figure 3, increased the Sedimentation rate of erythrocytes (SRE) and S-reactive protein in 1/2 of women and approximately their titer in 1/3 of men.

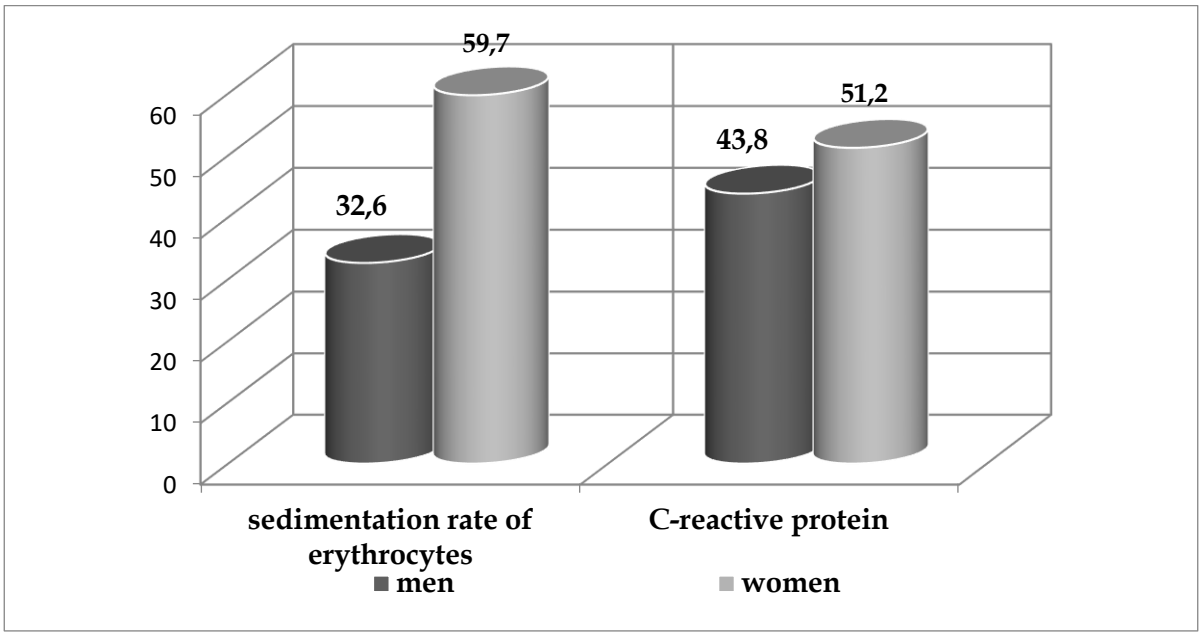

Figure 3. Percentage of patients with increased titers of inflammatory markers in patients diagnosed with OA (%). * - the degree of reliability of statistical results, calculated in the ratio of gender.

It is known that joint diseases, including disorders of the joint structure in OA, are reflected in radiological changes of typical appearance. In addition, the exacerbation of joint syndrome may be associated with dynamic changes in it. In a retrospective analysis, radiographs of 156 patients with OA were studied, with a

total mean age of 53.1 ± 11.2 years and an average duration of disease of 4.5 ± 1.9 years. According to the results of the X-ray image analysis, as shown in Figure 4, radiological stage I of OA occurred in 42.6% of men and was reliably differentiated from women (p <0.05). In turn, stage IV was predominant in women (p <0.05) and was detected in 47.1% of patients.

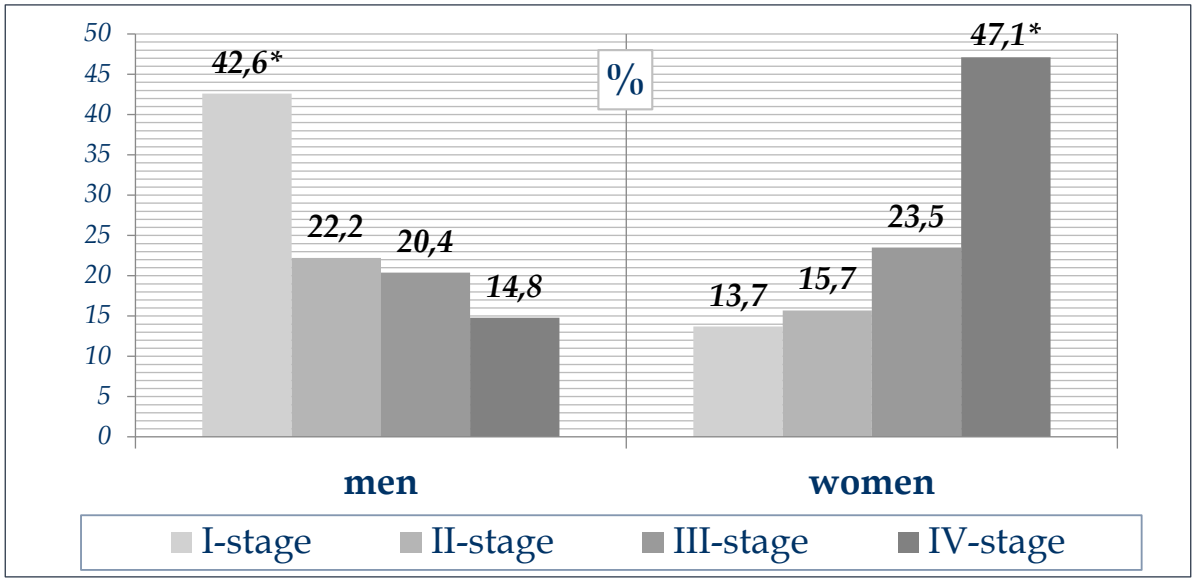

Figure 4. Distribution by radiological stages in patients diagnosed with OA. * - the degree of reliability of statistical results, calculated in the ratio of gender.

It should be noted that the change in the structure of the joints observed in women with OA is more pronounced.

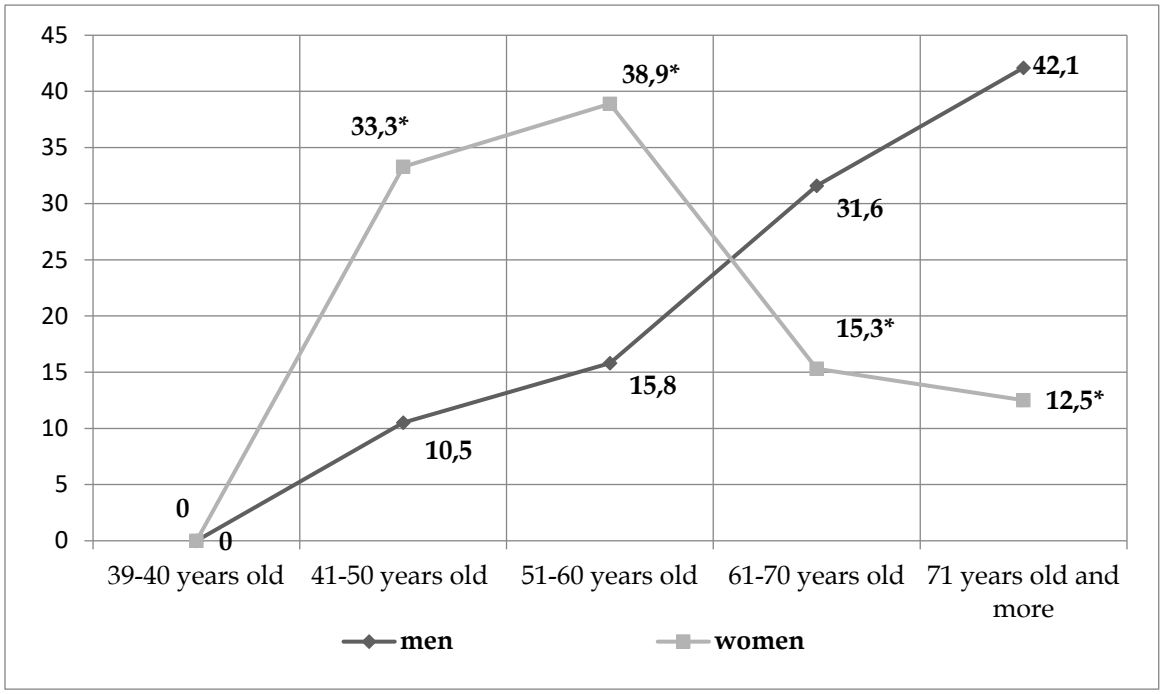

Figure 5. Distribution of radiological stages III-IV in patients diagnosed with OA according to the age of the patient. * - the degree of reliability of statistical results, calculated in the ratio of gender.

It should be noted that in 70.6% of women with OA, stages III-IV of radiological changes were recorded early. At the same time, as shown in Figure 5, 33.3% of cases were in women aged 41-50 years, and 38.9% were in stages III and IV of OA aged 41-50 years. In men, in turn, stage III-IV patients increased inversely with increasing age. It should be noted that due to the lack of timely treatment, the late stages of OA in women are formed early. Hence, the indication for joint arthroplasty in women differs with their early age.

In turn, X-ray imaging of the knee joint (Fig. 6) showed that epiphyseal osteoporosis was formed in 96.8% of cases and cystic symptoms in 21.4% of cases. Narrowing of the joint was detected in 64.7% of patients, and osteosclerosis was found in 56.4% of cases. Osteophytosis was observed in 1/3 of patients. In addition, periostitis occurred in 21.1% of patients.

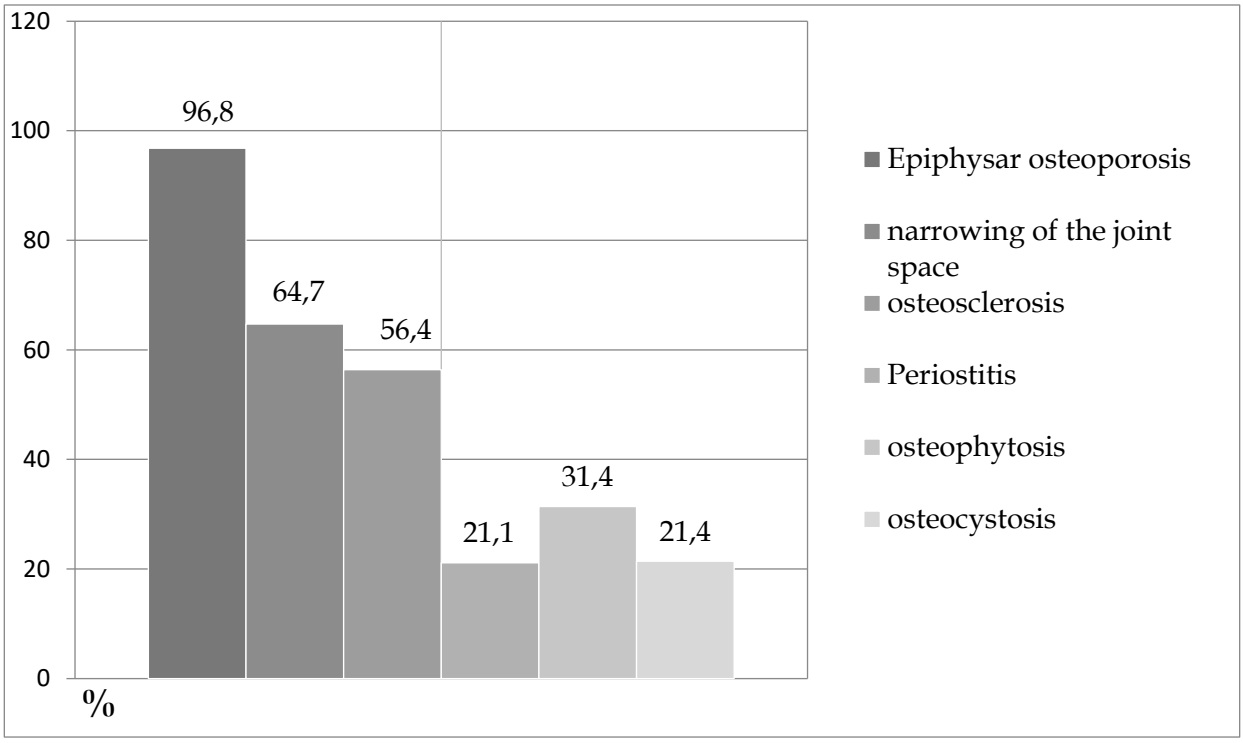

Figure 6. X-ray signs of the knee joint in patients with OA

CONCLUSION

According to the study, arthritis syndrome in patients with OA varies depending on the localization of the process and the number of affected joints, and changes in joint structure and functional limitations are more pronounced in women than in men, with radiological stages III-IV occurring early in 70.6%.

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POLYMORPHISM OF THE CYP2C19 ISOENZYME AS A RISK FACTOR FOR GASTROPATHIES INDUCED BY THE USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH PAIN SYNDROME

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ABSTRACT

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most widely used medicines: more than 30 million people take them every day in the world. The popularity and widespread use of NSAIDs is explained by their significant analgesic and anti-inflammatory effect in pain syndromes of different genesis. **The aim** of the study was to evaluate the role of genetic polymorphism of the CYP2C19 isoenzyme in predisposition to NSAID-gastropathies. **Research materials and methods:** the study is based on the examination data of 69 patients with pain syndrome (27 men, 42 women aged 56.4±9.1 years) who underwent inpatient treatment at the 3rd TMA clinic. 11 patients (15.9%) with gastropathies were identified among the examined. All patients necessarily underwent upper endoscopy and determination of Hp status by performing a ^{13}C-urea breath test. **Results of the study:** as a result of the study, we found that the frequency of carrying allele A in patients taking NSAIDs was 97.1%, in the control group – 98.9%. Whereas the frequency of the G allele was 2.6 times more common among patients with pain syndrome and corresponded to the expected Hardy-Weinberg equilibrium, $\chi 2=7.0$, $p=0.008$. Carriers of the G allele were found in 30.4% of patients taking NSAIDs, whereas in the control this allele was found in 1.1% of volunteers. **Conclusion:** The presence of the CYP 2C19 G allele is significantly associated with endoscopically confirmed NSAID-induced gastropathy and can be considered as a risk factor for their development, which is presumably explained by the participation of the CYP 2C19 isoenzyme in the metabolism of arachidonic acid, which plays a role in gastrocytoprotection; Patients with CYP2C19 polymorphism have accelerated metabolism of PPIs, which significantly reduces their clinical effectiveness.

Key words: NSAID, PPIs, Cytochrome P450, gastropathy, gastroduodenal damage.

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most widely used medicines: more than 30 million people take them every day in the world. The popularity and widespread use of NSAIDs is explained by their significant analgesic and anti-inflammatory effect in pain syndromes of different genesis. Unfortunately, the use of NSAIDs is significantly limited due to their undesirable complications, primarily gastrointestinal [6].

NSAID-gastropathy is an erosive and ulcerative lesion of the gastroduodenal zone of the gastrointestinal tract (gastrointestinal tract) that occurs when using NSAIDs and acetylsalicylic acid and has a characteristic clinical and endoscopic picture. Its diagnostic criteria are chronological connection with the use of NSAIDs, asymptomatic / erased clinical picture, high risk of bleeding manifestation, acute often multiple injuries, predominant localization in the antrum of the stomach, absence of an inflammatory shaft around ulcers, foveolar hyperplasia of the mucous membrane and sufficiently rapid healing with the abolition of NSAIDs. Gastroduodenal toxicity of NSAIDs is explained by the blockade of the production of cytoprotective prostanoids mediated by cyclooxygenase (COX)-1, such as prostaglandin E2 and prostacyclin. Highly selective COX-2 inhibitors cause less pronounced gastroduodenal damage than non-selective NSAIDs that inhibit COX-1 and -2, but they do not completely solve the problem of gastrotoxicity [6]. The extreme urgency of the problem is caused by a large number of hospitalizations and deaths associated with the use of NSAIDs, as well as high economic costs for the treatment of NSAID-gastropathy, steadily increasing every year. Ulceration and bleeding induced by the use of NSAIDs are still one of the main clinical problems of internal medicine.

According to various studies, approximately 25-40% of chronic NSAID users have erosions and peptic ulcers (PI) of the gastroduodenal zone, and 2-4% have bleeding or perforation. In many patients, especially the elderly, the use of NSAIDs can do more harm than good. The relative risk (RR) of bleeding, perforation and death due to NSAID-induced ulcers is 3; 6 and 7.6, respectively [6]. Pathologies associated with the use of NSAIDs are the causes of the development of diseases and deaths in many countries of the world. For example, in the USA, the side effects of NSAIDs are the 15th most common cause of death, and on average, gastrointestinal complications are noted in 30% of patients using NSAIDs even in the absence of ulcers on the mucous membrane. In the UK, NSAIDs have become the main class of drugs that cause side effects, which are

noted in 30% of over 18 thousand. hospitalized patients, and NSAID-induced ulcers and bleeding account for 61% of deaths associated with adverse drug reactions (NLR) [6]. Recently, scientific papers have appeared on the frequency and severity of NLR from the use of NSAIDs and their effectiveness depending on the polymorphism of various isoenzymes of the cytochrome P450 hepatic system (CYP 2C8, CYP 2C9, CYP 2C19), responsible for the metabolism of many drugs [2, 3, 4, 6, 11]. The CYP 2C cytochrome system isoenzyme subfamily includes 20% of the CYP 450 content in the liver and metabolizes 25-30% of commonly used drugs, in particular such clinically important ones as NSAIDs, proton pump inhibitors (PPIs), antidepressants, benzodiazepines and clopidogrel [7, 8]. CYP 2C isoenzymes also metabolize endogenous substances such as arachidonic acid and estrogens [9]. Three members of the CYP 2C subfamily (CYP 2C8, CYP 2C9, CYP 2C19) are highly polymorphic isoenzymes and have numerous single nucleotide polymorphisms (SNPs) with different frequency in different ethnic populations [13, 15]. Today, 14 CYP2C8-, 35 CYP 2C9- and 28 CYP2C19-coding ONPS are known, some of them are clinically significant because they can significantly alter the metabolism of various drugs.

Data from previous studies indicate that people with ONP in the genes encoding enzymes that metabolize NSAIDs have a higher risk of developing peptic ulcer and/or upper gastrointestinal bleeding, although the results obtained are quite controversial [2, 3, 12]. The results of a systematic review of the problem showed that it is currently very difficult to assess whether there is an interaction between the effects of NSAIDs and the presence of coding variants in the main NSAID-metabolizing systems of cytochrome P450, such as CYP 2C9, CYP 2C8 and CYP 2C19, and whether these variants increase the risk of NSAID gastropathy independently of each other [2, 3, 4].

In recent years, data have been obtained that ONP is possible not only with loss of function, but also with its enhancement, in particular in the CYP 2C19 isoenzyme. Relatively recently, it has been established that ONP in the CYP 2C19 family (CYP 2C19*17) can predispose to peptic ulcer by means of effects independent of the use of NSAIDs, in particular as a result of changes in the metabolism of arachidonic acid [12]. In addition, ONP in the CYP2C19 family may predispose to the development of peptic ulcer indirectly by altering the metabolism of NSAIDs [5, 8, 10].

Cytochrome P450 (P-450) enzymes are the main participants in the metabolism of xenobiotics. The genetic variability of the genes encoding these enzymes plays an important role in the manifestation of individual sensitivity to drugs [14]. CYP2C19 participates in the metabolism of a number of drugs, in

particular proton pump inhibitors (omeprazole, pantorazole, lansoprazole, rabeprazole and esomeprazole) [1].

Drug interactions are the leading cause of a decrease or complete absence of the effect of therapy and adverse drug reactions.

The aim of the study was to evaluate the role of genetic polymorphism of the CYP2C19 isoenzyme in predisposition to NSAID-gastropathies.

Research materials and methods: the study is based on the examination data of 69 patients with pain syndrome (27 men, 42 women aged 56.4±9.1 years) who underwent inpatient treatment at the 3rd TMA clinic. 11 patients (15.9%) with gastropathies were identified among the examined. All patients necessarily underwent upper endoscopy and determination of *Hp* status by performing a ^{13}C-urea breath test.

All patients were divided into two groups:

11 patients with gastropathies who developed during 2 weeks of NSAID use (main group);

58 patients without gastropathy who used NSAIDs before endoscopy (comparison group).

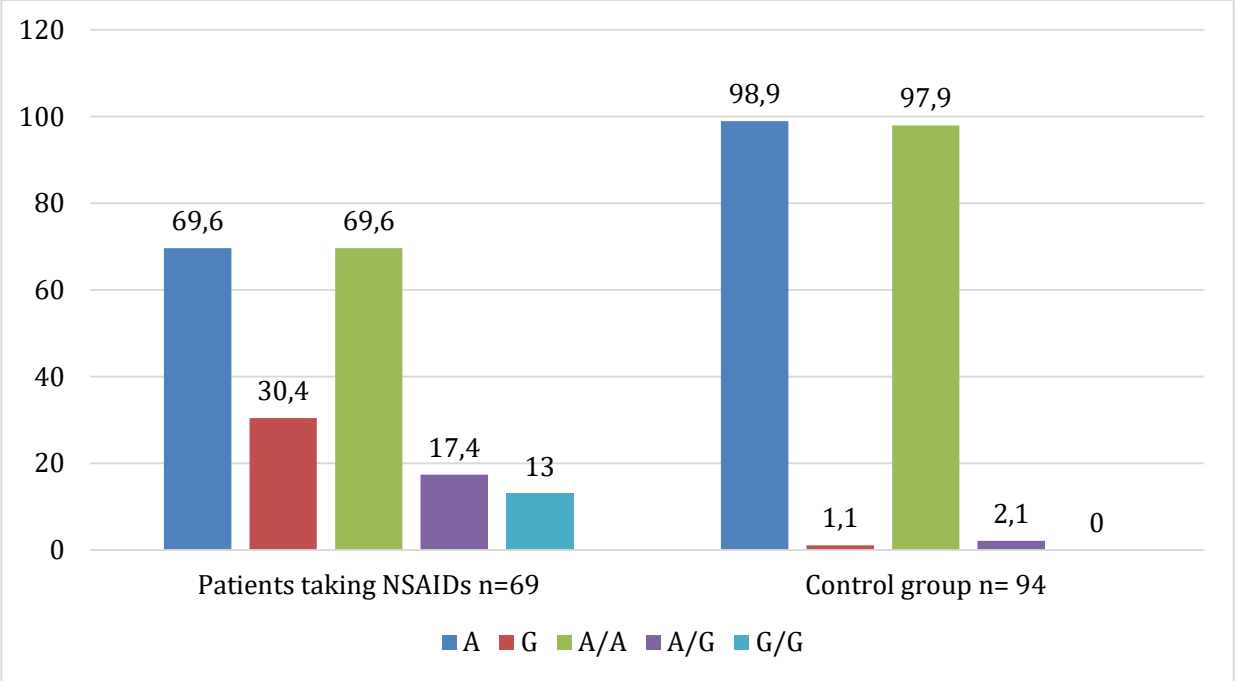
The control group included 94 healthy volunteers (control group)

Molecular genetic studies were carried out on the basis of the Laboratory of medical genetics of NIIG and the PC of the Ministry of Health of the Republic of Uzbekistan. Genotyping after isolation of genomic DNA from whole blood with the addition of ethylenediaminetetraacetate was carried out by multiplex polymerase chain reaction with a fluorescent scheme for detecting products in real time using LITECH CYP 2C19 ACE test systems (St. Petersburg, Russia).

Statistical processing of the results of the study was carried out: using the online calculator open api [https://www.openepi.com / TwobyTwo.htm]. The correspondence of the distribution of the observed frequencies of the genotypes of the studied genes in the control group, theoretically expected by the Hardy-Weinberg equilibrium, was evaluated by the criterion $\chi 2$. The calculation was carried out using an online calculator: http:// www.oege.org/software / hw em r-calc.shtml.

Results of the study: as a result of the study, we found that the frequency of carrying allele A in patients taking NSAIDs was 97.1%, in the control group – 98.9%. Whereas the frequency of the G allele was 2.6 times more common among patients with pain syndrome and corresponded to the expected Hardy-Weinberg equilibrium, $\chi 2=7.0$, $p=0.008$. Carriers of the G allele were found in 30.4% of patients taking NSAIDs, whereas in the control this allele was found in 1.1% of volunteers. The carriage of the heterozygous A/G allele in the CYP2C19 gene in

patients taking NSAIDs was noted in 17.4% of cases, whereas in the control in 2.1% of cases (Fig. 1).



OR=6,9 (CI 1,44-33,0); $\chi 2$=58,8, p<0,001

Fig. 1. Frequency of distribution of alleles and genotypes of polymorphism in the CYP2C19 gene in groups of patients depending on gender and control

A relationship was established between the G allele, the G/G genotype and the presence of NSAID gastropathy at both allele and genotype levels (Table 1).

Table 1

Identification of alleles and genotypes of polymorphism in the CYP2C19 gene depending on the presence of gastropathies among patients with pain syndrome taking NSAIDs

Allele/genotype	Gastropathies + (n=11)		Gastropathies - (n=58)		
	n	%	n	%	
A	14	63,6	82	70,7	$\chi 2$ =12,1; p=0,05; OR=0,25; 95% CI 0,11-0,56; df=0,014
G	8	36,4	34	29,3	
AA	6	54,5	42	72,4	$\chi 2$ =14,2; p=0,01; OR=8,25; 95% CI 2,56-26,6; df=0,030
AG	2	18,2	11	19,0	
G/G	2	18,2	5	8,6	

Why CYP2C19 is associated with gastropathies at the allele and genotype levels is not fully understood. As is known, CYP 2C19 is a common polymorphism with enhanced function, whose carriers have higher metabolic rates of some clinically important drugs (PPIs, escitalopram, sertraline, clopidogrel, etc.), followed by a decrease in their concentration in blood plasma and a weakening of the clinical effect (Goldstein J.A., 2001; Ingelman-Sundberg M. et al., 2007; Rosemary J., Adithan C., 2007; Baldwin R.M. et al., 2008; Hunfeld N.G. et al., 2008; Li-Wan-Po A. et al., 2010; Pedersen R.S. et al., 2010; Sibbing D. et al., 2010; Scott S.A. et al., 2012b; Zabalza M. et al., 2012; Musumba C.O. et al., 2013).

Nevertheless, based on a review of data on the functional and clinical consequences of carrying the CYP2C19 G allele, it was concluded that CYP2C19 has only a minor effect, which is unlikely to be clinically significant, with the exception of CYP 2C19* G homozygotes, and only for drugs with a narrow "therapeutic window" (Ingelman-Sundberg M. et al., 2007; Li-Wan-Po A. et al., 2010; Scott S.A. et al., 2012b).

On the other hand, in some recent studies, scientists have concluded that the carriage of the CYP2C19 allele in patients taking clopidogrel is associated with lower platelet reactivity, a reduced risk of cardiovascular complications and stent thrombosis, but with a higher risk of intense bleeding (Harmsze A.M. et al., 2012; Zabalza M. et al., 2012). Therefore, one of the possible explanations for the revealed connection may be that CYP 2C19 carriers have accelerated metabolism and a decrease in the clinical efficacy of PPIs, which cause a decrease in the gastroprotective ability of the mucous membrane to resist aggressive factors (for example, NSAIDs and *Hp* infections), thus predisposing to the occurrence of gastropathies.

In addition, CYP2C isoenzymes are involved not only in the metabolism of xenobiotics, but also in various endogenous substances (Ingelman-Sundberg M. et al., 2007; Scott S.A. et al., 2011; 2012a). For example, arachidonic acid is metabolized by three main enzymatic pathways: cyclooxygenase, lipoxygenase, and CYP 450-monooxygenase with CYP 2C19 (Kaspera R., Totah R.A., 2009; Musumba C.O. et al., 2013). The CYP 2C19 isoenzyme effectively metabolizes arachidonic acid into four types of epoxyeicosatrienic acids (EETC): 5,6-EETC; 8,9-EETC; 11,12-EETC and 14,15-EETC, which are species- and organ-specific and have a variety of physiological functions (including control of vascular tone, angiogenesis, cell migration, proliferation, inflammation) (Kaspera R., Totah R.A., 2009).

Although the effect of EETCS on the human gastrointestinal tract has not been fully studied, however, they presumably inhibit the production of prostaglandin E2 in smooth muscle cells and participate in the formation of reactive oxygen species in vascular endothelial cells, which contributes to ischemic lesions (Pilotto A. et al., 2007; Kaspera R., Totah R.A., 2009; Musumba C. et al., 2009). Therefore, one of the possible explanations for the relationship between gastropathies and CYP 2C19 can be considered that the latter alters the metabolism of arachidonic acid, as a result of which the protective properties of the mucous membrane of the gastroduodenal zone of the gastrointestinal tract decrease due to a combination of a decrease in the production of gastroprotective prostaglandin E2, increased vasoconstriction in the microcirculatory bed of the mucous membrane and the production of damaging reactive oxygen species (Musumba C. et al., 2009; 2012).

CONCLUSION

1. The presence of the CYP 2C19 G allele is significantly associated with endoscopically confirmed NSAID-induced gastropathy and can be considered as a risk factor for their development, which is presumably explained by the participation of the CYP 2C19 isoenzyme in the metabolism of arachidonic acid, which plays a role in gastrocytoprotection.

2. Patients with CYP2C19 polymorphism have accelerated metabolism of PPIs, which significantly reduces their clinical effectiveness.

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POLYMORPHISM OF THE CYP2C19 ISOENZYME AS A RISK FACTOR FOR GASTROPATHIES INDUCED BY THE USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH PAIN SYNDROME

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ABSTRACT

In the last decade, there has been a sharp increase in chronic kidney diseases (CKD) among children. In the US, Europe, Australia, Asian countries, it is noted that one-tenth of the world's population suffers from a violation of kidney function. In 50% of patients with SBK, the disease is detected at the 3-5 stage of chronic renal failure (CRF), in 10% of patients at the terminal stage. At present, insufficient research has been conducted in the country to study the features and complications of kidney disease in children (Umarov R.Kh. 2010; Sharipov A.M. 2012; Khamzaev K.A., 2019; Rakhmonova L.K. 2020; Karimova U.N., 2020;).

Key words: children, nephrotic syndrome, glucocorticosteroids.

INTRODUCTION

Nephrotic syndrome in children is characterized by proteinuria > 3,0 g/Day (>50 mg/kg of body weight per day or >40 mg/m^2 of body surface per hour), a decrease in the concentration of albumin in the blood < 25 g/l, the development of hyperlipidemia and tumors [1,2,3,5]. According to A.A. Baranov's data (2018), the annual incidence of nephrotic syndrome accounts for 2-7 primary cases per 100 000 children, while the prevalence rate in children – 12-16 cases per 100 000 children population. [4-7] Tsigin I.A., Komarov O.V. at al (2017) state that every 100 000 children under the age of 10 with primary nephrotic syndrome 2-13 years of age are eligible for the condition. NS in children is about 10% in children under 90 years of age, and in older children about 50%. The congenital form of nephrotic

syndrome is in the ratio of 0,9-1,2 incidence in every 10 000 newborns, this form is common in European countries, especially in Finland. [6-8,19,20]

New approaches to the nephrotic syndrome in children have shown that in recent decades, the results of the treatment of nephrotic syndrome due to the change in ideas about the etiology, pathogenesis and treatment tactics of nephrotic syndrome, the emergence of new therapeutic technologies, sung has shown that there are profound changes in other organs and systems, in particular, the digestive tract. Ignatova M.S., Dlin V.V. (2017). [3-6]

Glucocorticosteroids (GKS) are the main selective preparations used in the treatment of steroid-sensitive nephrotic syndrome (SSNS) in children. Approximately 40% of them would have died before the use of GKS and antibiotics [3]. In 80-90% of patients receiving GKS, ida occurs in the remission phase of the disease[1]. Depending on the response to GKS therapy, SSNS and steroid-resistant nephrotic syndrome (SRNS) are allocated [2].

According to the recommendations of international and Russian scientists, for the treatment of nephrotic syndrome, prednisolone is prescribed to drink at a dose of 60 mg/m^2 per day or 2 mg/kg per day (the dose is 60 mg per day.for 4-6 weeks, then the drug is recommended to take for 4-6 weeks at a dose of 40 mg/m^2 or 1.5 mg/kg (maximum one-day to 40 mg dose), a gradual reduction and a scheme of cancellation of the drug is recommended [1-4]. The total duration of GKS therapy is 4-5 months [7,16].

GKS is an alternative mode of admission, which increases the duration of remission compared to the intermittent mode of admission (continuous) [4-6,16]. Children with frequent recurrent (SSNS) and steroid - dependent nephrotic syndrome (FRNS), which are considered clinical variants of SRNS, need long-term GKS therapy, [9-15]. this leads to serious side effects, including damage to the mucous membranes of the stomach and duodenum [5-8]. Proceeding from the above, it is topical to determine the dependence of clinical-morphofunctional changes in gastroduodenal foci on long-term GKS therapy in children with nephrotic syndrome.

The purpose of the study: in children who have long received GKS therapy with nephrotic syndrome, the study is to investigate the clinical changes observed by the gastrointestinal tract.

Research materials and methods

Under our observation, the indicators in the form of dyspeptic complaints observed in children who received and did not receive GCS for 6 months before admission were analyzed in the multidisciplinary clinic of the Tashkent Medical Academy under the supervision of the Department of Nephrology in the period

from 2018 to 2020. Various clinical variants of nephrotic syndrome were analyzed in the medical documentation (history of the disease) of 298 children aged 4 to 14 years of age.

Results of the study.

According to the results of the analysis, it was found that despetic complaints and signs were observed in 244 (81,9%) children. These children were divided into groups of patients who received GKS for 6 months before hospitalization in 1-Group n=176 (72,1%) hospital hospitalization in two groups and who did not receive GKS within 6 months before hospitalization in 2-Group N=68 (27,9%) hospital. Based on clinical laboratory variants of nephrotic syndrome, it was divided into 3 groups. With the diagnosis of steroid-sensitive nephrotic syndrome (SSNS), in which 1-group was identified as primary and treated with GCS for 12 weeks and achieved remission, children were treated with 64 (26.2%), 2-group were treated with 86 (35.2%), 3-group prednisolone with a diagnosis of frequent recurrence (FR), which is considered a clinical variant of steroid-resistant nephrotic syndrome (SRNS), patients with steroid-dependent nephrotic syndrome (SDNS), which did not achieve remission after a course of weeks of treatment with Sung and 3 times a course of Solu-medrol, received 94 units (38,6%). it was.1-table. Most of the children were hospitalized several times.

Table 1

Clinical description of children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization.

Clinical variants of NS	1-group (***n*** = 176)		2- group (***n*** = 68)		P
	abs	%	abs	%	
SSNS=64	3	1,8	61	89,7	P< 0,01
SRNS or FRNS=86	79	44,8	7	10,3	P< 0,02
SDNS=94	94	53,4	0	0	-

Note: against the background of taking 1-group-maximal GKS dose, 2-group-during the most long-term remission of the disease, P-mail data reliability.

In the results of the analysis, 244 patients with dyspnea complaints and signs were analyzed according to age and sex of the children. The age of the children was divided into three age groups, taking into account the critical periods.

The first age group ranged from 4 years to 7 years of age 62 (25,4%), the second age group from 7 years to 10 years 95 (38,9%), the third age group ranged from 10 years to 14 years 87(35,6%), the average age of children was 8,8 ±1,3. P< 0,05.

Table 2

Description of the age and sex of sick children with NS diagnosis

Age	4-7 years (n=62)		7-10 years (n=95)		10-14 years (n=87)		P
Sex	абс	%	абс	%	абс	%	
Girls	18	29,0	26	27,3	38	43,6	P< 0,01
Boys	44	71,0	69	72,7	49	56,4	P< 0,01

Note: P-data reliability.

The results of the analysis showed that dyspeptic complaints and symptoms in children with NS were more common in boys when they were distributed by gender in all age groups than girls, which was generally consistent with the results of the study of many authors. [2-8]. When the social origin of the sick children was pushed, the rural population accounted for a large part (131 (74.3%) in the 1st Group and 54 (79.4%) in the 2nd Group, respectively. Data on the duration of the disease were as follows: 8 years from the onset of the disease in the 1st Group, an average of 5,1±1,8 years; in the 2nd Group-3 years, an average of 1,6±0,6 years. According to the results of the analysis, in isolated groups based on clinical laboratory variants of nephrotic syndrome, dyspnea complaints (pain in the abdomen, vomiting, constipation) were the same.

Table 3

Dyspeptic complaints in children with nephrotic syndrome (pain in the abdomen, vomiting, constipation).

Dispatch complaints	SSNS 1-group (***n=64)***	SRNS or FRNS 2-group (***n=86)***	SDNS 3-group (***n=94)***	**P**
Abdominal pain abs. (%)	11(17,1%)	71(82,5%)	82(87,2%)	P< 0,01
Vomiting abs (%)	13(20,3%)	68(79,0%)	78(82,9%)	P< 0,02
constipation abs. (%)	23(35,95)	54(62,7%)	67(71,1%)	P< 0,01

Note: P-data reliability.

Also, as a result of retrospective studies of the history of the disease, dyspeptic complaints were analyzed in children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization. In the 1-group 153 (86,9%) suffered with abdominal pain, vomiting 146 (82,9%), constipation 121 (68,7%) cases. Dyspeptic complaints among patients who did not receive GKS for 6 months or more before 2nd group

hospitalization were identified 11 (16,1%), vomiting 13 (19,1%), constipation 23 (33,8%), abdominal pain. In the 1st group, compared that then the 2nd group dyspeptic complaints vomiting abdominal pain, constipation was detected a lot, it corresponded to the data of the literature. [6-8].

Table 4

Dyspeptic complaints in children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization.

Index	Group 1 (n = 176)	Group 2 (n = 68)	P
Abdominal pain	153(86,9%)	11(16,1%)	P <0,01
Vomiting	146(82,9%)	13(19,1%)	P <0,02
Constipation	121(68,7%)	23(33,8%)	P <0,02

Note: 1 — group-against the background of taking the maximum dose of GKS, 2-group-during the most prolonged remission of the disease. P-reliability of data.

CONCLUSION

Dyspeptic complaints (pain in the abdomen, diarrhea, vomiting) were noted in 81,9% of patients who received glucocorticosteroids for a continuous 6 months in nephrotic syndrome, dyspeptic complaints were observed in 18,1% of children who received glucocorticosteroids for less than 6 months, and morphofunctional changes in the intestinal tract of the stomach were associated with the duration and continuaqtion. In the period of remission of the disease in children with a frequent recurrent form of nephrotic syndrome and sensitive to steroids, there was a significant decrease in the incidence of dyspeptic complaints (pain in the abdomen, diarrhea, vomiting), discontinuation of glucocorticosteroid drugs.

Predicting the effect on the state of the gastrointestinal tract in children with nephrotic syndrome, taking different courses of glucocorticosteroids, requires timely diagnosis and treatment of changes.

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TRENDS IN THE DEVELOPMENT OF HIGHER MEDICAL EDUCATION THROUGH THE INTRODUCTION OF DIGITAL ONLINE CONSULTATIONS IN SURGERY

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ABSTRACT

The digitalization of medicine has been actively introduced into medicine in recent decades. Telemedicine is a variation of this area. It has prospects in the form of conducting various online consultations of specialists in all corners of our Republic, when the use of electronic information, integrated digital and telecommunication technologies creates conditions for the exchange of data between doctors, as well as for management in the field of medical education and healthcare. With the help of telemedicine technology, doctors can urgently consult with each other. In serious cases, doctors themselves sometimes need the help of a more qualified specialist. If there is no such thing nearby (for example, if we are talking about remote medical institutions), then the only way out is a video call to an experienced colleague. Doctors can also send patient data to each other to view their medical history. Live broadcasts of surgical operations, during which doctors and students can ask their questions, which will qualitatively improve the educational process.

Key words: telemedicine, surgery, information technology.

INTRODUCTION

Digitalization is being introduced widely into all areas of health care, and telemedicine was the first of its kind. Despite the common perception that

telemedicine is young and not yet common in practice, it began long before the computer, in the days of the telegraph. Consultations with specialists by phone can also be classified as telemedicine. At the same time, the first videoconferencing session as a telemedicine tool was conducted in 1965. It was a broadcast of an aortic valve replacement operation on an artificial heart assisted by the eminent cardiac surgeon Michael DeBakey [2,5].

Since the 1960s there has been a significant increase in the use of videoconferencing amongst medical personnel including surgeons [7]. In recent years, the cost of equipment for this has become cheaper and high technical skills are not required to use the system. In 2004, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) introduced its definitions of telemedicine [8]. Videoconferencing is defined as a real-time, interactive programme in which one group of participants is at one or more locations and another group of participants is at another location. Videoconferencing permits interaction, including audio and/or video, and possibly in other ways, between at least two specialists [8]. A similar definition is used in Telemedicine Journal and e-Health [3].

The US Department of Health and Human Services defines telehealth as "the use of electronic information and telecommunication technologies to support and promote clinical care at a distance, patient education and professional medical education, public health and health care management" [4]. The Agency for Healthcare Research and Quality classifies telemedicine into 3 separate categories:

1. real-time telemedicine between patient and health care provider;
2. storing and forwarding telemedicine services, such as the exchange of medical images or data between service providers;
3. telehealth home monitoring, involving the use of telehealth to remotely monitor patients and their health status, also known as remote patient monitoring [4].

The greatest concern in the current pandemic is the enormous workload, psychological stress, emergencies and, even worse, transmission among health-care workers. As of 8 May 2020, 90 000 health workers were infected with the severe disease COVID-19 and many countries have reported a large number of deaths of health workers [13]. One potentially useful tool to reduce the aforementioned risks to the health system is the digitalization of medicine. Many surgical pathologies are known to have negative outcomes due to delayed treatment, leading to worse outcomes and increased patient mortality [3, 9].

Education and training is an important aspect of the practice of the academic surgeon. Residency training is hampered by reduced operating room hours, patients in clinics, and individual surgical training. Virtual learning environments via

videoconferencing have been used successfully for training trainees and students, as well as for tele-rehabilitation [10]. Distance learning is considered to be as effective as traditional instructor-led methods [11]. This method of teaching provides theoretical knowledge, but does not allow residents and medical students to acquire technical and surgical skills. Virtual patient cases have been studied as a substitute option for some patient meetings, and they have shown a moderate improvement in knowledge and appear to be useful for preparing or reinforcing face-to-face patient meetings [12].

A unified communication and information service for emergency medical care, comprising several levels and structural components, has been set up in the Republic. Transforming primary health care for the population, developing an emergency medical service and ensuring access to highly specialized medical care for the population remain priorities in the reform of the health-care system.

This service aims to provide the population with qualified specialized, high-tech emergency, urgent and emergency care, to organize a system of emergency medical care in line with international standards and to establish close cooperation with foreign specialized institutions. It is here that the implementation of digitalization for accessibility of medical services and training is relevant [6].

Air ambulance is one of the structures of emergency services, particularly surgery, where specialists need help in solving difficult and controversial clinical cases in a collegial way. Of course, this emergency service is relevant in all branches of modern health care, but when it comes to the economic efficiency of this service, here it is necessary to modernize it by implementing digitalization in the air ambulance service.

Material and methods. We analyzed the calls of employees of Department of general and pediatric surgery #1, based in department of purulent surgery and surgical complications of diabetes mellitus of multidisciplinary clinic of TMA in the year of 2020. A total of 109 patients were consulted, of whom the main contingent was 88 patients in whom surgical infection developed against the background of diabetes mellitus, less frequent were 16 patients with lung suppurative diseases and 9 patients with surgical soft tissue infections.

Table 1

Distribution of patients by nosology

Nosology	**Amount**	
	n	**%**
Acute purulent-destructive lung diseases	16	14,7
Soft tissue infections	9	8,3
Soft tissue infections due to diabetes mellitus	40	36,7
Diabetic gangrene of the lower limbs	44	40,3
	109	100

Results.

An analysis of the distribution of patients by regions of the Republic showed that patients from Tashkent and Tashkent province were consulted, patients from other provinces were consulted less frequently, while the number of patients with surgical infections in the regions of the Republic remained at a high level.

Table 2

Distribution of patients by regions of the Republic

Provinces	**Number of calls**	**(%)**
Tashkent city	55	50,5
Tashkent	24	22,1
Syrdarya	8	7,4
Jizzakh	7	6,4
Namangan	5	4,6
Andijan	2	1,8
Bukhara	1	0,9
Navoiy	3	2,7
The Republic of Karakalpakstan	2	1,8
Samarkand	2	1,8
Total	**109**	**100**

In reviewing the care provided to these patients, it was found that in 88.9% of cases the conservative treatment was corrected or the patients were subsequently transferred to our department and only 12 patients underwent surgery locally.

Table 2

Volume of care provided

Provinces	**Correction of treatment**	**%**	**Operation**	**(%)**
Tashkent city	52	47,8	3	2,7
Tashkent	19	17,4	5	4,6
Syrdarya	8	7,5	-	
Jizzakh	7	6,5	-	
Namangan	3	2,7	2	1,8
Andijan	2	1,8	-	
Bukhara	1	0,9	-	
Navoiy	3	2,7	-	
The Republic of Karakalpakstan	1	0,9	1	0,9
Samarkand	1	0,9	1	0,9
Total	**97**	**89,1**	**12**	**10,9**

Discussion.

To call a specialist to a distant facility requires the involvement of many specialists, in particular the consultant, dispatcher, driver and their financial incentives accordingly. Of course, if it is necessary and possible to carry out various types of surgical interventions on site, visiting of specialists is obligatory. But, today, the question is about the accessibility of specialists at all levels locally in the early stages of the disease, and here the main role is assigned to the digitalization. There are situations where doctors need help, because severe and complex cases are everywhere. At the same time, transporting the patient to a clinic in the capital or to a medical centre is not possible or not reasonable. The only option is an urgent video call, which can help you get the advice you need as quickly as possible, avoiding valuable time being wasted.

Digitization in this area allows trainees to see clinical situations clearly and to analyse complex cases together so that they can actually follow the patient's treatment online. In contrast to watching video recordings, the trainees can ask questions and receive detailed explanations, and can analyze difficult situations. In addition, it can display all of the patient's data, from clinical and laboratory tests to complex instrumental studies, which enables data transfer at any distance, long-term preservation and eliminates the paperwork that is ubiquitous today.

Conclusions.

Thus, the relevance of the emergency medical service and its structural subdivision - air ambulance - is beyond doubt, but there is a need for widespread implementation of digitalization in the form of preliminary online consultations, where all patient data and treatment performed will be demonstrated. This requires the improvement of the digital base and the involvement of specialist engineers who will create the software for the service. The special features of this digitalization are urgency, unlimited number of consultants, with consilium, accessibility and high cost-effectiveness.

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ASSESSMENT OF MEDICAL EXPOSURE IN PALLIATIVE THERAPY WITH SAMARIUM – 153

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ABSTRACT

The scientific article is devoted to an actual problem - medical exposure. **The aim** of the study is to assessment the doses of irradiation of organs and tissues during palliative treatment patients with metastasized bone cancer. Over the past 20 years, only samarium-153 has been used for these purposes in Uzbekistan. **Materials and methods.** For the study, data from radioisotope laboratories of Tashkent medical institutions, where palliative treatment is carried out, were used. Radionuclide therapy with samarium-153, oxabiphor, was performed on 78 women who were diagnosed with mammary cancer, who had multiple bone metastases and pain syndrome. Equivalent doses of irradiation of the organs of patients were calculated by multiplying the introduced activity in MBq by the dose coefficients of the absorbed dose in mGy for specific organs per 1 MBq of activity. **Results.** Depending on the weight of the patients, dose loads on the bladder were in the range of 1.2–2.0 Gy; liver - 0.01 -0.02 Gy; kidneys - 0.6 - 1.0 Gy; small intestine - 0.01 - 0.02 Gy; the lower part of the large intestine - 0.02 - 0.03 Gy; upper colon - 0.01 - 0.02 Gy; ovaries - 0.02 - 0.03 Gy; whole body - 0.2 - 0.03 Gy. **Conclusion.** Due to the selective accumulation and manifestation of deterministic effects in the bone tissue, a decrease in pain in patients with metastasized bone lesions is clearly expressed. Equivalent radiation doses to other organs are below critical levels, so the risk of deterministic damage is minimal. The bladder experiences the greatest dose loads, then the kidneys, the lower part of the large intestine, the ovaries, small intestine, and the upper colon.

Key words: radionuclide medicine, samarium-153, oxabiphor, equivalent dose of radiation, palliative therapy, radiopharmaceutical.

INTRODUCTION

According to the World Health Organization, 19.3 million people fell ill with cancer in the world in 2020, 10 million people died as a result of this disease. The situation became more complicated due to the COVID-19 pandemic, when health systems were working at the limit of their capabilities and all resources were directed to the fight against coronavirus [1].

In the structure of the incidence of malignant neoplasms (MN) for 2021, breast, stomach and cervical cancers retain leading positions with incidence rates of 9.8; 5.1; and 4.8 per 100 000 population, respectively. The structure of oncological morbidity among the female population is as follows: breast MN - 19.5; cervical MN - 9.7 and ovarian MN - 4.9 per 100,000 population, and among the male population: stomach MN - 6.2; bronchial and lung MN - 5.4 and prostate MN - 3.0 per 100,000 population [2].

Metastatic bone damage is one of the most common complications of solid cancer. According to the literature, the frequency of such lesions of the bone system in breast cancer at different stages of the disease is 47-85%, prostate cancer — 33-85%, lung cancer — 30-60%, kidney — 33-40%, thyroid cancer — 28-60% [3,4]. At the initial stages, metastatic bone damage is often clinically asymptomatic, but later manifests itself as malignant hyperkalemia, fractures and pain syndrome, which significantly reduces the quality of life of patients [5].

Radionuclide therapy of multiple metastatic skeletal lesions has been widely used in the world since the late 80s of the last century [6,7,8]. The greatest experience of the successful use of radionuclides in palliative therapy has been accumulated in prostate cancer and BPH, which is explained by the nature of the lesion of the bone system (the presence of a pronounced blast component) [9]. In world practice, isotopes 32P, 89Sr, 186Re, 188Re, 153Sm and 177Lu are actively used for palliative therapy of bone metastases [10]. The use of radionuclide therapy for the treatment of bone metastases is due to the ability of some beta-emitting isotopes to selectively accumulate in pathological foci with increased mineralization and increased metabolism of bone tissue. Local "internal" irradiation with β-particles equally affects both the manifesting and subclinical foci of bone destruction, which makes it possible to achieve reduction of tumor infiltration and provide anesthesia [11,12].

The formation of maximum doses of the drug in the most functionally active metastases provides a basis for achieving rapid and effective suppression of pain syndrome [13].

Due to the presence of gamma quanta in the 153Sm radiation spectrum, the scintigraphic picture obtained with any labeled phosphate compound before treatment is completely comparable to the distribution of the radiopharmaceutical (RFP) in the bones after its administration.

According to the literature, 153Sm is characterized by a rapid response to the introduced activity, which is its distinctive feature compared to phosphorus and strontium. On average, the effect of the therapy occurs 2-7 days after the introduction of RPF and lasts an average of 4-12 weeks [14]. The overall clinical

efficacy of samarium-153 therapy depends on the primary localization of the tumor process. Evaluation of the results of repeated injections showed that therapy carried out after 3 and 6 months is also effective.

Work with the drug should be carried out in accordance with SanPiN No. 0193-06 "Radiation safety standards (NRB-2006) and basic sanitary rules for radiation safety (OSPORB-2006)".

The aim of the study was to evaluate the doses of irradiation of organs and tissues during palliative therapy with Samarium in 153 patients with metastasized bone cancer.

Materials and research methods. For the last 20 years in Uzbekistan, only Samarium-153 has been used for palliative treatment of metastasized bone cancer.

Samarium-oxabiphor, 153Sm is a colorless transparent solution for intravenous administration. The 153Sm isotope emits beta radiation with an energy of 640 keV, 710 keV, 810 keV with yields of 30%, 50% and 20%, respectively, and gamma rays with an energy of 103 keV. Half-life of 153Sm - 46.2 h.

For the study, data from radioisotope laboratories of medical institutions in Tashkent were used, in which palliative therapy of patients with metastatic bone cancer with Samarium-153 oxabiphor is carried out. Radionuclide therapy with samarium-oxabiphor, 153Sm was carried out in 78 breast cancer patients with multiple bone metastases and pain syndrome. The age of the patients ranged from 28 to 70 years (mean 48.7 years). The duration of the disease before the start of radionuclide therapy ranged from 6 to 240 months. (average 61.5 months). Of the 78 patients, bone metastases were already present in 10 women when the disease was detected, in 68 they appeared after the diagnosis was established. All patients previously received various treatment: hormone therapy, radiation, chemotherapy, surgical treatment. Samarium-oxabiphor, 153Sm was injected intravenously. Women who first came to receive palliative care were selected. In Uzbekistan, for palliative therapy of bone cancer, samarium-153 oxabiphor is administered to patients at the rate of 1 mCi of activity per 1 kg of the patient's weight, 1 mCi is equal to 37 MBq. This treatment is carried out only in patients over 18 years of age.

Table 1 shows the distribution of patients by body weight in the range of 5 kg.

Table 1

Distribution of patients with metastasized bone cancer participating in the study, by body weight

Number of patients	Weight of patients, kg						
	45-50	51-55	56-60	61-65	66-70	71-75	76-80
78	5	19	21	18	8	6	1

The effectiveness of treatment was assessed by the dynamics of the pain syndrome for 3 months after drug injection. For this, a 10-point visual analogue scale was used (0 points - no pain, 10 points - the most severe pain). The effect was self-assessed by the patient one, two and three months after the injection.

The dynamics of the "quality of life" was determined according to the Karnovsky scale, according to which the patient's activity is assessed: 0-40% - unable to serve himself, hospital care is required, rapid progression of the disease is possible; 50-70% - loss of ability to work, living at home is possible, for the most part is able to serve himself, care is required in a different amount; 80-100% - normal daily activity is preserved, medical care is not required [15].

Equivalent doses of irradiation of the organs of patients were calculated by multiplying the introduced activity in MBq by the dose coefficients of the absorbed dose in mGy for individual organs per 1 MBq of activity.

With intravenous administration of the solution, there is a high and selective accumulation of Samarium - 153 oxabiphor in metastatic organs and rapid excretion from healthy tissues. A preliminary assessment of the accumulation of radiopharmaceuticals can be carried out, if necessary, using bone scintigraphy with technefor or pyrfotech preparations containing radioactive technetium-99. According to the officially approved instructions for use of the drug, compiled on the basis of the electronic edition of the Vidal 2014 guide, updated on December 7, 2019, the absorbed doses of various organs in mGy per 1 MBq of the administered activity of Samarium-153 oxabiphor were determined, which amounted to - 0.702 mGy/MBq, liver - 0.0067, kidneys - 0.351, small intestine - 0.00783, lower large intestine - 0.00999, upper large intestine - 0.0051, testicles - 0.00756, ovaries - 0, 00918. For the whole body, the coefficient for determining the effective equivalent dose is 0.01161 mSv/MBq. In the palliative treatment of metastatic bone cancer, determining the effective dose is not so important, because the concept of effective dose was introduced to assess the long-term effects of human exposure to low doses. Small doses mean that they cannot have deterministic effects, i.e. cause radiation damage to any tissue. The goal of radionuclide therapy (RNT) is the opposite - to cause the death of tumor tissue, therefore, radiation exposure in RNT is described by equivalent doses in individual organs and target tissues.

For statistical data processing, the main methods of descriptive statistics were used: measures of central tendency and measures of variability. From the measures of the central tendency, the arithmetic mean was determined, from the measures of variability, the standard deviation.

Distributions (samples) were checked for normality using the Kolmagorov-Smirnov test. Significant differences between the samples were determined using

the Mann-Whitney U-test. Statistical analysis was carried out using statistical programs OriginPro 8.6, SPSS Statistics 17.

Results and discussion. After intravenous administration, the drug selectively accumulated in the skeletal system, mainly in foci with increased mineral metabolism (metastases). The presence of gamma radiation (103 keV) in 153Sm made it possible to obtain a scintigraphic image on gamma cameras.

The decrease in pain intensity began to appear in most cases (in 48 of 78 patients - 61.5%) in the interval from one to two weeks after the injection. In 19 (24.3%) patients, pain began to decrease earlier than this period, and in 11 (14.2%) patients, later. It was difficult to accurately determine the day of onset of anesthesia due to the gradual manifestation of the clinical effect. The dynamics of the pain syndrome looked like this on a 10-point visual analogue scale. At the beginning of therapy, the average figures for the intensity of bone pain were 6.5 points, after 2 weeks and within 3 months, the pain was, according to a 10-point scale, at the level of 3.2 + 0.3 points. The minimum average pain intensity score was 2.41 points. The data is presented in Figure 1.

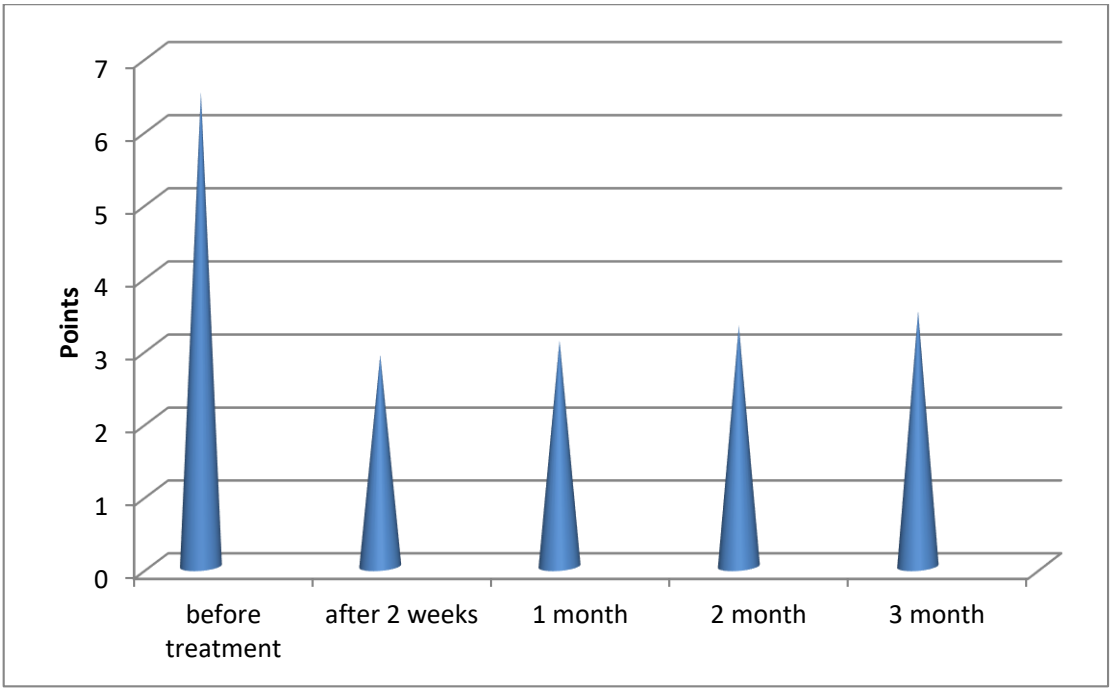

Fig. 1. Dynamics of average values of pain syndrome in patients with breast cancer with bone metastases after therapy with samarium-oxabiphor, 153Sm, according to the visual analogue scale of pain from 0 to 10 points

Before the start of treatment, in most of the observed female patients, the "quality of life" according to the Karnovsky scale was at the level of 55-60%, after 2 weeks and within 3 months - at the level of 70 + 5%. The data is shown in Figure 2.

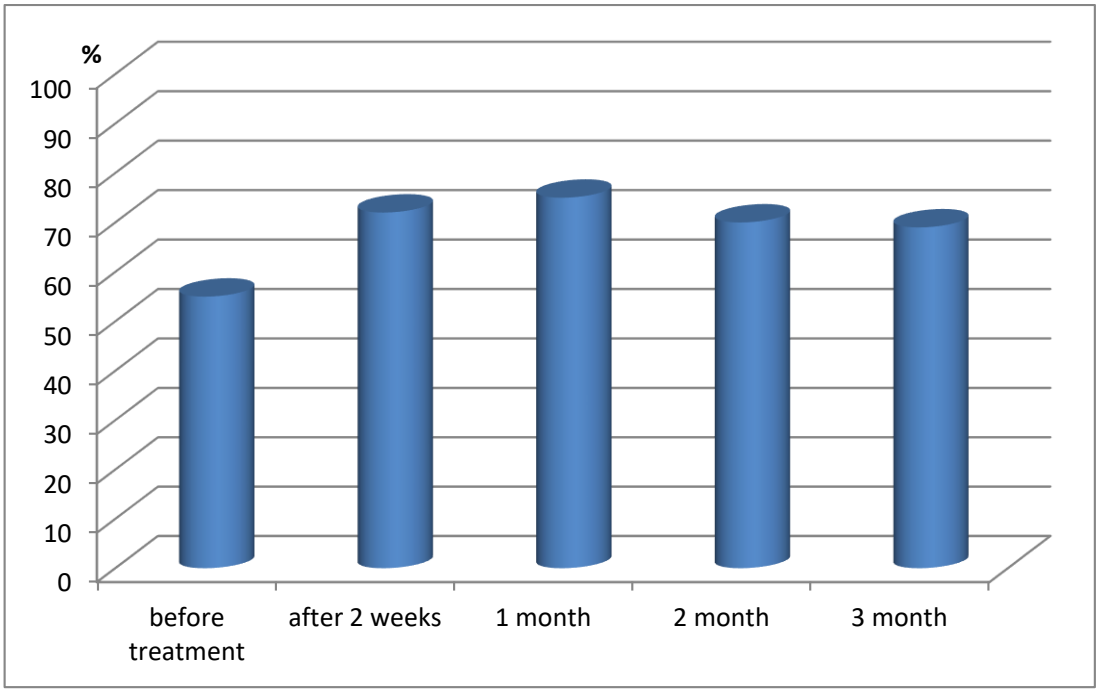

Fig.2. Dynamics of "quality of life" in patients with breast cancer with bone metastases after the therapy with samarium - oxabiphor, 153Sm, based on the Karnovsky scale in the range of 0-100%

Based on the introduced activities per 1 kg of body weight of patients, the equivalent doses of organ irradiation were determined. The average and total values of the activities administered to patients, depending on the weight and number of patients, are presented in Table 2.

Table 2

Average values of the obtained radiopharmaceutical activity by pations with metastasized bone cancer depending on the patient's body weight

Weight of patients, kg	**Number of patients**	Total injected activity, MBq	Average values of injected activity, MBq
45-50	5	8806,9	1761,20 ± 47,36
51-55	19	36630,5	1952,66 ± 50,22
56-60	21	45695,7	2175,71 ± 198,16
61-65	18	42294,1	2314,41 ± 43,80
66-70	7	18093,8	2504,22 ± 44,33
71-75	5	13651,2	2693,07 ± 40,77
76-80	3	8875,1	2904,50 ± 18,50
45-80	78	174047,3	2231,38 ± 264,87

Table 3 shows the calculated equivalent doses of irradiation of organs and tissues during palliative treatment with Samarium-153 oxabifor.

Table 3

The results of determining the equivalent doses of irradiation of organs and tissues during radionuclide therapy with Samarium-153

Organs	Equivalent doses, mGy						
	Weight of patients, kg						
	45-50	51-55	56-60	61-65	66-70	71-75	76-80
bladder	1236,4 ± 33,2	1370,8± 35,3	1527,4± 139,1	1624,7± 30,7	1757,9± 31,1	1890,5± 28,6	2038,9± 12,9
liver	11,80 ± 0,31	13,08 ± 0,33	14,58 ± 1,32	15,50 ± 0,29	16,77 ± 0,29	18,04 ± 0,27	19,46 ± 0,12
kidneys	618,2 ± 16,6	685,4 ± 17,6	763,7± 69,6	812,3± 15,3	878,9± 15,5	945,3± 14,3	1019,4± 6,5
small intestine	13,8 ± 0,4	15,3 ± 0,4	17,0 ± 1,5	18,1 ± 0,3	19,6 ± 0,3	21,1 ± 0,3	22,7 ± 0,1
lower part of the colon	17,6 ± 0,5	19,5 ± 0,5	21,7 ± 1,9	23,1 ± 0,4	25,0 ± 0,4	26,9 ± 0,4	29,0 ± 0,2
upper part of the colon	8,9 ± 0,2	9,9 ± 0,3	11,1 ± 1,0	11,8 ± 0,2	12,8 ± 0,2	13,7 ± 0,2	14,8 ± 0,1
ovaries	16,4 ± 0,3	17,9 ± 0,4	19,9± 1,6	21,3 ± 0,4	23,0 ± 0,4	24,7 ± 0,4	26,7± 0,2
whole body	20,4 ± 0,5	22,7 ± 0,6	25,3 ± 2,3	26,9 ± 0,50	29,1 ± 0,5	31,3 ± 0,5	33,7 ± 0,2

From the obtained results of the study, it can be seen that in the case of palliative treatment with Samarium-153, in addition to the selective accumulation of radiopharmaceuticals in metastatic and inflammatory-destructive foci of bone tissue, the bladder experiences a large dose load, then the kidneys, the lower part of the large intestine, ovaries, small intestine, upper section of the large intestine. These data are shown in Figures 3-5.

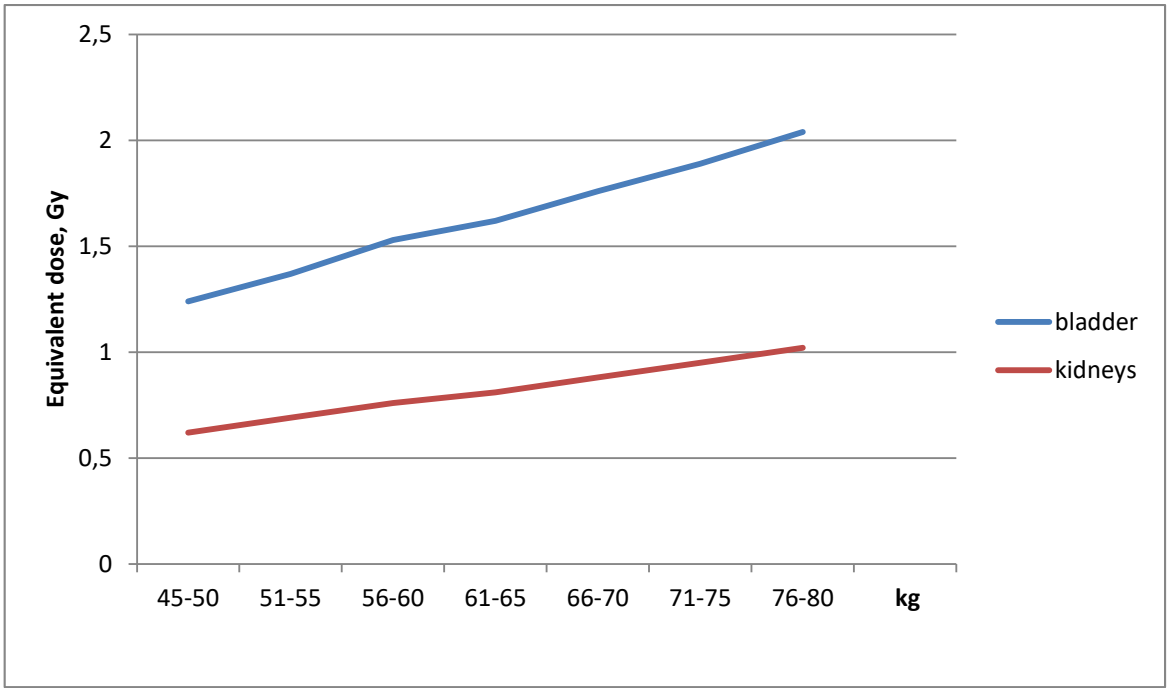

Fig.3. Dynamics of values of equivalent doses of irradiation of the bladder, kidneys, depending on body weight of patients

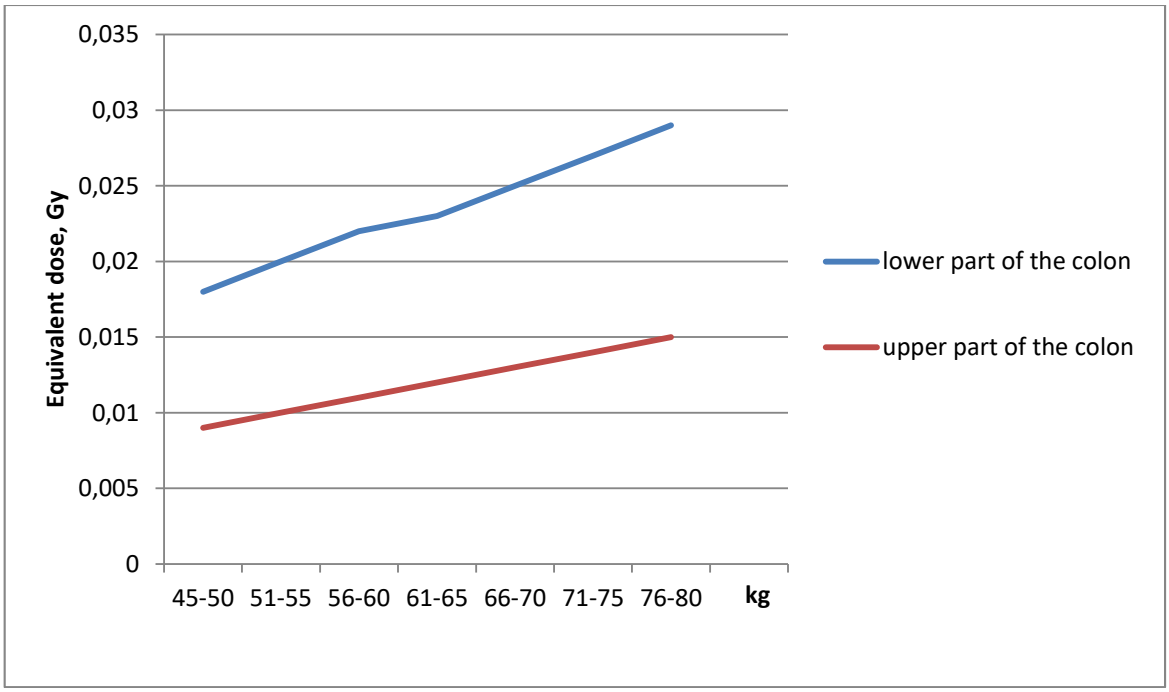

Fig.4. Dynamics of the values of equivalent doses of irradiation of the lower and upper parts of the colon, depending on body weight of patients

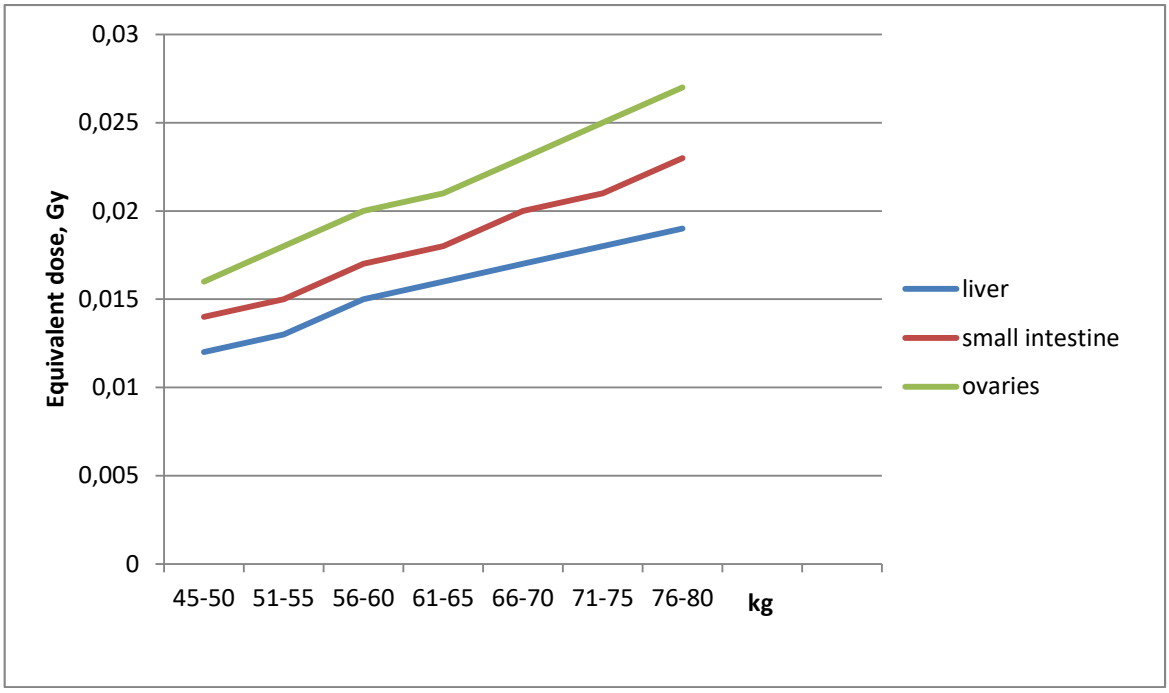

Fig.5. Equivalent of values doses dynamics of irradiation of the liver, small intestine, ovaries depending on body weight of patients

The equivalent dose to the whole body is in the range of 20.44 - 33.72 mSv. All received equivalent doses are below the dose thresholds required to produce deterministic effects.

The advantages of Samarium-153 oxabiphor are rapid excretion from healthy tissues, relatively low toxicity of the drug, and a good analgesic effect.

Conclusion.

The results of the conducted studies prove that despite the irradiation of all organs and tissues during radionuclide therapy with Samarium-153, the benefits of this procedure are greater than the harm. Due to the selective accumulation and manifestation of deterministic effects in the bone tissue, a decrease in pain in patients with metastasized bone lesions is clearly expressed. Equivalent radiation doses to other organs are below critical levels, so the risk of deterministic damage is minimal. The greatest dose load is experienced by the bladder, then the kidneys, the lower part of the large intestine, the ovaries, the small intestine, and the upper part of the large intestine.

The use of radionuclide therapy in the complex treatment of metastatic lesions of the skeletal system in malignant tumors of various localization confirms the need for greater introduction into medical practice, the development of new radiopharmaceuticals that have a high specificity of accumulation in the focus, a pronounced analgesic effect with minimal side effects.

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ESTIMATING THE ACTUAL DIET AND FOOD STATUS OF OBSESS MEN

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ABSTRACT

Obesity is a chronic relapsing disease, today it is one of the most widespread non-communicable diseases: in 1998, there were 250 million obese patients in the world, and by 2025, according to WHO experts, their number will exceed 300 million.

The aim of this work was to study the actual nutrition and nutritional status, as well as physical activity of obese men.

Materials and methods. The study involved 250 men aged 40 to 55 years old, diagnosed with obesity of 1-11 and 111 degrees, living in the city of Tashkent and the Tashkent region. 30 men made up the control group. The study was carried out at the Levelmed clinic in Tashkent.

Results and discussion: The diet of obese men is characterized by quantitative and qualitative deficiencies: body mass index, waist and hip circumference are above normal. Violated the diet in the form of irregular food intake, food at the late hours of the day, massive consumption of high-calorie foods: saturated animal fats, salt and sugar.

Key words: obesity in men, BMI, nutritional status in obese men.

INTRODUCTION

Obesity is a chronic recurrent disease, today it is one of the most common non-communicable diseases: in 1998, 250 million obese patients were registered in the world, and by 2025, according to WHO experts, their number will exceed 300 million (1,16,17,18). Obesity is one of the most important public health problems in the twenty-first century, and therefore this problem is given great attention. It is proved that the increase in the number of diseases associated with overweight and obesity, atherosclerosis, hypertension, coronary heart disease, decreased glucose tolerance, metabolic disorders, bone and joint (osteochondrosis, deforming osteoarthritis) and endocrine systems (insulin-dependent diabetes mellitus, diabetes mellitus type-2), many forms of cancer (cancer of the rectum, breast, prostate), reproductive system, secondary immunodeficiencies are caused by several "external" factors, the leading of which is a rapid non-evolutionary change in nutrition (the ratio of the main groups of nutrients) and lifestyle (decrease in physical activity and increased stress). The fundamental reasons for this change are recognized as industrialization, urbanization and globalization of the food and services market, which have changed not only food production, but also the stereotype of food choice (9,10,11,12,20,21). Every year, diseases associated with overweight cause more than one million deaths in the Central Asian region 9).

In recent years, there has been a sharp increase in the prevalence of obesity worldwide, which stimulates interest in the consequences for the health and quality of life of this population (22,23). Persons suffering from various forms of obesity make up 20-30% of the total population. In developed countries, obesity is already considered the fifth most important risk factor and one of the leading causes of disability. (WHO.2003). In addition, obesity leads to a decrease in life expectancy and increases the risk of arterial hypertension, dyslipidemia, type 2 diabetes mellitus, coronary heart disease. Targeted studies regarding the study of actual nutrition, morbidity, the development of new food products in obese men aged 30 to 60 years in the Republic of Uzbekistan have not been conducted. The quality of life of obese patients is an important issue that needs to be considered more carefully. Unfortunately, the effect of weight loss on sexual function and quality of life is not well understood.

The aim of this work -was to study the actual nutrition and nutritional status, as well as physical activity of obese men.

Materials and methods. The study involved 250 men aged 40 to 55 years old, diagnosed with obesity of 1-11 and 111 degrees, living in the city of Tashkent and the Tashkent region. 30 men made up the control group. The study was carried out at the Levelmed clinic in Tashkent. Obese men were under outpatient control. The diagnosis was made on the basis of anamnestic, anthropometric data and the

results of examination by hygienists, endocrinologists and therapists, as well as on the basis of anamnestic, anthropometric data. During the outpatient examination, the activity and mood of the patients were assessed. Anthropometric studies included bioimpedance control of body composition with the determination of its mass, body mass index (BMI), waist and hip circumference (W/H); amount of fat mass. The measurements were carried out using a Martin anthropometer, caliper, and standard medical scales.

During the outpatient examination, the nutritional status, as well as the well-being, activity and mood of the patients were assessed. In the conducted studies, actual nutrition was studied using a questionnaire card. The collection of material was carried out under expeditionary conditions 2 times a year (winter-spring and summer-autumn periods) with registration in individual sheets of products actually eaten by men for 7 days. The content of the main nutrients and energy was calculated from the tables of the chemical composition of food products (14,15).

The results obtained were compared with the average daily rational norms of food consumption for the population of the Republic of Uzbekistan (SanPiN - 0105-01; SanPiN: Sanitary rules and regulations - 0250-08) (13).

To study the nutritional status in the clinic, a clinical and outpatient examination was conducted simultaneously, including clinical blood and urine tests, as well as a biochemical blood test with the determination of amylase, total protein, albumin, fibrinogen, bilirubin, creatinine, cholesterol in its serum. The obtained data were subjected to statistical processing on a Pentium 1V Microsofi office Excell – 2003 computer.(4,7).

Research results and discussion. When studying the quality of nutrition according to a questionnaire survey, the diets of obese men were characterized by a predominance of bakery, fatty and salty foods, low physical activity; unhealthy eating habits - systematic overeating, adherence to cheap high-calorie foods (fatty, flour, sweet, "fast food"); decreased metabolic processes of the body due to age; violations in the endocrine system; stressful and depressive states that have led to both changes in eating habits and metabolic disorders. There was a high content of saturated fats, salt and sugar in the daily diet against the background of non-compliance with nutrition standards for fresh vegetables and fruits (dietary fiber deficiency in the diet was 80%). In the main group, the content of meat and meat, fatty products (red meat, lamb meat, smoked sausages, chickens, sausages, etc.) in the diets is significantly higher than normal. It was noted that 48% of the surveyed 40-year-olds with obesity consume fatty foods (pilaf, kovurdok, kebabs), fast foods, hamburgers, hot dog, fried potatoes, Coca Cola, fanta and other soda drinks. were consumed daily during meals. One of the factors determining the

development of obesity, an important role is given to physical activity, which plays an essential role in the formation and functioning of a healthy organism. Among the surveyed 35% of men from 40 to 50 years of age are engaged in light gymnastics in the morning (10 minutes). Men from 50 to 55 years of age regularly engaged in physical exercises. 65% of men aged 40 to 50 years, 80% of men aged 45 to 55 years are around the TV after dinner and watch TV shows, movies, etc. 34% of men aged 40-50 work around a computer during the day. The analysis of the provision of men with basic foodstuffs showed that the actual nutrition of men with obesity is generally not balanced and is deficient in some foods, due to the characteristic irrational hierarchy of food sets. According to the questionnaire survey, the diets of obese men are characterized by a predominance of bakery, flour-grain and confectionery products, a high content of saturated fats, salt and sugar was noted in the daily diet against the background of non-compliance with nutrition standards for fresh vegetables and fruits (dietary fiber deficiency in the diet was 80%). The study of the provision of men with basic foodstuffs of men in the control group showed that the average daily consumption of meat and meat products is significantly higher than normal, milk and dairy products, eggs and fish, vegetables, berries and fruits, as well as vegetable oil is significantly lower than normal (Table 1).

Table 1

The average daily set of basic foods in the diets of obese men aged 40 to 55 years of age

Products, g *	Norma * g	Obese men (BMI 25-29, and above)		Men without obesity (BMI 18-24, I)	
		Winter-spring period	Summer-autumn period	Winter-spring period	Summer-autumn period
Meat and meat products (calculated as meat)	150	169 (112,7)	162 (108,0)	148 (98,7)	140 (93,3)
Milk and dairy products (calculated as milk)	491	480 (97,8)	420 (85,5)	410 (83,5)	380 (77,4)
Fish and fish products	35	25 (71,4)	22 (62,9)	19 (54,3)	16 (45,7)
Eggs, pcs	1,0	0,9 (90)	0,8 (80)	0,8 (80)	0,7 (70)
Bread and bakery products (in terms of bread)	314	495 (157,6)	443 (141,1)	427 (136,0)	398 (126,8)
Potato	181	238 (131,5)	221 (122,1)	215 (118,8)	196 (108,3)

Animal fat	21	30 (142,9)	28 (133,3)	19 (90,5)	16 (76,2)
Vegetable oil	16	18 (112,5)	17 (106,3)	15 (93,8)	14 (87,5)
Vegetables and gourds	296	250 (84,5)	300 (101,4)	275 (92,9)	318 (107,4)
Fruits and berries	325	230 (70,8)	340 (104,6)	245 (75,4)	330 (101,5)
Sugar and confectionery (in terms of sugar)	67	85 (123,2)	76 (110,1)	70 (101,4)	65 (98,5)

* When compiling the table, the recommended set and the number of products for one day according to SanPiN 0105-01 and 0250-08 are taken into account

In the main group, the content of meat and meat products (sausage, sausages, etc.) in the diets is much higher than the norm. In a week without restriction, fast-foods (hamburgers, hot dogs, french fries, etc.) were consumed by obese men. Ration calculations showed that the excess consumption of meat and meat products in children over the age of 12.1% in the winter-spring period, 8% in the summer-autumn period, and in the control group there is a shortage of these products by 1.3 and 2.75%.

Among dairy products, milk, cheese and feta cheese and cottage cheese turned out to be in obvious deficit; the range of these products included mainly kefir, kurt (a product made from salted curd), kaimak, and sometimes curdled milk, especially in the winter-spring period and, accordingly, below the recommended norms, the deficit ranged from 39.2% to 45.0%, and in summer-autumn period from 29.8 to 37%., and in the control group of the above products were not found in the diet of kaymak, kurt, but milk and dairy products, however, were below the norm by 16.6 and 22.6% . The deficit of vegetable fat (mainly cottonseed) turned out to be relatively small. In some cases, there was even an excess of the norm of fats, mainly of animal origin. The largest excess of animal fat consumption was 2-4 times. Butter, lamb and beef were used as animal fat. A clear deficiency (almost 2 times less than the norm) in the consumption of vegetables, melons, fruits and berries was found in obese men and in the control groups.

Fried potatoes turned out to be a favorite dish for every third surveyed, which exceeded the norm by 30 and 22%, in the control group it also exceeded the norm by 18 and 8%. Sugar and confectionery in the main group increased by 23 and 30%, in the control group by 1.4% in the winter-spring period, and in the summer period the deficit is 1.5%.

Analysis of the collected data showed that the energy value of the diet of obese men was 27% higher than in the control group, due to the excessive

consumption of high-calorie foods: saturated fats, salt and sugar, as well as bakery products (Table 2).

The calculation of the biological value of the diets of obese men showed that the content of total protein is 1.2 and 1.4% higher than the norm. In the control group, in the winter-spring period, the protein deficiency was 4.7%, and in the summer-autumn period, 2.2%. The diet was dominated by fats of animal origin, which amounted to 66.5±1.3%, i.e. 6.7% higher than the norm in the winter-spring period, (62.7±2.1) 10.0% higher than the norm in the summer-autumn period. In the control group (51.5±1.7) by 9.6% and (50.8±1.2) 8.2% below the norm. In comparison with the data of the control group, the consumption of animal protein significantly prevailed in obese children and adolescents (P>0.001).

When analyzing food intake, the most negative changes, characterized by an increase in the absolute and relative fat content, were noted in obese men. The content of fats in the daily diet exceeded the physiological norms by 30.8 and 20.0%, and in the control it was below the norm by 3.7 and 2.2%. The optimal ratio of consumption of fats of vegetable and animal origin is the content of animal fat in the daily diet is less than 21%, and vegetable fat is more than 16%. The diet was dominated by fats of animal origin, which amounted to 121.6±4.2 (130.8) in the winter-spring period, 111.6±4.9 (120.0) in the summer-autumn period, with a norm of 21.

The level of consumption of animal fat significantly differed from that in the control group and was 1.2 times higher (P> 0.001.) According to Olson R.E. (2000) the excess of fat in the daily diet by more than 30-40% of energy requirements leads to obesity, and also contributes to the development of metabolic syndrome, sugar insulin and dependent diabetes.

The main sources of fat in the diet were: fatty fast food meat products (fatty pilaf, fried meat products, flour dishes with fat, smoked meat and chicken, fast foods: hot dogs, hamburger, daily scrambled eggs (breakfast), hot dishes and etc., from dairy products (kaimak, sour cream) Despite their calorie content, fast foods, hamburgers are not very nutritious, contain a large amount of animal fat and are very poor in B vitamins and dietary fiber. An excess of saturated fatty acids increases the concentration of cholesterol and the development of coronary heart disease.Dietary cholesterol also has a significant effect on blood cholesterol levels (15).

The problem of qualitative and quantitative consumption of carbohydrates deserves special attention. In the compared groups, in the diets of actual nutrition, an excess of the amount of carbohydrates was noted: in obese men by 32.5 and 25%, and in the control group by 10 and 3%. Compared to the control group,

58.9% of obese men significantly more often dominated the consumption of carbohydrates (P>0.001).

A high content of mono and disaccharides in the daily diet was revealed, apparently due to the availability of high-calorie confectionery products (cake, muffins) for obese men. The structure of consumed sugars did not meet sanitary standards and recommendations for a balanced diet: an increase in the consumption of refined products in relation to polysaccharides was revealed. The main suppliers of simple carbohydrates were sugar and sugar-containing foods. As you know, the supply of energy with these sugars is not accompanied by the supply of essential nutrients, which leads to the displacement of foods with nutritional value (polysaccharides, proteins) from the diet. When assessing micronutrients in the daily diet, the following indicators were revealed: in the main group, the calcium content was slightly higher than the norm (by 4 and 5%); (in the control group - below the norm by 28.4%), 1.1 times the recommended level of magnesium, probably due to an excess of cereals, (in the control group - below the norm by 21 and 17%); the phosphorus content corresponded to the norm (in the control it was below the norm by 17.8 and 19.8%).

When assessing micronutrients in the daily diet, iron deficiency was detected, the intake of which was 13.3±2.4 and 13.8±2.8 mg/day in obese men, 12.6±2.9 and 13.1 in the control group. ±2.1 mg/day at the required level of 16.5 mg. The content of iodine in the diet of men is below the norm, despite the use of only iodized salt in recent years. An analysis of the daily intake of vitamins in obese men revealed a reduced intake of vitamins A, E and C compared to the norm, and their combined use is known to be a powerful antioxidant factor (13). The content of vitamin A in the diets of obese men was below the norm in the winter-spring period by 53.3%, in the summer-autumn period 47.8, and in the control group 62.0 and 58.0%. The content of vitamin B1 in obese men exceeded the norm by 41.7, and in the control group by 33.3%; vitamin B2 is below the norm by 1.2-1.5 times (29%), and in the control group by 1.5 times (28.5%). The content of vitamin PP in the diets of the main group was above the norm by 10 and 5%, and in the control group below the norm by 7.6% and 4%. 2-7%.

Reduced levels of vitamin C content in the diet were established. Our studies showed that the deficiency of vitamin C- (ascorbic acid) in the body of obese men ranged from 20 to 22.5%, and in the control group up to 20.0%. (Table 2.).

Table 2

The average daily content of the main nutrients in the diets of obese men (45-55 years old) (M ± m), abs. (% of the norm).

Nutrients	^ Norm	Obese men, BMI 25-29.9 and above (% of normal)		Non-obese men, BMI 18-24 (% of normal)	
		Winter-spring period	Summer-autumn period	Winter-spring period	Summer-autumn period
Proteins, g	93	100±3,8 (107,5)	95±3,2 (102,2)	90,0±3,5* (96,8)	88±3,1* (94,6)
including animal	57	68,5±3,3 (120,2)	66,7±2,7 (117,0)	50,0±2,6 *** (88,7)	48,0±2,1*** (84,2)
Fats, g	93	131,1±4,4 (141,0)	120,6±3,7 (129,8)	99,0±3,2*** (106,5)	90,0±2,8* (96,8)
Carbohydrates, g	395	600,0±18,6 (151,9)	580,7±16,7 (147,0)	412,8±11,6*** (104,5)	405,4±10,7*** (102,6)
Calorie content, kcal	2787	3770,0±33,2 (135,3)	3600,0±29,8 (129,2)	2800,5±22,7*** (100,5)	2787,7±25,1*** (100)
Vit A, mg	0,9	0,54±0,03 (60,0)	0,55± 0,04 (61,1)	0,45±0,02* (50,0)	0,40±0,03** (44,4)
Vit C, mg	70	57,7±3,4 (82,4)	60,6±3,1 (86,6)	54,8±2,9 (78,3)	55,5±2,8 (79,3)
Vit B1, mg	1,4	1,9±0,05 (135,7)	1,8±0,06 (128,6)	1,7±0,05** (121,4)	1,6± 0,04** (114,3)
Vit B2, mg	1,6	1,5±0,04 (93,8)	1,8±0,03 (112,5)	1,6± 0,03* (100,0)	1,8±0,05 (112,5)
Vit PP, mg	25	30,8±2,5 (123,2)	28,3± 2,2 (113,2)	26,0±2,4 (104,0)	28,0±2,4 (1121,0)
Calcium, mg	1200	1300,0±20,6 (108,3)	1250,0±19,7 (104,2)	961,0±18,5*** (80,1)	988,0±19,4*** (82,3)
Magnesium, mg	300	320,0±8,8 (106,7)	330,0±9,1 (110,0)	240,0±7,3*** (80,0)	251,0±7,6*** (83,7)
Phosphorus, mg	1800	1880,0±22,6 (104,4)	1899,0±23,8 (105,5)	1668,0±19,4*** (92,7)	1647,0±18,3*** (91,5)
Iron, mg	16,5	18,3±1,6 (110,9)	17,8±1,7 (107,9)	16,0±1,4 (97,0)	17,0±1,6 (103,0)

Note: ^ - when compiling the table, the recommended set and the number of products for one day according to SanPiN 0105-01 and 0250-08 were taken into account;
* - compared with the nutrition of children of the main group (* - P<0.05, ** - P<0.01, *** - P<0.001)

The low content of vitamins A and C in the diet of the examined children correlates with the proportion of vegetables, fruits, and berries.

The main indicator that is used to diagnose and assess the severity of obesity is the body mass index - the ratio of body weight in kilograms to the square of height in meters. Normally, it ranges from 18.5 to 25.0. Criteria for the diagnosis of overweight and obesity are body mass index values of 25.0-29.9.0 and > 30.0, respectively (16). When assessing the nutritional status, it was found that among the surveyed main group, 25 surveyed men had obesity of the 2nd degree, in 10 patients of the 3rd degree, in the rest of the 1st degree. BMI was 32.2+1.10.

Hip circumference 109.8±0.66 cm; waist circumference 107.3±0.89cm, fat mass 89.1±1.06%. In the control group, overweight and obesity were not detected. The physical performance of the surveyed compared with the men of the control group was reduced. In the study of total protein and albumin in the blood, slight changes were revealed, that they corresponded to the norm, indicators of nitrogen metabolism (blood urea) were also normal. Indices of blood glucose, taken on an empty stomach in the morning, exceeded the permissible level by 2% -3% (in 13 men with grade 11 obesity).

The analysis of the diet revealed a number of features. So, on average, 68% of obese men violate the diet: four meals with a long interval (5-6 hours), high energy value of food taken in the evening up to 45-58% (of the total daily calorie content). 42% of the surveyed take food 1-2 hours before going to bed. Revealed low physical activity, prevailing food intake at night, the predominant carbohydrate nature of nutrition. In the control group, the diet is more established. Both the assortment list of products and the structure of nutrition had a fundamental difference on weekdays and weekends.

It should be noted that only 10 to 15% in both groups, 45% of men have an idea about rational nutrition. Wives are sources of information about healthy eating (in 52% of cases). Only 10-15% have sources such as the media and medical personnel. Only 22% of men (control group) could independently and objectively assess their diet.

One of the factors determining the development of obesity is physical activity, which plays a significant role in the formation and functioning of a healthy body. Among the surveyed, 35% of men from 40 to 50 years of age do light gymnastics in the morning (10 minutes). Men between 50 and 55 years of age did not exercise regularly. 65% of men aged 40 to 50 years of age, 80% of men aged 50 to 60 years of age after dinner are near the TV and watch television programs, movies, etc. 34% of men aged 40-50 during the day work about computer.

Thus, the analysis of the nutrition of obese men showed not only quantitative and qualitative inferiority, but also non-compliance with hygiene standards in almost all respects. A more pronounced imbalance of nutrients in their diet is a

significant risk factor for the development of functional disorders in men and requires mandatory correction.

CONCLUSIONS:

1. The diet of obese men is characterized by quantitative and qualitative inferiority. Actual nutrition is inadequate to energy costs in the direction of their excess, is characterized by a high level of consumption of animal fats and carbohydrates and is not fully adequate in terms of the content of vegetable fats, polysaccharides, fiber, a number of vitamins (A, E and C) and minerals.

2. The nutritional status of obese men is inadequate for age and gender norms: body mass index, waist and hip circumference are above normal.

3. The diet is disturbed in the form of irregular meals, eating late in the day, massive consumption of high-calorie foods: saturated animal fats, salt and sugar.

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PREDICTION OF LONG-TERM NEUROLOGICAL CONSEQUENCES OF CORONAVIRAL INFECTION USING NEUROTROPIC AUTOANTIBODIES

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ABSTRACT

Today, amid the ongoing COVID-19 pandemic, it has become clear that SARS-CoV-2 infection can have long-term consequences, even after asymptomatic or mild acute cases, raising concerns about the consequences of COVID-19. The terms “long-COVID-19”, “chronic COVID-19”, “post-COVID-19 syndrome” have appeared. Patients who have had COVID-19 often have fatigue, cognitive and psycho-emotional disorders, which are often referred to as "brain fog", and the possibility of developing neurodegenerative diseases is also discussed. The exact pathophysiological mechanisms of the development of the neurological long-term consequences of COVID-19 have not been established, but at the same time, numerous links are emerging between the post-COVID-19 syndrome, immunological changes, and neurotransmission dysfunction in the brain. Using method of immunochemical analysis ELI-Neuro-Test, developed by Professor A.B. Poletaev, we analyzed an individual profile of serum immunoreactivity, depending on changes in the relative content of IgG autoantibodies directed to 12 autogens of the nervous system. We identified in patients who underwent COVID-19 immunochemical signs of damage to the GABAergic (58.6%), opioid (37.9%), serotonergic (20.7%), cholinergic (13.8%) neurotransmitter systems, and also markers of axonal damage (20.7%), demyelination (10.3%) and reactive astrogliosis (24.1%). However, given the small sample size, further research is required.

Key words: COVID-19, nervous system, neurotropic autoantibodies, early diagnosis, ELI-Neuro-Test.

INTRODUCTION

At the end of 2019, the SARS-CoV-2 virus was discovered in China, which caused a new disease – COVID-19 and the second viral pandemic in human history. More than 420 million cases of the disease have been registered, the pandemic continues to grow, it is believed that the number of unreported cases of infection is several times higher. More than 35% of COVID-19 patients develop neurological symptoms [31], such as anosmia, ageusia, headaches, dizziness, cognitive decline, seizures, depression, as well as acute cerebrovascular disease, acute disseminated encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, Guillain-Barre syndrome and etc. Neurological complications of COVID-19 are caused not only by cytokine storm, hypoxia, disorders in the hemostasis system, but can also be a direct result of the neurovirulent properties of SARS-CoV-2 [43]. Some scientists suggest that all viruses can reach the CNS under the right conditions depending on viral factors (mutations in specific virulence genes) and host factors (immunosuppression, age and comorbidities) [21]. To date, several studies provide direct evidence for SARS-CoV-2 neurotropism [13]. The receptor for the entry of SARS-CoV-2 into the host cell is ACE2 [17]. ACE2 is expressed in most areas of the brain [7]. RNA of SARS-CoV-2 was detected in brain dissection samples [35] and in the cerebrospinal fluid of patients with COVID-19 [46]. Immunological detection in preparations of brain organelles revealed the presence of the membrane (M) protein SARS-CoV-2 mainly in the soma of neurons, as well as in neurites [5]. Electron microscopy also demonstrated the presence of SARS-CoV-2 in neurons [42]. These facts point to the neuroinvasive properties of SARS-CoV-2.

It is known that some neurotropic viruses, such as the pathogens of measles, rubella, herpesviruses, retroviruses, can cause a disease of the nervous system several years after infection, and this list may be supplemented by SARS-CoV-2 in the future. So far, little is known about the long-term impact of COVID-19. Viruses with neuroinvasive properties activate the immune response in the brain and can cause long-term damage similar to those seen in some neurodegenerative diseases [47]. SARS-CoV-2 infection itself may be a factor contributing to the risk of developing neurological disorders throughout life [43]. In a pandemic, this poses the risk of a significant increase in patients with neurological disorders in the coming years.

It is clear that the clinical symptoms of damage to organs and systems may not appear immediately after the start of the pathological process, since the body has enormous compensatory capabilities. Even biochemical changes in the blood, although ahead of clinical manifestation, appear after the loss of a significant

number of cells in organs and tissues. It is appropriate to pose the question, is there a method that can reveal with great accuracy an increased risk of developing neurological disorders after the pathological process has started, but even before changes appear in the indications of traditionally used methods for early diagnosis of a developing neurological disease?

Our cells of organs and tissues are constantly, but at different rates, renewed, as well as the nervous system. This is not only about neurogenesis, the rate of which is incomparably slow relative to the rate of cell division in other organs. The brain not only of a child, but also of an adult is surprisingly constantly changing its structure, which is called neuroplasticity [14]. This process is based on the formation of new neural networks, new synapses (synaptogenesis) appear in the process of assimilating new information [39]; the connection between neurons is strengthened, which are activated during frequently repeated actions; and synapses that have not been used for a long time are lost (partial apoptosis of a neuron - its processes).

What happens to the remnants of dead organ cells, to the destroyed processes of neurons? They are phagocytosed [8]. But the set of phagocyte receptors is not provided for recognizing the entire variety of protein structures to be utilized. And here a very interesting point is observed - specific autoantibodies are attached to the protein components of the destroyed structures - a special label is put on the protein to be cleared in a peculiar way, through which the phagocyte unmistakably identifies and phagocytes the required object. Therefore, it is not surprising that normally all people have a large set of autoantibodies [30], corresponding to the set of proteins of the body, which was named by Professor A.B. Poletaev "Immunculus" [34], like the well-known homunculus of Penfield to neurologists. Although traditionally autoantibodies are associated with autoimmune diseases, they are present in minimal amounts in all healthy individuals [27]. As stated by the immunologist P. Matzinger [28], the main function of the immune system is precisely the recognition of harmful antigens (in our case, harmful decay products of cellular structures), regardless of infectious or non-infectious nature, and exogenous or endogenous origin. There is a whole spectrum of serum antibodies autoreactivity: from congenital poly-reactive IgM, which cleanse tissues of post-apoptotic debris [11] mainly arising from the constant renewal of tissue and cell structures, to conditionally pathological IgGs, which act as an adaptive mechanism for the selective purification of pathology-specific debris [30]. When, under the influence of various etiological factors, the process of cell destruction is accelerated, the immune system begins to produce more IgG autoantibodies so that the clearance process proceeds at an appropriate rate. This is a very important

point, since it is the increase in the levels of specific IgG autoantibodies that is the very early and sensitive marker indicating the start of the pathological process long before the appearance of biochemical preclinical shifts. Disease-induced changes in IgG autoantibody profiles can be identified and used as diagnostic biomarkers of diseases with a high degree of sensitivity and specificity [15, 29]. Since many diseases exhibit cell and tissue-specific damage, identification of characteristic disease-induced changes in autoantibody profiles can be used as a successful diagnosis for a wide range of diseases [30].

Patients after COVID-19 have been noted to have fatigue, cognitive and psycho-emotional disorders, and the development of neurodegenerative diseases is also discussed. The mechanism for the development of long-term symptoms has not been definitively established. Our goal was to study the involvement of different neurotransmitter systems in the pathological process in patients who underwent COVID-19 using neurotropic autoantibodies. We believe that this will help to better understand the pathogenesis of post-COVID syndromes, as well as change the traditional attitude towards neurotropic antibodies as exclusively pathogenic agents.

Methods

The method of immunochemical analysis ELI-Neuro-Test (registered in 2009 in the Russian Federation), developed by Professor A.B. Poletaev, makes it possible, long before the appearance of neurological symptoms, to predict diseases of the central nervous system with a high probability. According to the instructions, the ELI-Neuro-Test kit is used for the semi-quantitative determination of IgG autoantibodies that interact with antigens of neurons (NF200), glial cells (GFAP), nerve fibers (MBP) and neurotransmitter receptors by enzyme-linked immunosorbent assay. Using this method, an individual profile of serum immunoreactivity is analyzed, depending on changes in the relative content of IgG autoantibodies directed to 12 autogens of the nervous system: neurofilament factor (NF200), glial fibrillar acidic protein (GFAP), myelin basic protein (MBP), voltage-gated calcium channels (VGCC), calcium binding protein S100β, N-cholinergic receptors, glutamate receptors, dopamine receptors, serotonin receptors, GABA receptors, μ-opiate receptors, and β-endorphin. Such a multiparametric analysis eliminates the influence of the general reactivity of the immune system on the results of the study (this prevents false-negative results against the background of general immunosuppression and false-positive results against the background of general hyperactivation of the immune system).

It is known that the basis of the functioning of the nervous system is the synaptic transmission of the nerve impulse. The structural components that make

up the synapse have specific proteins. The presynaptic part is usually the terminal section of the axon. Axon-specific protein is phosphorylated neurofilament H (pNF-H/NF200), axon-covering myelin sheaths (oligodendrocytes) specific protein is myelin total protein (MBP), and voltage-gated calcium channels (VGCC) are specific for axon terminal thickenings. Specific proteins for postsynaptic membranes (to a lesser extent for presynaptic ones) are receptors for various neurotransmitters. In addition, synapses are enveloped by processes of astrocytes, which are involved in the regulation of their activity [1]. Characteristic proteins for astrocytes are the S100 protein and glial fibrillary acidic protein (GFAP). Thus, the set of autogens of the ELI-Neuro-Test panel makes it possible to comprehensively assess the state of neurotransmitter systems.

We examined blood serum samples from 29 apparently healthy adult patients (14 males and 15 females, aged 21 to 71 years) with a history of COVID-19 (confirmed by PCR with a nasopharyngeal swab test or serum testing for anti-SARS-CoV-2 antibodies) mild (17 patients) and moderate (12 patients) severity. At the same time, in order to minimize the effect of hypercytokinemia on the results of research, we selected persons who recovered from COVID-19 at least 2 months ago before the time of blood sampling. During acute infection, patients with COVID-19 experienced respiratory symptoms, fever, and non-specific nervous system symptoms (headache, dizziness, anosmia, ageusia). Patients with neurological complications of COVID-19, such as acute cerebrovascular accidents, acute encephalitis and encephalomyelitis, acute demyelinating processes, onset of neurodegenerative diseases, and convulsive syndrome, were excluded. At the time of the study, some patients complained of recurrent headaches, hyposmia, fatigue, and difficulty concentrating. Additional inclusion criteria were: a) the absence of neurological and psychiatric disorders prior to COVID-19, b) the absence of a previous diagnosis of chronic or current diagnosis of acute and chronic somatic and endocrine diseases that could potentially affect the nervous system, c) the absence of dyspnoea at the time of examination, d) no treatment with corticosteroids, antihistamines, antihypertensives, diuretics, hypnotic drugs at the time of study.

We determined the serum content of autoantibodies to 12 antigens of the nervous system using the ELI-Neuro-Test method on an enzyme immunoassay analyzer using the test kits of the same name manufactured by the Medical Research Center "Immunculus" (Moscow, Russian Federation). In the ELI-Neuro-Test kit, there is a mandatory control serum, which is used in parallel for each reaction setting (the kit contains panels designed to simultaneously determine the serum levels of autoantibodies of 3 patients and control serum). The calculation of

the results obtained was carried out using an appropriate computer program developed by the staff of the Medical Research Center "Immunculus".

Results and discussion

In our study, all serum samples showed a decrease in individual mean immunoreactivity (immunosuppression state), against which the absolute concentrations of all neurotropic autoantibodies were lower than in control serum, which did not allow the use of absolute values for interpretation. Therefore, the results of the study reflect deviations in the immunoreactivity of autoantibodies of each specificity, expressed as a percentage of the individual average level of serum immunoreactivity of the subject. The level of activity of the patient's immune system is taken as zero. In the normal state of organs and systems, there are only small dynamic fluctuations in serum concentrations of organ-specific autoantibodies ranging from -15% to + 10% around the individual average serum immunoreactivity.

In our study, 25 (86.2%) of 29 blood serum samples had a pathological profile of neurotropic autoantibodies (Table 1).

Table 1

Individual profiles of immunoreactivity based on serum levels of neurotropic autoantibodies in persons who have had an infection SARS-CoV-2.

Patients (age in years, gender)	anti-NF200	anti-GFAP	anti-S100β	anti-MBP	anti-VGCC	anti-N-Cholinergic receptors	anti-Glutamate receptors	anti-GABA receptors	anti-Dopamine receptors	anti-Serotonin receptors	anti-Opiate receptors	anti-β-endorphin	Number of rejected indicators
№1 (44, f)	-8%	28%	3%	-6%	-5%	-2%	-4%	6%	-9%	-1%	-5%	0	1
№2 (32, m)	1%	22%	-6%	-4%	-2%	0	-3%	11%	-8%	-7%	-5%	3%	2
№3 (59, m)	6%	3%	18%	-4%	-13%	1%	0	11%	-8%	-7%	-5%	4%	2
№4 (31, f)	-14%	-10%	-8%	19%	-11%	-4%	28%	5%	-7%	-1%	-8%	7%	2
№5 (33, m)	-10%	-1%	3%	-5%	-6%	-5%	6%	7%	2%	0	-3%	13%	1
№6 (39, m)	-5%	9%	1%	-4%	-7%	8%	0	0	-5%	4%	2%	-2%	0
№7 (69, m)	-8%	13%	7%	-8%	-6%	8%	4%	-1%	-6%	3%	-4%	-6%	1
№8 (31, f)	-11%	-6%	-1%	-1%	-4%	11%	3%	5%	-6%	5%	-4%	10%	2
№9 (57, f)	-26%	-16%	-4%	-2%	-5%	12%	4%	23%	4%	7%	0	3%	4
№10 (38, m)	-13%	0	-4%	-8%	-3%	9%	-2%	17%	1%	4%	-1%	5%	1
№11 (35, m)	-7%	1%	-3%	-1%	0	-3%	3%	12%	1%	2%	2%	-1%	1
№12 (31, m)	-12%	3%	-1%	-18%	-12%	8%	0	14%	-7%	5%	6%	15%	3
№13 (21, m)	-9%	-3%	-2%	-4%	-1%	1%	9%	6%	6%	3%	-1%	1%	0
№14 (30, f)	-9%	-3%	2%	0	-1%	1%	2%	5%	1%	6%	-1%	0	0
№15 (21, f)	-25%	-23%	-7%	-10%	-4%	-5%	2%	29%	3%	10%	17%	10%	6
№16 (22, f)	-8%	-2%	-7%	-11%	-3%	4%	3%	11%	2%	12%	-3%	4%	2
№17 (22, f)	-16%	-6%	6%	-16%	-4%	1%	-2%	31%	0	4%	-3%	10%	4
№18 (27, f)	-17%	-9%	-3%	-8%	-12%	18%	3%	17%	-4%	10%	-2%	13%	5
№19 (37, f)	-7%	8%	-1%	-8%	-5%	11%	1%	3%	-5%	9%	-3%	-3%	1
№20 (42, f)	-11%	8%	1%	-7%	1%	1%	-2%	15%	-1%	0	-5%	-4%	1
№21 (59, f)	-12%	-5%	-2%	-7%	-2%	1%	-2%	13%	0	12%	1%	2%	2
№22 (28, m)	-7%	5%	-2%	-6%	-3%	6%	-2%	13%	-3%	0	-3%	5%	1
№23 (71, f)	-12%	-4%	-2%	-11%	26%	1%	-15%	16%	-10%	-1%	2%	12%	3
№24 (21, m)	9%	-3%	-1%	-9%	-14%	-7%	-6%	4%	0	6%	-3%	20%	1
№25 (40, m)	-10%	8%	0	-8%	-10%	1%	4%	9%	-3%	6%	4%	0	0
№26 (48, m)	-14%	4%	-8%	-4%	-9%	3%	-5%	10%	-1%	5%	1%	16%	2
№27 (36, f)	-13%	-3%	-6%	1%	-4%	-2%	-1%	9%	2%	12%	4%	0	1
№28 (57, f)	-28%	-19%	-11%	-8%	-11%	6%	13%	28%	2%	9%	11%	9%	5
№29 (28, m)	-40%	-20%	-6%	-5%	-5%	-1%	9%	28%	13%	11%	3%	17%	6
Number of cases is higher than the individual norm		3 (10,34%)	1 (3,45%)	1 (3,45%)	1 (3,45%)	4 (13,80%)	2 (6,90%)	17 (58,62%)	1 (3,45%)	6 (20,69%)	2 (6,90%)	10 (34,48%)	48
Number of cases is below the individual norm	6 (20,69%)	4 (13,80%)		2 (6,90%)									12
Total number of cases of deviations from the individual norm	6 (20,69%)	7 (24,14%)	1 (3,45%)	3 (10,34%)	1 (3,45%)	4 (13,80%)	2 (6,90%)	17 (58,62%)	1 (3,45%)	6 (20,69%)	2 (6,90%)	10 (34,48%)	11 serum samples (37,93%)

* The level of activity of the patient's immune system is taken as zero. Deviations ≥10% or <(- 15%) may indicate an emerging or existing change in the respective structures.

The neurotropic properties of coronaviruses allow them to elude the host's immune response and reach a latency period. This makes them a potent contributor

to acute and late neurological effects [22]. SARS-CoV-2 can be dormant in the neurons of patients recovering from the acute effects of COVID-19, which increases the risk of long-term effects, causing demyelination and neurodegeneration [25]. Kumar et al. suggest that in the medium to long-term, an influx of patients with mental and cognitive problems who were otherwise healthy before contracting COVID-19 is expected. Early detection and prevention of neuropsychiatric and cognitive problems should be a long-term goal of health services and governments around the world, as this can be presented as next wave of a pandemic [22].

Although the exact mechanisms responsible for the long-term complications of SARS-CoV-2 infection remain unknown, there are a number of pathophysiological mechanisms that may explain the neurological long-term consequences of COVID-19, some of the proposed mechanisms include direct viral lesion, systemic inflammation, and cerebrovascular changes [9]. Of particular interest are data showing that neuronal cells express specific molecules that may act as immune receptors to modulate the innate immune response in the brain [4]. Since these molecules also play an important role in neuroplasticity and the organization of neural networks and synapses, such autonomous activation of neuronal cells using innate receptors during viral infections may compromise neuroplasticity and provoke subsequent neuronal dysfunction [47]. Also, neuroimmunological mechanisms may be involved in the development of long-term consequences of coronavirus infection, such as fatigue, impaired concentration, attention and memory, mood changes and sleep disturbances [41]. For example, autoantibodies targeting neurotransmitter receptors have the potential to cause depression-like symptoms [48]. Depression is often associated with various neurodegenerative disorders [12]. Depression correlates with decreased neurogenesis in adults [18]. Numerous clinical reports underscore the frequency of olfactory impairments in patients suffering from major depressive disorders [40]. Anosmia is associated with impaired neurogenesis [36]. New neurons formed in the subventricular zone in adulthood migrate to the olfactory bulb, where they finally differentiate into GABAergic inhibitory interneurons that contribute to olfactory function [24]. GABAergic transmission regulates neurogenesis in adults [33]. GABAergic deficiency linked to depression [26], along with serotonergic and dopaminergic neurotransmission disorders [10]. Adult hippocampal neurogenesis has been implicated in cognitive processes [2]. Several studies have identified the involvement of GABA in learning and memory [16, 20, 37]. Cortical GABAergic activity decreases in post-COVID-19 patients with cognitive disturbances and fatigue [45]. Fatigue is a dominant complaint in “long COVID” [38]. Fatigue is

considered as neuroimmune exhaustion [6]. Thus, there are numerous links between clinical symptoms, dysfunction of neurotransmitter systems and immunological disorders. Many scientists consider IgG autoantibodies to be potentially pathogenic, although there is a need to clarify causal relationships. For example, Vargas et al. demonstrated the importance of autoreactive IgG antibodies in the nervous system. Anti-myelin IgG contribute to the removal of tissue debris after damage to peripheral nerves, and in their absence, axonal regeneration is hampered [44].

The most informative pathological processes in the body can be reflected in changes in the ratio between different autoantibodies. According to the instructions of the ELI-Neuro-Test, which is intended for the simultaneous quantitative assessment of changes in the content of 12 neurotropic autoantibodies IgG, it can be used as an indicator of existing or emerging disorders in the nervous system. A steady rise in the production of specific autoantibodies IgG reflects the activation of the processes of apoptosis of specialized cells or the decay of subcellular structures. These immunological changes are the earliest sign of beginning pathological processes, which can reach the stage of characteristic clinical disorders only after a few months or even years.

In our small study, we identified in patients who underwent COVID-19 immunochemical signs of damage to the GABAergic (58.6%), opioid (37.9%), serotonergic (20.7%), cholinergic (13.8%) neurotransmitter systems, and also markers of axonal damage (20.7%), demyelination (10.3%) and reactive astrogliosis (24.1%). In general, this does not contradict the results of previous studies. According to other authors, the onset of cognitive symptoms after COVID-19 may indicate an underlying neurodegenerative process [22]; SARS-CoV-2 infection causes reactive astrogliosis in the central nervous system [23]; an increase in plasma GFAP levels may indicate damage to the central nervous system in patients with COVID-19 [19]; in COVID-19, cases of demyelinating Guillain-Barre syndrome have been reported [3, 32]; Versace et al. revealed a general decrease in cortical GABAergic and, to a lesser extent, cholinergic activity in post-COVID-19 patients using transcranial magnetic stimulation [45].

At the same time, the results of our study have some limitations, in particular, a small sample size reduces the reliability of our results; secondly, subclinical pathological processes reflected in changes in immunoreactivity profiles in reality, under certain circumstances, may not reach the stage of clinical manifestation; thirdly, most neurotransmitter systems have several receptor subtypes, sometimes with opposite effects, which is not taken into account in our method, this causes difficulties in interpreting the results obtained. But in general, we consider

Professor Poletaev's approach to diagnosing neurological diseases to be very promising and interesting.

Thus, changes in neurotropic autoantibodies reflect the pathological intensification of apoptosis of neurons and glial cells and their subcellular structures, which is the very first stage in the formation of neurological diseases, far ahead of the appearance of any other signs of damage to the nervous system. In our opinion, this will also help to capture the moment when functional disorders develop into structural changes, as well as to critically reconsider the blurred line between "functional disorders" and "morphofunctional disorders". The study of individual profiles of immunoreactivity according to the serum level of neurotropic IgG autoantibodies in patients who have undergone COVID-19 makes it possible to identify the onset of subclinical changes and predict the neurological long-term consequences of coronavirus infection, which, according to the results of our study, will mainly affect GABAergic, opioid, serotonergic and cholinergic neurotransmitter systems. Also, the use of this approach makes it possible to understand in more detail the violations of which neurotransmitter systems are associated with the existing clinical symptoms of long-COVID, which, in our opinion, provides an opportunity to select a more targeted treatment, but this requires further research.

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Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Abbreviations

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; ELI-Neuro-Test, enzyme-linked immuno-neuro-test; IgG, immunoglobulin G; IgM, immunoglobulin M; NF200, neurofilament factor; GFAP, glial fibrillar acidic protein; MBP, myelin basic protein; VGCC, voltage-gated calcium channels; S100β, calcium binding protein; GABA, γ-aminobutyric acid; CNS, central nervous system; PCR, polymerase chain reaction.

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ROLE OF GENITIC FACTORS IN PATHOGENESIS WITH COMPLICATED DUODENAL ULCER WITH BLEEDING

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ABSTRACT

Aim: Study N-acetyltransferase activity and type of acetylation in patients with and without complication of ulcer disease. **Methods:** N-acetyltransferase activity and type of acetylation were studied in 163 patients; of these 63 had noncomplicated and 65 had complicated ulcer disease, while 35 were healthy (control group). Eighteen patients with complicated ulcer disease had perforation, 18 bleeding, and 29 stenosis. Results: In our studies, in the examination of patients with complicated course of peptic ulcer disease according to the most important clinical symptoms, a relationship was found between the activity of the acetylation process and clinical and laboratory indicators of peptic ulcer complicated by bleeding, perforation, and pyloroduodenal stenosis.

Conclusion: Our results suggest that it would be useful to identify acetylation phenotype to aid prediction of the character and clinical course of gastric and duodenal ulcer disease. Peptic ulcer is a chronic recurring polyetiological disease that occurs as a result of the interaction of exogenous and endogenous factors: a hereditary predisposition from 5.5 to 50%, the type of nervous system, endocrine systems, psychoemotional features, metabolic characteristics, biochemical reactions, immune status, cytokine profile and environmental factors, resulting in a violation between the factors of “aggression” and “protection” of the mucous membrane of the gastroduodenal zone. In the etiology of peptic ulcer, a certain role is played by hereditary burden. Therefore, when studying the nature of the hereditary predisposition to peptic ulcer of the stomach and duodenum, an important area is the identification of genetic markers.

Key words: Helicobacter pylori, N-acetyltransferase, Gastric ulcer, Duodenal ulcer, Bleeding.

INTRODUCTION

Many issues of surgical tactics in gastric (GU) and duodenal ulcer (DU) remain controversial. This is due to the variety of options for the clinical course, timing and nature of complications. The development of prognostic criteria makes it possible to choose the most rational treatment tactics, in many patients to prevent relapses and complications, rather than affect the already frolicing severe pathological process.

Peptic ulcers account for 28% to 59% of nonvariceal upper gastrointestinal (GI) hemorrhage with duodenal ulcers responsible for 17% to 37% and gastric ulcers 11% to 24%.1 Peptic ulcer disease has reduced in prevalence, probably owing to improved nonsteroidal antiinflammatory drug prescribing practice, increased testing, and treatment of Helicobacter pylori infection in addition to more widespread use of proton pump inhibitors. However bleeding from peptic ulcers continues to result in significant morbidity and mortality, with the latter reported at 2% to 11%. Mortality for inpatients with upper GI bleeding is higher, owing to the increased comorbidities and older age of these patients. Over the years, endoscopic techniques and therapies have improved the management of peptic ulcer bleeding, with endotherapy becoming more accessible and technologically advanced. A 2007 audit of upper GI bleeding in the UK reported data on 6750 patients, 36% of whom had peptic ulcer bleeding.

Upper gastrointestinal bleeding is a medical condition routinely encountered in clinical practice. Overt upper gastrointestinal bleeding usually presents as melena or hematemesis but can also present as hematochezia in cases of brisk bleeding. The initial evaluation of a patient with suspected upper gastrointestinal bleeding begins with assessment of hemodynamic status, identification of potential risk factors, and appropriate triage of level of care. After resuscitation measures, endoscopic evaluation can be performed to diagnose and potentially treat the source of bleeding. Risk factors that increase the propensity for recurrent bleeding should be identified and addressed.

Upper gastrointestinal bleeding (UGIB) develops in the oesophagus, stomach or duodenum and has an incidence of 47/100,000. Lower GIB (LGIB) develops in the small bowel, colon or anorectum and has an incidence of 33/100,000. Where the incidence of UGIB has fallen, driven by helicobacter pylori eradication and the use of proton pump inhibitors, the incidence of LGIB may be increasing.

Acute upper gastrointestinal bleeding (UGIB) remains a public health burden with a persistent high mortality despite advances in modern day management. Proton pump inhibitors (PPI) as medical therapy is an attractive adjuvant to

endoscopic treatment in UGIB but the method and dose of PPI therapy remains controversial.

Peptic ulcer disease continues to be a source of significant morbidity and mortality worldwide. Approximately two-thirds of patients found to have peptic ulcer disease are asymptomatic. In symptomatic patients, the most common presenting symptom of peptic ulcer disease is epigastric pain, which may be associated with dyspepsia, bloating, abdominal fullness, nausea, or early satiety. Most cases of peptic ulcer disease are associated with Helicobacter *pylori* infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), or both. In this review, we discuss the role of proton pump inhibitors in the management of peptic ulcer disease, highlight the latest guidelines about the diagnosis and management of *H. pylori*, and discuss the latest evidence in the management of complications related to peptic ulcer disease, including endoscopic intervention for peptic ulcer-related bleeding. Timely diagnosis and treatment of peptic ulcer disease and its sequelae are crucial in order to minimize associated morbidity and mortality, as is prevention of peptic ulcer disease among patients at high risk, including those infected with *H. pylori* and users of NSAIDs.

Literature data on the prediction of ulcer complications are scarce. As prognostic criteria, various indicators are used that are associated with the pathogenesis of peptic ulcer. There is evidence that the development of complications is facilitated by the severe course of diseases with frequent relapses, a family ulcerative history, high acid-forming function of the stomach, and a decrease in the level of gastric mucus glycoproteins. The authors recommend clinical endoscopic data as prognostic criteria. In the etiology of peptic ulcer, a certain role is played by hereditary burden. In this regard, the approach to the study of N - acetyltransferase involved in the implementation of genetic information and the clarification of the relationship of hereditarily determined traits with ulcer pathology are fundamentally important. Recently, research has been carried out to obtain real biomodels and the creation of highly specific species primers for the N-acetyltransferase-1 and N-acetyltransferase-2 genes. According to published data, there is a correlation between the process of acetylation and the etiology and pathogenesis of a number of diseases: peptic ulcer of the stomach and duodenum, ulcerative colitis, heart failure, with infertility and peritoneal form of endometriosis, acute coronary syndrome, with pneumonia. And also, when studying the state of the processes of acetylation of a number of diseases, a correlation was revealed between the activity of these processes and the severity of diseases, as well as their progression.

Over the past few years, foreign and domestic gastroenterologies have claimed that peptic ulcer is a local infectious process caused by contamination of the mucous membrane of the stomach or duodenum of H. pylori (HP). In contrast, most scientists studying ulcer consider that the presence of hydrochloric acid in the stomach is one of the prerequisites for the occurrence of a peptic ulcer in the coolant or bulb of the duodenum. In the past and at present, in the treatment of ulcer, drugs that suppress the secretion of hydrochloric acid (antacids, H2 - blockers, proton pump inhibitors), as well as surgical interventions (ranging from various types of vagotomy to gastrectomy) are mainly used.

There are differences in geographical distribution (between West and Asia), time trends, sex and peptic ulcer ratio, seasonal rates and behavioral response. HP is one of the main causes of peptic ulcers; other environmental and genetic factors contribute to ulcer formation. It should be noted that, in addition to genetic factors, the environmental factor claimed an etiological role in peptic ulcer disease: non-steroidal anti-inflammatory drugs, cigarette smoking, stress and dietary factors.

Until the 19th century, ulcerative ulceration was a rarity, whether in the East or the West. The level of infection varies widely between Asians. It is low in Malays and Indonesians, in whom stomach ulcers and stomach cancer are rare. It is very high in India, where a duodenal ulcer is common, but a stomach ulcer and cancer are not. In the Chinese and Japanese, cancer is common, high, but the Chinese have a greater frequency of duodenal ulcer than the Japanese. It is believed that HPi is the main cause of ulcer, other environmental and genetic factors contribute to the formation of ulcers, supporting the concept of etiological heterogeneity.

Proponents of the infectious origin of ulcer consider the use of anti-Helicobacter pills as the main principle of its treatment. At present, numerous researchers have found that the number of patients with HP-negative forms is gradually increasing from 8 - 56%. Epidemiological studies have established that HP infection is widespread in the world: up to 60% of the population of all continents of the planet in all entic groups of the population is infected with HP, starting from childhood. About 70% of them, however, are healthy bacteria carriers, often throughout life. At the same time, gastric and duodenal ulcer affect only 12-15% of those infected with HP. The authors found in the gastric mucosa, in addition to HP and mucous microflora, which have adhesive properties and high virulence. Unfortunately, there is almost no discussion in the literature of the significance of mucosal microflora in the pathogenesis of ulcer and its relapses. Zimmerman et al. believe that the antiulcer drugs used not only act on HP, but also on mucous microflora. Tkachenko E.I. considers HP to be low virulent

bacteria, distinguishing them from highly virulent surgical infection. The authors of found that the cytotoxic gene is found in patients with ulcer, gastric cancer, gastroduodenal dyspepsia, with chronic gastritis, as well as in healthy bacteria carriers. Zimmerman et al. consider that the pathogenic HP strain has a cytotoxic effect when the body's immunity is reduced. According to the literature and our data, we can conclude that the role and importance of HP in the pathogenesis of ulcer in the literature are discussed debatably, the absence of HP in the gastric mucosa contributes to a deeper change in metabolic processes.

MATERIAL AND METHODS

Genitic factors were studied in 163 patients; of these 63 had noncomplicated and 65 had complicated ulcer disease, while 35 were healthy (control group). Eighteen patients with complicated ulcer disease had perforation, 18 bleeding, and 29 stenosis. N-acetyltransferase activity and type of acetylation were determined by micromethod modified by Bulovskaya L.N. Following on overnight fast, each subject was given orall sulfadimesin at a dose of 0.5 g for body weight up to 51 kg, 0.75 g for body weight of 51 - 83 kg and -1 g for body weight over 83 kg. The concentration of acetylated sulfademesin was determined in blood samples obtained five hours later with the degree of sulfadimesin acetylation determined by this method showing N-acetyltransferase activity. Subjects with acetylation activity lower than 50% were concidered as slow acetylators, while those who had acetylation activity higher than 50% were termed as fast acetylators. For evaluation of reliable differences, the criteria of nonparametric statistics was used. A thorough history wascollected from all patients and a comprehensive clinicallaboratory, endoscopic, functional examination was carried out. Statistical data processing was performed using Microsoft Office 2016

METHOD FOR DETERMINING THE PHENOTYPE OF N - ACETYLTRANSFERASE ACTIVITY

Along with the study of clinical and medical history data, all patients who received a complicated gastroduodenal ulcer underwent routine clinical and biochemical studies: a general analysis of blood and urine, residual nitrogen, urea, blood creatinine, total protein and its fractions, sugar, bilirubin (total, direct and indirect), blood enzymes (AST, ALT), electrolytes and blood chlorides, indicators of the coagulation system, diastasis of blood and urine. All patients underwent ECG, fluoroscopy or radiography of the lungs, and other studies as needed. The motor-evacuation function of the stomach (or its stump) was studied by X-ray examination of the stomach using barium sulfate. Esophagogastroduodenofibroscopy was performed for all patients and, if necessary, repeatedly in dynamics.

The acetylation phenotype was determined according to the Evans method in the modification of L. Bulovskaya. The method is based on the oral administration of sulfadimesin as a substrate of N - acetyltransferase, and the determination of reaction products in blood samples after 5 hours. Patients are given sulfadimezin orally on an empty stomach at a rate of 10 mg / kg body weight 2 hours after taking the drug, a light breakfast (1 cup of tea and bread), after 5 hours, take blood from a finger and determine the amount of free, acetylated and total sulfadimesin, then calculating the percentage of free sulfadimesin to total, which is an indicator of the activity of polymorphic N-acetyltransferase . 0.1 ml of whole blood or serum is introduced into a centrifuge tube with 1.4 ml of distilled water and the proteins are precipitated by pouring 0.5 ml of 20% trichloroacetic acid. The precipitate is carefully transferred with a glass rod and left for 5-10 minutes; then centrifuged for 20 minutes at 3000 rpm. 0.5 ml centrifuge in two identical tubes. In both test tubes, 0.1 ml of 4 p. HCL and one of them is placed for 45 minutes. in a boiling water bath for hydrolysis, then cooled at room temperature.

Then both tubes are cooled in the refrigerator at 40 ° C for 30 minutes. After cooling, diazotization and azo coupling are carried out: 0.1 ml of 1% ammonium sulfamic acid is poured into the samples, shaken and after 2 minutes 0.2 ml of 0.1% NED are added. Samples are left in the dark for 60 minutes, periodically shaking, and photometric on a photo-calorimeter - MKPM at a wavelength of 540 nm in a socket with an optical path length of 10 mm. For the calculation, a calibration curve is constructed using a standard solution of sulfadimezin with a concentration of 2.5; 5; 7.5 and 10 mcg. In hydrolyzed samples, total sulfadimesin is determined, and in non-hydrolyzed samples it is determined free, the amount of acetylated sulfadimesin is calculated by the difference. The type of acetylation is determined by the ratio of the activity of the enzyme N-acetyltransferase, expressed as a percentage. The level of N-acetyltransferase activity is determined by the percentage of sulfadimesin acetylation in the blood.

RESULTS AND DISCUSSION

The distribution of the acetylation phenotype in the control group and in the group of patients under consideration is presented in Table 1. When studying the activity of N-acetyltransferase, the bimodal distribution of the sulfadimesin acetylation phenotype was established in both healthy individuals and patients with uncomplicated peptic ulcer disease. In the control group, 68.6% of slow and 31.4% of fast acetylators were detected.

Among the examined individuals with uncomplicated peptic ulcer disease, patients with a slow type of acetylation predominated, and the ratio of slow and fast acetylators was 87.3 and 12.7%. The enzyme activity in slow acetylators in the control group ranged from 0 to 20%, in fast - from 50% to 60%. (table 1). The

average level of N-acetyltransferase activity in this group for slow acetylators was 15.0%, for fast - 53.3%.

Table 1.

Change in the ratio of slow and fast acetylators and level acetylation in patients with uncomplicated duodenal ulcer (M±m).

Researched groups	number of subjects		Acetylation activity, %	
	“slow”	“fast”	“slow”	“fast”
Control, n=35	24 (68,6%)	11 (31,4%)	15,0±1,12	53,3±1,8
Noncomplicated ulcer disease, n=63	55 (87,3%)	8 (12,7%)	22,0 ±1,36*	63,0 ±2,81*

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

Results of N-acetyltransferase activity determination showed that gastroduodenal ulcer occurred both among subjects with slow acetylation and those with fast phenotype. However, there were significant differences in frequency of the presence of both phenotypes between the study and control group (table 1). Thus, in the group of healthy subjects, the number of subjects with slow and fast acetylation type accounted for 68.6% and 31.4%, respectively. In patients with noncomplicated ulcer disease, there was a relative increase of slow acetylators by 27.3% and decrease of fast acetylators by 59.6% comparing with the control group (table 2).

During the progress of ulcer disease and development of complications one directional changes were noted in the proportion of slow and fast acetylators. Thus, in patients with nonperforated gastroduodenal ulcers there was increase in slow acetylators of 37.6% and a decrease in fast acetylators of 82.2% in comparison with the control group, - - and of 8.1 and 56.0% respectively, in comparison with noncomplicated ulcer disease. In patients with gastroduodenal ulcer complicated by bleeding, the increase in slow and decrease in fast acetylators was 13.7% and 30.0%, respectively, in comparison with the control group. However, in contrast to the non - perforated group of patients, when comparison with non-complicated ulcer was made, the decrease in the number of slow acetylators was 10.7% and the increase in fast acetylators was 73.2%.

In patients with pyloroduodenal stenosis, an increase in slow acetylators of 20.6% and decrease in fast acetylators of 44.9% was noted in comparison with control subjects, while noncomplicated ulcer disease slow acetylators decreased by 5.3%, and fast acetylators increased by 36.2%.

Table 2.

Percentage of changes between slow and fast acetylators and acetylation level in patients with gastroduodenal ulcer

Study groups	number of subjects				Acetylation activity, % (means±SEM)	
	"slow"		"fast"		"slow"	"fast"
	n	%	N	%		
Control, n=35	24	68.6	11	31.4	15.0±1.12	53.3±1.8
Noncomplicated ulcer disease, n=63	55	87.3	8	12.7	22.0 ±1.36*	63.0 ±2.81*
- bleeding, n=18	14	78	4	22	26.0 ± 3.8**	55.0 ± 3.12

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

Along with change in proportion of slow and fast acetylators in noncomplicated and complicated ulcer disease, the increase in N-acetyltransferase activity level was noted at the limits of its phenotype in both slow (by 46.7%) and fast (by 18.2%) acetylators in the group of patients with ulcer disease, complicated with bleeding, the acetylation level of which did not differ from the control group.

In patients with gastro-duodenal ulcer complicated by perforation, acetylation activi-ty was 26.7% hiqher in slow acetylators and 50.7% hiqher in fast acetylators than control subjects. However, it should be noted that in comparison with indicators in patients with noncomplicated ulcer disease, the acetylation level in slow acetylation type patients with perforated ulcer was 13.6% lower. At the same time, the average level of N-acetyltransferase activity in fast acetylators in this group was the highest, exceeding the acetylation le-vel of noncomplicated ulcer disease patients by 27.5%. The average level of enzyme activity in slow acetylator patients with ulcer disease complicated by bleeding, was also highest, ex-ceeding control levels by 73.3%, and noncomplicated ulcer disease levels by 18.2%. Acetylation activity was 40.0% higher in slow acetylators with pyloroduodenal stenosis than control pati-ents and 17.3% higher in fast acetylators, but levels were stable in uncomplicated ulcer disease.

Results showed changes in levels of N-acetyltransferase activity associated with in-dividual fluctuations of sulfadimesin acetylation activity in patients with noncomplicated and complicated ulcer disease, ranging from 0% -49.0% in slow phenotypes, significantly higher than changes in healthy subjects (from 0% to 20%). In fast acetylators, healthy subjects activity changes ranged from 50% -

59%, whilst they were significantly higher (50% - 80%) ($p<0.05$ by Rosenbaum Q criteria) in patients with ulcer disease.

Fluctuations in individual levels of sulfadimesin acetylation activity in patients with complicated ulcer disease showed an interrelationship between the development of complica-tions of ulcerative pathology and change of N-acetyltransferase activity.

According to the literature, individual levels of N-acetyltransferase activity in humans are stabilized by control of gene-modifiers [11]. On the basis of this evidence, it may be suggested that an increase in levels of N-acetyltransferase activity in progressive ulcera-tive pathology, reflects a change in the control of gene-modifiers.

Differences and changes of acetilation actyvity in slow and fast acetylators, leads us to conclude that patients with complicated ulcer disease and fast phenotype of acetylation have a different predisposition to the complications of ulcer disease. Current evidence suggest that fast acetylators are heterogeneous and those with heterozygote heredity acetylate slower than homozygotes [11,12]. It may therefore be concluded that heterozygotes prevailed in the group of patients with complicated ulcer. In this context it is clear why, in spite of an increase in N-acetyltransferase activity during the development of complicated ulcer disease, enzyme activity in patients with bleeding does not exceed control levels.

An increase in the average level of N-acetyltransferase activity in the group of patients due to the appearance of individuals with an “intermediate” phenotype. The results obtained suggest the pathogenetic role of acetylation in the pathogenesis of uncomplicated peptic ulcer of the stomach and duodenum.

When studying the state of the processes of acetylation of a number of diseases, a correlation was revealed between the activity of these processes and the severity of diseases, as well as their progression. An increase in N-acetyltransferase activity was observed within its phenotype as the tumor process progressed [17], an increase in the adhesion process was noted in women with high activity of the N-acetyltransferase enzyme [3,4,7,18], and an increase in acetylation with the progression of lymphogranulomatosis in children [4,7,11,15,16].

Based on literature data, we investigated the activity of acetylation processes in patients with peptic ulcer disease with complications of bleeding, perforations, and pyloroduodenal stenoses.

The results of the study showed (table 3) unidirectional changes in the ratio of slow and fast acetylators in the group of patients with gastroduodenal bleeding

compared with those in the group of patients with uncomplicated peptic ulcer disease.

Table 3.

Change in the ratio of slow and fast acetylators and acetylation levels in patients with bleeding gastroduodenal ulcer (M±m).

Study groups	number of subjects		Acetylation activity, %	
	"slow"	"fast"	"slow"	"fast"
Control, n=35	24 (68,6%)	11 (31,4%)	15,0±1,12	53,3±1,8
Noncomplicated ulcer disease, n=63	55 (87,3%)	8 (12,7%)	22,0 ±1,36*	63,0 ±2,81*
Complicated ulcer disease: - perforated, n=18	14 (78,0%)	4 (22,0%)	26,0 ± 3,8**	55,0 ± 3,12

Notes: Differences reliability * in relation to control;
** in relation to noncomplicated ulcer disease by Rosenbaum Q criteria (P<0,05).

There was also an increase in the number of slow and a decrease in fast acetylators in this group compared with the control, which amounted to 13.7 and 29.9%, respectively. The change in the average level of N-acetyltransferase activity is associated with significant individual fluctuations in sulfadimesin acetylation activity in patients with bleeding and slow acetylators (from 0 to 49%), which is significantly ($p < 0.01$) higher than the fluctuations in the group of healthy individuals (from 0 to twenty%). In the fast type, the indicators of acetylation activity were at the level of control data.

When comparing indicators with a group of patients with uncomplicated ulcers, a difference was found in the ratio of phenotypes: a decrease in the number of slow acetylators by 10.7% and an increase in fast ones by 73.2%. The average level of enzyme activity in slow acetylators among patients with peptic ulcer complicated by bleeding exceeded the control level in uncomplicated ulcers by 18.2% ($p < 0.01$).

Thus, acetylation processes play a role in the development of complications of peptic ulcer bleeding: a large predisposition of fast acetylators to the development of bleeding and the appearance of individuals with an "intermediate" phenotype.

Along with a change in the phenotype ratio, a slight increase in the average level of N-acetyltransferase activity was noted in this group compared with the control data. Among slow acetylators, the enzyme activity did not differ from that in the group of patients with uncomplicated ulcers, and among fast acetylators, a significant increase in enzyme activity was noted compared with the

uncomplicated course of peptic ulcer disease (p <0.01). When analyzing individual fluctuations in acetylation activity in slow acetylators, it should be noted that 52.9% of patients had activity ranging from 0 to 9%, and 47.1% patients had activity ranging from 20% up to 49%, i.e. had an intermediate phenotype.

Thus, as the results showed, a perforated ulcer developed mainly in slow acetylators. However, its development is not excluded also in fast acetylators, but, apparently, with a very high level of activity of acetylation processes. The development of perforated ulcers in slow acetylators is more characteristic of patients with the lowest enzyme activity (from 0 to 9%) and with an “intermediate” phenotype, the enzyme activity of which ranged from 20% to 49%

It is known that numerous factors can significantly change the intensity of acetylation, including the treatment of diseases. Thus, according to [12,17], a decrease in N-acetyltransferase activity was observed with successful chemotherapy in patients with malignant lymphomas and after radical surgery in patients with lung and gastrointestinal tract cancer, and with successful treatment and improvement of the condition of sick children with lymphogranulomatosis, a decrease in N- acetyltransferase activity [8,12].

The results of studying the activity of acetylation after traditional therapy for patients with peptic ulcer disease showed that the average level of enzyme activity decreased by 53%.

Thus, traditional therapy and surgical intervention contribute to a decrease in the level of N-acetyltransferase activity in patients with gastroduodenal ulcer. In some cases, in the course of all types of treatment, the acetylation phenotype changes: fast to slow and slow to fast.

It is known that the majority of diseases are based on changes in the chemical homeostasis of the body, the causes of which are metabolic disorders in chemical compounds. A very important enzyme system supporting internal chemical homeostasis is the N-acetylation system. Violation of the metabolic function of this system leads to serious negative consequences. This is confirmed by data on the close relationship between the activity of acetylation processes and clinical indicators of the course of individual pathological conditions [8,10].

In our studies, in the examination of patients with complicated course of peptic ulcer disease according to the most important clinical symptoms, a relationship was found between the activity of the acetylation process and clinical and laboratory indicators of peptic ulcer complicated by bleeding, perforation, and pyloroduodenal stenosis [7].

CONCLUSIONS

1. This study showed that noncomplicated and complicated gastro-duodenal ulcer occur-red in patients with both slow and fast phenotype of acetylation, and that the incidence of both phenotypes differs from healthy controls (increase in slow acetylators and decrease in fast acetylators). Moreover, there an increase in the average level of acetylation was noted in the study group patients.

2. Moreover, there an increase in the average level of acetylation was noted in the study group patients.

3. A more significant increase in levels of N-acetyltransferase activity in slow acetylators was found in patients with ulcer disease complicated by bleeding, than among fast acetylators in patients with perforated ulcer.

4. In conclusion, our results suggest that it would be useful to identify acetylation phenotype to aid prediction of the character and clinical course of gastric and duodenal ulcer disease.

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MOLECULAR AND CELLULAR MECHANISMS OF ACTION OF SORBENTS USED IN MEDICINE

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ABSTRACT

The article provides an overview of the literature data on the effectiveness of the use of sorbents of various origins in diarrhea with various etiological causes. Enterosorbents, despite their very ancient use in medicine, are still relevant drugs. The use of this group of drugs has gone far beyond gastroenterology and makes it possible to effectively help patients with various diseases, including such "diseases of civilization" as cardiovascular pathology, disorders of lipid and carbohydrate metabolism. It is very valuable that the natural and safe composition of drugs, especially of domestic production, is also useful for healthy people in order to prevent diseases of the digestive system and prevent metabolic disorders: it allows achieving a higher quality of life - a priority task of medicine.

Key words: intoxication, diarrhea, sorbents, diagnosis, treatment, pathobiochemistry.

INTRODUCTION

Intestinal intoxication is poisoning that occurs when the body is unable to cope with the influence of toxic substances on its own. With intestinal intoxication, the body continues to secrete enzymes that are incompatible with the normal operation of its systems. The symptoms of intoxication are very extensive and have different expressions. Their manifestations are due to the nature of the toxic substance, physical and chemical properties, affinity to certain organs, systems of physiology, subcellular structures, body tissues, enzymes produced and available receptors. It can be stated that infectious diseases still occupy a significant place among the causes of mortality of the population worldwide [1]. Intoxication can

be exogenous, when toxins enter the human intestine from the outside, and endogenous - when toxins appear as a result of a violation of the organ itself. The degree of intoxication depends on how much of the toxic substance has entered the human body. At the same time, it is important not so much how much of the toxin was absorbed, but what dose of it was absorbed and distributed through the body through the blood.

Common causes of intoxication are poisoning:

- medicines;
- alcohol, tobacco, narcotic substances;
- due to the release of decay products by parasites.

Clinical manifestations are determined by the gastrointestinal tract (GT) lesion syndrome: dyspepsia, vomiting, diarrhea, abdominal pain of various localization [2]. Each toxin causes specific symptoms, but the leading symptoms in this condition are most often diarrhea (diarrhea).

Diarrhea (diarrhea or loose stools) is a rapid emptying of the intestine, usually with an increase in the amount of feces and a change in their consistency (dilution), sometimes with the appearance of pathological impurities (mucus, blood). Diarrhea can be acute or chronic [3].

Acute diarrhea is a sudden increase in stool up to 3 times / day, usually accompanied by a change in its consistency. Only E.coli has six pathological species that can cause acute diarrhea [4].

Chronic diarrhea - frequent stools more than 3 times / day, lasting longer than 1 month.

The causes of acute and chronic diarrhea can be different conditions:

Causes of acute diarrhea:

- Acute intestinal infections (viral, bacterial, parasitic)
- Food toxicoinfections
- Poisoning with certain substances or medications
- Neuropsychiatric disorders ("bear disease")
- Intoxication caused by internal factors (uremic diarrhea

Causes of chronic diarrhea

- Inflammatory bowel diseases (ulcerative colitis, Crohn's disease)
- Taking certain medications (laxatives, antibiotics, iron preparations, etc.)
- Malignant tumors of the gastrointestinal tract
- Hyperthyroidism, AIDS
- Infections (giardiasis)
- Variants of the syndrome of impaired absorption (celiac disease, pancreatic diseases, etc.)

- Functional motor disorders (irritable bowel syndrome).

Based on the features of pathogenetic mechanisms, four types of diarrhea are distinguished: secretory, hyperexudative, hyperosmolar, hyper- and hypokinetic.

Secretory diarrhea is caused by increased secretion of sodium and water into the intestinal lumen. A classic example is diarrhea in cholera, the causative agent of which, cholera vibrio, multiplies only on the surface of the epithelium of the small intestine, but the cholera toxin disrupts intracellular regulation, as a result, the intestinal epithelium begins to actively secrete water with electrolytes into the lumen. Hypersecretion of water and electrolytes is also caused by toxins of other bacteria (Salmonella, Escherichia, klebsiella), enteropathogenic viruses, bile acids, prostaglandins and other biologically active substances. The secretory form is characterized by painless, abundant water diarrhea, calculated in liters per day.

Hyperexudative diarrhea is characteristic of inflammatory bowel diseases. It develops with bacterial OCI caused by shigella, salmonella, clostridium, Escherichia, etc. bacteria. In this case, they are also called invasive (English invasion - invasion, invasion). The stool is liquid, often with pathological impurities (mucus, blood, pus). Similar diarrhea is also observed in non-infectious diseases: ulcerative colitis, Crohn's disease, malignant intestinal tumors.

Hyperosmolar (osmotic) diarrhea develops due to malabsorption in the small intestine. Of the infectious agents, it is most often caused by rotaviruses, which multiply in the epithelium and disrupt the activity of enzymes of the intestinal mucosa. Because of this, disaccharides cannot split into monosaccharides and be absorbed. Disaccharides remain in the intestinal lumen and attract water. Under the influence of intestinal microflora, disaccharides ferment with the formation of gases (flatulence) and water, which leads to pain and "watery" diarrhea.

Hyperosmolar diarrhea is observed with malabsorption syndrome, with a deficiency of digestive enzymes (congenital enteropathy, chronic pancreatitis, etc.). With osmotic diarrhea, the stool is plentiful, liquid, often contains a large amount of half-digested food residues.

Hyper- and hypokinetic diarrhea occurs with an increase or decrease in intestinal motility, which is accompanied by a violation of the transit of intestinal contents. Hyperkinetic diarrhea is caused by neurogenic factors (stress), laxatives, secretin, pancreosimin, gastrin, prostaglandins and serotonin. This type of diarrhea is characteristic of patients with irritable bowel syndrome. With hyperkinetic diarrhea, the stool is liquid or mushy, frequent, but not abundant. Hypokinetic diarrhea is less common and is associated with excessive bacterial contamination of the small intestine.

Etiology and pathogenesis

Various factors lead to the activation of enterocyte adenylate cyclase, further increases intracellular cAMP, which leads to disruption of the transport of Na and Cl ions through the membrane of enterocyte cells with their accumulation in the intestinal lumen. After that, there is an intense secretion of fluid into the lumen of the digestive canal, copious watery diarrhea, vomiting.

Mechanisms of diarrhea development:

- increased secretion of electrolytes by the intestinal epithelium, causing massive fluid loss (secretory diarrhea);
- decreased absorption of electrolytes and nutrients from the intestinal lumen, developing due to damage to the brush border of the epithelium of the large or small intestine (exudative diarrhea);
- increased osmolarity of intestinal contents due to deficiency of saccharolytic enzymes and lactose intolerance (hyperosmolar diarrhea);
- violation of intestinal motor activity (hyperkinetic diarrhea).

Antibiotic-associated diarrhea caused by the proliferation of Clostridium difficile against the background of suppression of the growth of normal microflora is well known. This diarrhea is mixed – exudative and secretory.

Antibiotic-associated diarrhea is a complex of symptoms that develop against the background of quantitative and qualitative changes in the composition of the intestinal microflora during antibiotic therapy. The incidence of such a complication, according to various authors, is 5-39%. It is also known that when a patient takes six or more drugs at the same time, the probability of adverse reactions reaches 80% [5]. A decrease in the number of anaerobes against the background of antibacterial therapy leads to a violation of the metabolism of carbohydrates and fiber. Accumulating in the lumen of the large intestine, carbohydrates and fiber contribute to the secretion of water and electrolytes. As a result, osmotic diarrhea develops. Some anaerobic bacteria are involved in the metabolism of bile acids in the intestinal lumen. When antibiotics suppress such bacteria, there is a violation of the cleavage of bile acids. An excess of primary bile acids leads to secretory diarrhea. One of the mechanisms of the development of diarrheal syndrome against the background of antibiotic therapy can be attributed to the direct effect of an antibiotic on intestinal motility. Thus, macrolides are stimulators of motilin receptors. Such stimulation causes a contraction of the antrum of the stomach and duodenum and leads to such clinical manifestations: spastic abdominal pain, vomiting and diarrhea.

One of the common causes is also poisoning with ethyl alcohol. Poisoning with ethyl alcohol for a long period occupies a leading place among household poisoning by the absolute number of deaths.

Alcohol has a toxic effect on a number of human organs. Alcohol-related mortality is, according to WHO, 6.3% in men and 1.1% in women [6]. However, this is the average data for the world, whereas in a number of countries, alcohol mortality rates can reach a very high level. Disorders of the gastrointestinal tract are an indispensable attribute of acute alcohol intoxication and post-intoxication. They are manifested by acute pain in the stomach and diarrhea. Diarrhea in this condition is a consequence of a rapidly occurring lactase deficiency and the associated decrease in lactose tolerance, as well as impaired absorption of water and electrolytes from thin substances [7] substances. Alcoholic beverages worsen the absorption of nutrients from food, disrupt many links of metabolism in the body: proteins, carbohydrates, fats, mineral salts. As a result, acidic products accumulate in organs and tissues, the acid-base balance is disturbed, and this leads to serious metabolic disorders[7]. The strength of ethanol depends on the dose, tolerance to the toxicant (liver hypertrophy) and the degree of individual expression of isoenzymes, depending on the genome. With ethanol poisoning, glycogenolysis develops; nausea, vomiting and dehydration are characteristic. Thiamine deficiency is typical due to malabsorption.

Toxins have a damaging effect on membranes and receptors, in particular, affecting the subunits of G-proteins that mediate signal transmission from the receptor to the effector structures of the cell. One of the subunits of the cholera toxin penetrates into the cell and catalyzes the attachment of ADP-ribose to the GS protein, the manifestation of GTP-phosphatase activity of the aS subunit is inhibited, dephosphorylation of GTP does not occur, the cycle of functioning of the GS protein stops at the stage of activation of adenylate cyclase, the increased activity of which persists for a long time. Excess cAMP accumulates in the cells of the intestinal epithelium, causing the secretion of electrolytes and water into the intestinal lumen, damage to intestinal cells occurs, dehydration of the body and death after a few hours (8).

Antihistamines. Histamine is a neurotransmitter capable of influencing the gastrointestinal tract (intestinal colic, stimulation of gastric secretion), smooth muscles of the intestine [9]. There is an opinion that it is antihistamines that can cause the most severe and complex form of intoxication of the body. After all, it often happens that during the course of an allergy, a person can take more pills, and sometimes even take two or more different antihistamine pills at a time that are incompatible with each other. Symptoms of antihistamine poisoning: general

weakness, severe dilation of the eyeball pupil, manifestation of hallucinations in humans, causeless mental agitation, nausea, vomiting, diarrhea. Under the action of various damaging factors, the non-selective permeability of the CPM and intracellular membranes for electrolytes and water increases, the systems of passive and active electrolyte transport are disrupted. A decrease in the activity of Na+/K+-ATPase leads to an increase in the intracellular content of Na+ ions and leakage of K+ ions. Stoichiometry of Na+/K+-ATPase under optimal conditions 3/2/1 (during hydrolysis of one ATP molecule, three Na+ ions are removed from the cell and two K+ ions enter the cell). A decrease in the potassium content in the cell leads to a decrease in this ratio to 1/1/1, the membrane potential decreases and the intracellular sodium content increases. The hydrate number of the K+ 25 ion is 10.5, and the Na+ ion is 16.6 water molecules per ion, i.e. Na+ are characterized by greater hydrophilicity compared to K+, therefore, an increase in the intracellular content of Na+ leads to cell hydration. An increase in the concentration of intracellular Ca2+, associated with a decrease in the activity of Ca2+-ATPase and Na+/Ca2+-ion exchange mechanism, leads to the opening of highly selective Ca2+-dependent potassium channels and an increase in the rate of leakage of K+ from the cell, which is accompanied by further development of cell hydration. Hyperhydration of the cell can cause excessive stretching of the CPM and intracellular membranes, followed by their damage (osmotic cell death). Despite the widespread prevalence of OCI, many aspects of their pathogenesis in adults have been studied extremely insufficiently.

For the correction of gastrointestinal disorders developing in acute diarrheal infectious diseases, eubiotics, enzyme preparations, antispasmodics and a number of other groups of medicines are used in clinical practice, among which enterosorbents have been given increasing importance in recent years.

Enterosorbents (gr. enteron-gut; lat. sorbens - absorbing) are substances with a high sorption capacity that do not break down in the gastrointestinal tract, effectively binding and removing endogenous and exogenous toxic compounds, supramolecular structures and cells from the body, used for the treatment and prevention of diseases [10,11,12]

Enterosorbents as therapeutic agents have been known since ancient times. Even the healers of Ancient Egypt, India, Greece used charcoal, clay, crushed tuffs, burnt horn inside for the treatment of poisoning, diarrhea, jaundice and other diseases, as well as externally for the treatment of wounds. Healers of Ancient Russia used birch or bone charcoal. Avicenna (Abu Ali ibn Sina) in his Canon of Medical Science, out of the seven postulates of the art of preserving health, put the method corresponding to the modern understanding of enterosorption in the third

place. The researcher I.e. Lovitz (1785), studying the chemical properties of charcoal, justified its use for the same purposes.

The most important medical requirements for modern enterosorbents are a high sorption capacity relative to the components to be removed and the ability to sorb molecules and bacterial cells of different sizes and weights, the absence of toxic and traumatic effects on the mucous membranes of the gastrointestinal tract; they must be well evacuated from the intestine and not cause loss of useful ingredients, not have a negative effect on the secretion processes and intestinal microflora. As it passes through the intestine, the bound components should not be desorbed. Enterosorbents should not penetrate the gastrointestinal mucosa, therefore, they do not have systemic pharmacokinetics. Preparations for enterosorption should have a convenient dosage form and have good organoleptic properties [13].

The role of sorption materials in medicine is significant. Due to its developed porous structure, carbon materials are effectively used for detoxification of the body and are used for hemo-, enterosorption and application. They bind toxic substances on their surface and remove them from the body naturally, through wound discharge, etc. [14]. However, the use of non-selective sorbents significantly complicates their predicted use and can lead to negative consequences, in particular, due to the nonspecific sorption of substances useful for the body - hormones, vitamins, enzymes. Therefore, the development and use of selective and biospecific sorbents has become an urgent direction in the development of sorption therapy methods.

With the help of polymers with molecular imprints in biomedical research, medicinal substances (phenytoin [15], theophylline [16], propranolol [17], 7-hydroxycoumarin [18], bupivacaine [19], antibiotics (ampicillin [20], gatifloxacin [21]), acyclovir [22], celecoxib [23], berberine [24] and tizanidine [25]), biological markers (epinephrine [26], cholesterol [27], glutathione [28]), toxicants (bisphenols [29], hydroxypyrene [30]), narcotic substances (tetrahydroxycannabiol and its metabolites [31]) and phytoestrogens (biohanin A, daidzein and genistein [32]).

The interaction of sorbents with the removed components is realized in four main ways: adsorption, absorption, ion exchange and complexation [33,34]. During adsorption, the interaction between the sorbent and the removed substance occurs at the interface of the media. Absorption is the process of absorption of a substance by a liquid sorbent as a result of dissolution. Ion exchange is the process of replacing ions on the sorbent surface with sorbate ions. The pathogenetic

mechanisms of enterosorption depend on the type of sorbent and the structure of the sorbed particles.

Sorbents have different properties and may differ in a number of features [35].

By dosage form and physical properties: granules, powders, tablets, pastes, gels, suspensions, colloids, encapsulated materials, food additives

According to the chemical structure, sorbents can be divided into several groups:

1. Carbon sorbents (activated carbon, Carbolong, Carbovite, Carbospherite, saturated spherical carbonite - SCN, Anthralene, etc.).

2. Silicon containing enterosorbents (Polysorb, Sillard P, white clay, Smekta, Neosmectin, etc.).

Natural and synthetic enterosorbents are distinguished among silicon-containing enterosorbents. Of the natural ones, the most famous is white clay, the suspension of which has enveloping and adsorbing properties. In addition to white clay, smectites and sodium montlorilonites, etc. are used in medicine.

Of the synthetic enterosorbents, currently the most widely used preparation is a synthesized gel of methylsilicic acid hydroxide. Having a high sorption activity, it is characterized by a selective action: binds and removes only medium-molecular toxic substances.

The main characteristics of enterosorbents are: 1) the sorption capacity indicator is the amount of substance that can absorb the sorbent per unit of its mass; 2) the ability to bind molecules of different sizes and weights, as well as bacterial agents; 3) the active surface of the enterosorbent is the total area of the adsorbing surface per unit mass of the drug [36].

The main route of administration of enterosorbents is oral, sometimes enterosorbent is administered through a probe when the patient is unable to take the drug on his own or there are obstacles due to esophageal stenosis or pyloric stomach. With probe administration, the sorbent can be withdrawn (usually with an exposure of up to 30 minutes) and a new portion of the drug is introduced. Sometimes, according to indications, enterosorbents are injected with enemas into the colon.

The mechanisms of action of enterosorbents are divided into 4 groups:

1. Intestinal absorption of exotoxins, xenobiotics, bacteria, bacterial and endogenous toxins

2. Contact effect on the structures of the gastrointestinal tract.

3. Elimination of endotoxins from the internal environment of the body into the intestinal cavity.

4. Enhancement of metabolism and elimination of endotoxins by natural detoxification organs [37].

The therapeutic effect of enterosorbents is carried out as a result of their direct and indirect effects on pathogenetic mechanisms.

The direct action of enterosorbents is aimed at binding and elimination from the gastrointestinal tract of toxic metabolic products and the inflammatory process, pathogenic bacteria and their toxins, viruses, biologically active substances, binding gases formed in excess during the putrefactive process.

The indirect effect is due to the prevention or weakening of the clinical manifestations of endotoxicosis, toxic-allergic reactions, diarrheal syndrome. The use of enterosorbents reduces the metabolic load on the liver and kidneys, contributes to the normalization of the motor, evacuation and digestive functions of the gastrointestinal tract, has a positive effect on the functional state of the immune system [38].

Enterosorption is included in the group of efferent therapy means (Latin efferens - to remove), i.e. therapeutic measures aimed at stopping the action of toxins of various origins and their elimination from the body. Enterosorption in intestinal infectious diseases is a pathogenetically justified method of therapy.

Targeted clinical studies on the effectiveness of domestic enterosorbents were started in the mid-80s of the last century [39]. At that time, only carbon sorbents were used in practice, which, along with positive properties, had a relatively small sorption capacity and side effects and a number of contraindications. The creation of new drugs derived from other groups of sorbents has expanded the possibilities of using enterosorption in the complex treatment of OCI. The first of them was Enterodesis, a drug of low molecular weight polyvinylpyrrolidone, which was used in the complex therapy of 144 patients with OCI (men - 71, women - 73), 124 of whom were diagnosed with food toxicoinfection, 20 - shigellosis. In 105 (72.9%), the course of the disease was of moderate severity, in 37 (25.9%) — mild, in 2 (0.015%) — severe. The drug was prescribed, as recommended by the manufacturer, in dissolved form (5 g in 100 ml of water) 2-4 doses per day for 3 days. The therapeutic effect was registered in all patients: abdominal pain, flatulence, nausea, vomiting were stopped; after 6-12 hours from the start of treatment, body temperature normalized in 75.6% of patients. Parenteral rehydration was not required in all patients treated with enterodesis on the first or second day of the disease. The pronounced clinical effect, the absence of adverse reactions (also controlled by laboratory biochemical studies) made it possible to include this drug in the complex of remedies for the treatment of patients with acute diarrheal infections.

According to infectious disease doctors and pediatricians, timely, i.e. early use of enterosorbents in acute infectious diarrheal diseases of an invasive type has a rapid and pronounced detoxification, hypothermic and antidiarrheal clinical effect [40].

Such results were obtained with the combined use of enterosorbents with antibacterial drugs or probiotics in the treatment of OCI. According to some authors, the clinical efficacy of enterosorbents in mild and moderate forms of OCI is not inferior to antibacterial drugs widely used in clinical practice [41,42].

A. A. Novokshonov et al. (2002) used enterosorbent for the treatment of 60 children with mild and moderate forms of OCI, of which 40 patients received the drug as a means of etiotropic monotherapy (20) or in combination with furazolidone (20). It has been established that "etiotropic" monotherapy with enterosorbent is more effective than treatment with furazolidone, and significantly increases when they are used together in the treatment of moderate forms of acute bacterial etiology of an invasive type of diarrhea. Along with the rapid and pronounced detoxification clinical effect, the sanitizing effectiveness of combination therapy also increased markedly: repeated seeding of the causative agents of AKI was not registered, while with furazolidone monotherapy, a third of patients had repeated seeding of salmonella and Pseudomonas aeruginosa at the end of the 5-day course. The authors note that "the high antibacterial activity of enterosorbents not only contributes to the rehabilitation of the gastrointestinal tract from pathogens, but also can have an indirect immunomodulatory effect due to detoxification and prevention of antigenic overload of the immune system, which creates favorable conditions for the relief of the infectious process [43].

In the complex treatment of 63 patients aged 19 to 34 years who were admitted to the hospital with a diagnosis of "food toxicoinfection", we also used enterosorbent. As a control, a group of 23 patients who met the age and other criteria of the first group, received detoxification and rehydration therapy, was observed. Due to the fact that according to the clinical and epidemiological characteristics confirmed by laboratory studies, the etiological agents were opportunistic bacteria or rotaviruses (in 14), antibacterial drugs were not prescribed to patients. All patients were admitted in a state of moderate severity. Enterosorbent treatment was carried out in accordance with the manufacturer's recommendation: 2-3 tab. 3 times a day an hour before meals and taking other medications. The duration of use of the drug averaged 4 ± 0.3 days. As a result, in patients receiving enterosorbent, a decrease in the duration of fever and manifestations of intoxication was registered to 2.3 ± 0.4 days, in the control group this indicator was 3.2 ± 0.3 days ($p > 0.05$), the duration of diarrhea decreased,

which in the groups under consideration was 1.6 ± 0.5 and 2.8 ± 0.7 days, respectively ($p > 0.05$). The use of enterosorbent contributed to an earlier cessation of pain syndrome - after 1.4 ± 0.2 days ($p < 0.05$), which in patients of the control group lasted up to 2.6± 0.3 days, the time of disappearance of such manifestations as flatulence was less - 1.9±0.2 days ($p<0.05$), in the control group - up to 3.7±0.4 days, lethargy and anorexia 1.8±0.3 and 3.1± 0.4 days ($p<0.05$), respectively. The tolerability of the drug was good, no adverse reactions were noted. Thus, the inclusion of enterosorbent in the complex treatment of patients with food toxicoinfections had an obvious therapeutic effect, expressed in a reduction in the time of disappearance of manifestations of intoxication and functional disorders of the gastrointestinal tract.

The given examples of the use of the drug indicate the good effectiveness of an enterosorbent based on hydrolysis lignin - a polymer of plant origin with a high sorption capacity, capable of removing toxins, pathogenic microorganisms, and their waste products from the body, as well as contributing to the restoration of microflora and normalization of intestinal motility. Drugs of this group are actively being introduced into medical practice, especially in pediatrics, because they can be prescribed to children starting from infancy.

In the domestic manuals on infectious diseases, manuals for doctors and special scientific literature of recent years, recommendations on the use of enterosorbents in the complex treatment of acute infectious diarrheal diseases are constantly present [44].

However, it should be noted that the list of recommended drugs is relatively small. There is little information about their use in intestinal infectious diseases of a viral nature, which, as many researchers have shown, occupy a significant share among diarrheal diseases. Thus, compared to the previous year, the incidence of rotavirus gastroenteritis increased by more than 50%, the Norwalk virus was registered 1.8 times more often [45]. In this regard, more studies have been conducted by infectious diseases pediatricians, which is quite natural given the wider spread of viral diarrheal diseases among children. Currently, specific immunoglobulins, interferon inducers and immunomodulatory drugs are used as etiotropic therapy agents for these diseases, and probiotics and enterosorbents are used for etiopathogenetic therapy. It should be borne in mind that not all known enterosorbents are effective enough for viral diarrheal diseases, but some of them have a noticeable etiotropic effect, which is due to the ability to sorption and elimination of viruses and opportunistic bacteria from the intestine. A number of enterosorbents (dioctahedral smectite, preparations based on hydrolysis lignin) prevent the introduction of viruses through the protective intestinal mucosal

barrier, absorb excess disaccharides, intestinal gases, reduce flatulence and abdominal pain caused by it; normalize the absorption of water and electrolytes, the composition of the intestinal microflora; have a pronounced detoxification and antidiarrheal clinical effect.

N. Mazankova et al. [46] noted a noticeable positive effect when using an enterosorbent of natural and artificial origin in the treatment of OCI in children, where the etiological agents were bacteria and rotaviruses. Enterosorbents were prescribed to patients from the moment of admission against the background of oral rehydration and diet therapy. Already from the first days of treatment, a positive effect of sorbents on general toxic and local OKA syndromes was noted in the form of fever relief, reduction in the frequency or complete cessation of vomiting, improvement of appetite, elimination of abdominal pain and flatulence, reduction of the frequency of defecation and improvement of the general condition of patients. According to V. F. Uchaykin et al. (2008), the inclusion of another well-known enterosorbent drug (dioctahedral smectite) in the complex therapy of AKI of viral (osmotic) and viral-bacterial etiology (invasive osmotic type of diarrhea) in children, it contributes to the faster disappearance of symptoms of intoxication and exicosis, fever, relief of flatulence, abdominal pain and diarrheal syndrome.

Most modern enterosorbents are known to practitioners of various specialties. However, many registered enterosorbents have not yet found wide application due to various reasons: due to insufficient awareness of doctors of medical institutions about the role of enterosorbents in the treatment of infectious and non-infectious diseases of the gastrointestinal tract, ignorance of the advantages and disadvantages of certain sorbents in a particular pathology and the actually existing skeptical attitude of doctors to enterosorption. In one of the conclusions of Academician of the Russian Academy of Sciences V.F. Uchaykin et al. [47], who have extensive experience in the use of enterosorbents, it is said that "in gastroenterological pathology, including acute respiratory infections, enterosorbents are a means with multifaceted effectiveness, determined not only by their pathogenetic (detoxification, antidiarrheal, etc.), but also etiotropic action against both pathogenic bacteria and viruses."

In the domestic manuals on infectious diseases, manuals for doctors and special scientific literature of recent years, recommendations on the use of enterosorbents in the complex treatment of acute infectious diarrheal diseases are constantly present [48]. However, it should be noted that the list of recommended drugs is relatively small. There is little information about their use in intestinal infectious diseases of a viral nature, which, as many researchers have shown,

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Thus, enterosorbents, despite their very ancient use in medicine, are still relevant drugs. The use of this group of drugs has gone far beyond gastroenterology and makes it possible to effectively help patients with various diseases, including such "diseases of civilization" as cardiovascular pathology, disorders of lipid and carbohydrate metabolism. It is very valuable that the natural and safe composition of drugs is also useful for healthy people in order to prevent diseases of the digestive system and prevent metabolic disorders: it allows achieving a higher quality of life - a priority task of medicine.

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