eISSN 2181-1326
9 772181 132009

CAJM

Central Asian Journal of Medicine

Tashkent Medical Academy Press

eISSN: 2181-1326

Scientific Journal

This journal had been publishing since 2018

1
2023

MINISTRY OF HIGHER AND SECONDARY SPECIALIZED EDUCATION OF THE REPUBLIC OF UZBEKISTAN

2030 | UZBEKISTAN RESEARCH ONLINE

OAK.uz Supreme Attestation Commission at the Cabinet Ministers of the Republic of Uzbekistan

Digital Commons Network

Google Scholar

Ministry of Health of the Republic of Uzbekistan
Tashkent Medical Academy

Central Asian Journal of Medicine

№ 1 / 2023

Tashkent

1083
certificate

Central Asian Journal of Medicine

№1/2023

Journal edited and printed in the computer of Tashkent Medical Academy editorial department

Editorial board of Tashkent Medical Academy

Head of the department: M.N. Aslonov

English language editor: A.Kh. Juraev

Designer corrector: S.R. Sultonova

Organizer: Tashkent Medical Academy

eISSN 2181-1326

9 772181 132009

Central Asian Journal of Medicine

POTENTIAL ROLE OF A PREDICTIVE BIOMARKER IN THE PROGRESSION OF FATTY LIVER DISEASE

Dinora A. Parpiboyeva[1], Nodirbek Sh. Ergashov[2], Muharram A. Musayeva[3], Xikmat Q. Boltaboyev[4]

1 MD, Associate Professor, Head of the Department of Clinical modelling of Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: parpibaeva.d.a@gmail.com

2 Assistant of the Clinical modelling department of Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: Nodirbek_tta@mail.ru

3 Assistant of the Clinical modelling department of Tashkent Medical Academy, Tashkent, Uzbekistan

4 Assistant of the Clinical modelling department of Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in industrialized countries, affecting about 25.24% of the general population. NAFLD is a benign disease, but it can develop into more serious diseases, including non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and finally hepatocellular carcinoma (HCC). Liver biopsy is still the gold standard for diagnosing NAFLD. Due to the risks associated with liver biopsy and the inability to apply it on a large scale, it is now necessary to identify non-invasive biomarkers that can reliably identify patients at increased risk of progression. Thus, in this review, we report on biomarkers used in clinical practice for diagnosing NASH as well as for staging fibrosis, and secondly, we draw attention to new biomarkers, miRNAs, long non-coding RNAs, for diagnosing and staging fibrosis. This review discusses the potential role of miRNAs in the pathogenesis of fatty liver disease.

Key words: biomarkers; miRNA; NAFLD, intestines, triglyceride, glycemia, fibrosis.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in industrialized countries, and this is associated with an increase in morbidity and mortality. NAFLD is a hepatic manifestation of the metabolic syndrome, which is

considered systemic disease, as it affects various organs, including the pancreas [1], kidneys, adipose tissue and intestines [2,4]. It is estimated that NAFLD affects about 25% of the total population [5], although the actual prevalence is unknown due to the lack of specific and sensitive diagnostic tests. NAFLD includes several pathological conditions ranging from from simple steatosis to non-alcoholic steatohepatitis (NASH), the latter characterized by non-hemorrhagic inflammation of the liver and rapid progression towards fibrosis, cirrhosis and, finally, hepatocellular carcinoma (HCC) [5,8]. Liver biopsy is still the gold standard for differentiating simple steatosis from NASH and stages of fibrosis. Over the past few years, the identification of non-invasive biomarkers Differentiating simple steatosis from NASH and stages of fibrosis has become one of the most prevalent research objectives in the field of hepatology. This question is very important because the high prevalence of NAFLD in the general population, the potential for progression to more serious disease, and the inability to use liver biopsy on a large scale dictate large-scale studies.

Biomarkers. The diagnosis of NAFLD includes the definition of hepatic steatosis (defined as the histological presence of triglyceride accumulation in 5% of hepatocytes) as an exception there was a selection among those examined with liver damage not taking or taking a limited amount alcohol <20/30 g per day for women and men, respectively [9,10]. According to the literature, several indices and scales for the diagnosis of hepatic steatosis have been developed over the past decades [13,14]. FLI (fatty liver index) includes BMI, waist circumference, serum triglycerides and GGT (gamma-glutamyl transferase). FLI has a moderate diagnostic efficiency (AUC = 0.84), it has a low accuracy in determining several degrees of steatosis [16]. The LSI (Liver Steatosis Index) is a panel of biomarkers that includes ALT/AST, BMI, gender, and the presence of type 2 diabetes, and this index has a moderate diagnostic detectability for hepatic steatosis [17], which is significantly reduced in children with obesity (AUC = 0.67) [18]. In addition, like FLI, it has low accuracy in determining several degrees of hepatic steatosis [16]. A more efficient and sensitive method is the assessment of liver fat in NAFLD; by means of magnetic resonance, this method detects abnormalities in the liver. This indicator has a good diagnostic efficiency for diagnosing liver steatosis [19]. SteatoTest is a panel that includes more specific parameters for diagnosing steatosis. It combines the six elements of FibroTest (α2-macroglobulin, haptoglobin, apolipoprotein A1, GGT, total bilirubin and ALT) in addition to BMI, cholesterol, triglycerides and glycemia. The SteatoTest is adjusted for sex and age but has moderate accuracy for predicting hepatic steatosis confirmed by liver

biopsy (AUC = 0.80) [20]. This test is not widely used because it does not distinguish between different degrees of steatosis.

Visual biomarkers. Imaging techniques are often used in clinical practice and are used to diagnose NAFLD. To date, elastography has a high diagnostic accuracy in distinguishing between moderate and severe steatosis [21]. However, this method has some limitations: unable to detect steatosis when it is less than 20%, and depends on the skill of the operator [11]. Magnetic proton density resonance imaging of the fat fraction (MRI) is a non-invasive method that displays fatty degeneration of the liver. MRI is more accurate in detecting multiple degrees of steatosis in patients with NAFLD [23]. Based on the foregoing focus on biochemical and molecular biomarkers involved in specific pathways of progression of pathological process is the main point in the prognosis and diagnosis of various complications of NAFLD. Scientists from Harvard University in the nematode C. e legance [1] discovered the first miRNA, named lin-4, a quarter of a century ago. Scientists found that the lin-4 gene did not encode a protein, but two small RNAs - a precursor of 61 nucleotides in length and micro-RNA itself, of 22 nucleotides, which suppressed the expression of the lin-14 nematode gene, preventing it from developing normally. For a long time it was believed that microRNA is such an evolutionary exotic, a property of the nematode genome, until seven years later, in 2000, the second miRNA molecule, let-7, was discovered [2]. It suppressed the expression of several genes at once and was then described in a number of living organisms, including humans. And after that, the "dam broke" – microRNA discoveries began to follow one after another[15].

Circulating RNA to determine the stage of fibrosis. Fibrosis associated with NASH includes various stages, from no fibrosis (F0) to liver cirrhosis (F4). From a clinical perspective, fibrosis is defined as clinically significant (F2–F4) or severe/severe fibrosis (F3–F4). It is widely known that there are several risk factors that can predict the onset of fibrosis, including age, severe obesity, type 2 diabetes mellitus, high AST/ALT ratio, hypertension, dyslipidemia, and the presence of metabolic syndrome [31,34]. The stage of liver fibrosis may be the most important factor in determining the prognosis of NAFLD and preventing the risk of progression to cirrhosis and its associated complications [35]. Biological fluids contain RNA molecules belonging to different classes, including messenger RNAs (mRNAs), long non-coding RNAs (lncRNAs), circular RNAs (cirRNAs), and microRNAs. Circulating miRNAs are extremely stable because they are not present in the circulation in free form, they are encapsulated in membrane vesicles, alternatively complex with RNA-binding proteins, or associated with lipoproteins. All these mechanisms protect RNA from degradation [37]. Another aspect that

makes RNA molecules optimal biomarkers is that the methods used to detect them are extremely sensitive. Unlike proteins, nucleic acids are detected and quantified using PCR-based methods. Other studies have reported that differential expression profiles of circulating RNAs correlate with various physiological and pathological conditions [38]. MicroRNAs are widely known to be involved in the pathogenesis of NAFLD, and their dysregulation has been described in NASH-associated fibrosis. Although there are many studies reporting the role of microRNAs in pathogenesis, very few studies have evaluated circulating microRNAs as biomarkers of fibrosis in NAFLD populations. MicroRNA-122 expression was analyzed in 67 NAFLD patients with multiple degrees of fibrosis. MicroRNA-122 levels were significantly lower in patients with severe fibrosis compared with mild fibrosis. The diagnostic performance of miRNA-122 was also evaluated and compared with other fibrosis biomarkers such as hyaluronic acid and type IV collagen. MicroRNA-122 had a higher diagnostic accuracy compared to hyaluronic acid and type IV collagen. These studies support the use of RNA molecules as non-invasive biomarkers. Akuta et al. analyzed miRNA-122 expression levels in patients with NAFLD. They observed that in patients with improved histopathological parameters, serum levels of miRNA-122 expression were reduced at the second biopsy compared to the first biopsy. In addition, there was a significant correlation between miRNA-122 expression levels and histopathological score variations. The authors also observed a relationship between miRNA-122 expression levels and common clinical parameters such as AST and ALT [39]. The study reported that miRNA-21 levels were also reduced in patients with NAFLD compared with the control group [40]. Yamada et al. analyzed the expression of 5 miRNAs involved in lipid homeostasis (miRNAs -21, -34a, -122, -145, -451) in a total of 403 subjects. Serum levels of four of these miRNAs were higher in subjects with NAFLD compared to controls (92/403) (miRNA-21, -34a, -122, -451); in addition, miRNA-122 expression levels correlated with the degree of steatosis [16]. Cermelli et al. in 2013, reported in more detail the increase in miRNA-122, -16 and -34a expression levels in 34 NAFLD patients compared to 19 controls. On average, miRNA-122 showed a 7.2-fold increase in changes, miRNA-34a showed a 5.3-fold increase in changes, and miRNA-16 was not detected in control samples, while pathological samples had 1000 copies per ml. MicroRNA-122 and -34a increased further in patients with NASH compared with those with simple steatosis, with a fold change of about two and three times, respectively. Another important study by Pirola et al. in 2015 was aimed at determining biomarkers for the differential diagnosis of NAFLD and NASH. They profiled the expression of 84 miRNAs in patients with NAFLD,

NASH, and controls (n = 48) and consistently confirmed activation (FC > 2) of a panel of six miRNAs in an independent cohort (n = 96): miR -122, -192, -19a , -19b, -125 and -375. Only three of them, miRNA-122, -192 and -375, correlated with histological severity and were significantly overexpressed in patients with NASH compared to those with NAFLD. miRNA-122 and -192 were further confirmed by Becker et al. as indicators of histological severity. In more detail, they analyzed the expression of four microRNAs, i.e. miRNA-122, -192, -21 and -223, in 137 NAFLD patients with moderate or severe obesity (87 NASH and 50 with simple steatosis (PS) compared to 61 patients. In addition, they performed a correlation analysis between miRNA expression level and common biomarkers such as AST, ALT. Among the miRNAs analyzed, miRNA-122 and miRNA-192 were increased in severely obese NASH patients compared to severely obese CVD patients.

Conclusion. Today, NAFLD poses a global health risk due to its high prevalence in the general population. We know from multicenter studies that the majority of patients with NASH are at high risk of developing liver cirrhosis [29,30]. Therefore it is extremely important early identification of patients with NASH The ability to correctly identify patients with NASH among patients with NAFLD and determine the stage of fibrosis is an important clinical challenge. Currently, liver biopsy is still the gold standard for diagnosing NASH and the stage of fibrosis. However, because of the risks associated with biopsy, biochemical and imaging tests are often used by clinicians, even if they have limited diagnostic performance [13,14,21]. The introduction of new molecular genetic technologies, in particular miRNAs, will make it possible to identify patients with NAFLD in order to determine the stages of fibrosis for the subsequent prognosis of complications.

REFERENCES

1. Filippello A., Scamporrino A., Di Mauro S., Malaguarnera R., Di Pino A., Scali R., Purrello F., Piro S. Direct Effects of D-Chiro-Inositol on Insulin Signaling and Glucagon Secretion of Pancreatic Alpha Cells. Biomolecules 2020, 10, 1404. [CrossRef]

2. Armutcu F., Akyol S., Vura H. Metabolic Syndrome is an Important Cornerstone in the Health-disease Line and Pathological Organ Interaction. J. Cell. signal. 2020, 1, 70–75.

3. Filippello A., Di Mauro S., Scamporrino A., Malaguarnera R., Torrisi S.A., Leggio G.M., Di Pino A., Scali R., Purrello F., Piro S. High Glucose Exposure Impairs L-Cell Differentiation in Intestinal Organoids: Molecular

Mechanisms and Clinical Implications. Int. J. Mol. sci. 2021, 22, 6660. [CrossRef] [PubMed]

4. Filippello A., Urbano F., Di Mauro S., Scamporrino A. Di Pino A., Scali R., Rabuazzo A.M., Purrello F., Piro S. Chronic Exposure to Palmitate Impairs Insulin Signaling in an Intestinal L-cell Line: A Possible Shift from GLP-1 to Glucagon Production. Int. J. Mol. sci. 2018, 19, 3791. [CrossRef]

5. Younossi Z.M., Koenig A.B., Abdelatif D., Fazel Y., Henry L., Wymer M. Global epidemiology of nonalcoholic fatty liver disease-meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology 2016, 64, 73–84. [CrossRef] [PubMed]

6. Di Mauro S., Ragusa M., Urbano F., Filippello A., Di Pino A., Scamporrino A., Pulvirenti A., Ferro A., Rabuazzo A.M., Purrello M., et al. Intracellular and extracellular miRNome deregulation in cellular models of NAFLD or NASH: Clinical implications. Nutr . metab . Cardiovasc. Dis. 2016, 26, 1129–1139. [Cross Ref]

7. Scicali R., Di Pino A., Urbano F., Ferrara V., Marchisello S., Di Mauro S., Scamporrino A., Filippello A., Rabuazzo A.M., Purrello F., et al. Analysis of steatosis biomarkers and inflammatory profile after adding on PCSK9 inhibitor treatment in familial hypercholesterol subjectsemia with nonalcoholic fatty liver disease: A single lipid center real-world experience. Nutr. metab. Cardiovasc. Dis. 2021, 31, 869–879. [CrossRef] [PubMed]

8. Masarone M., Rosato V., Aglitti A., Bucci T., Caruso R., Salvatore T., Sasso F.C., Tripodi M.F., Persico M. Liver biopsy in type 2 diabetes mellitus: Steatohepatitis represents the sole feature of liver damage. PLoS ONE 2017, 12, e0178473. [Cross Ref]

9. Chalasani N., Younossi Z., Lavine J.E., Charlton M., Cusi K., Rinella M., Harrison S.A., Brunt E.M., Sanyal A.J. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver diseases. Hepatology 2018, 67, 328–357. [Cross Ref]

10. Rinaldi L., Pafundi P.C., Galiero R., Caturano A., Morone M.V., Silvestri C., Giordano M., Salvatore T., Sasso F.C. Mechanisms of Non-Alcoholic Fatty Liver Disease in the Metabolic Syndrome. A Narrative Review. Antioxidants 2021, 10, 270. [CrossRef]

11. Zhou J.H., Cai J.J., She Z.G., Li H.L. Noninvasive evaluation of nonalcoholic fatty liver disease: Current evidence and practice. World J. Gastroenterol. 2019, 25, 1307–1326. [CrossRef] [PubMed]

12. Piazzolla V.A., Mangia A. Noninvasive Diagnosis of NAFLD and NASH. Cells 2020, 9, 1005. [CrossRef]

13. Wong V.W., Adams L.A., de Ledinghen V., Wong G.L., Sookoian S. Noninvasive biomarkers in NAFLD and NASH—current progress and future promise. Nat. Rev. Gastroenterol. Hepatol. 2018, 15, 461–478. [CrossRef] [PubMed]

14. Kogachi S., Noureddin M. Noninvasive Evaluation for Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Clinic. Ther. 2021, 43, 455–472. [CrossRef] [PubMed]

15. Parpibaeva D.A., Karimov M.Sh., Shukurova F.N. The role of micro-RNA in the formation and course of liver diseases, Therapeutic Bulletin of Uzbekistan 2020. No. 2

16. Fedchuk L., Nascimbeni F., Pais R., Charlotte F., Housset C., Ratziu V., Group L.S. Performance and limitations of steatosis biomarkers in patients with nonalcoholic fatty liver disease. Aliment. Pharmacol. Ther. 2014, 40, 1209–1222. [Cross Ref]

17. Lee J.H., Kim D., Kim H.J., Lee C.H., Yang J.I., Kim W., Kim Y.J., Yoon J.H., Cho S.H., Sung M.W., et al. Hepatic steatosis index: A simple screening tool reflecting nonalcoholic fatty liver disease. Dig. LiverDis. 2010, 42, 503–508. [Cross Ref]

18. Koot B.G., van der Baan- Slootweg O.H., Bohte A.E., Nederveen A.J., van Werven J.R., Tamminga-Smeulders C.L., Merkus M.P., Schaap F.G., Jansen P.L., Stocker J., et al. Accuracy of prediction scores and novel biomarkers for predicting nonalcoholic fatty liver disease in obese children. Obesity 2013, 21, 583–590. [Cross Ref]

19. Kotronen A., Peltonen M., Hakkarainen A., Sevastianova K., Bergholm R., Johansson L.M., Lundbom N., Rissanen A., Ridderstrale M., Groop L., et al. Prediction of non-alcoholic fatty liver disease and liver fat using metabolic and genetic factors. Gastroenterology 2009, 137, 865–872. [Cross Ref]

20. Poynard T., Ratziu V., Naveau S., Thabut D., Charlotte F., Messous D., Capron D., Abella A., Massard J., Ngo Y., et al. The diagnostic value of biomarkers (SteatoTest) for the prediction of liver steatosis. Comp. Hepatol. 2005, 4, 10. [CrossRef]

21. Hernaez R., Lazo M., Bonekamp S., Kamel I., Brancati F.L., Guallar E., Clark J.M. Diagnostic accuracy and reliability of ultrasonography for the detection of fatty liver: A meta-analysis. Hepatology 2011, 54, 1082–1090. [CrossRef] [PubMed]

22. Karlas T., Petroff D., Sasso M., Fan J.G., Mi Y.Q., de Ledinghen V., Kumar M., Lupsor-Platon M., Han K.H., Cardoso A.C., et al. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. J. Hepatol. 2017, 66, 1022–1030. [CrossRef] Int. J. Mol. sci. 2021, 22, 11905 14 of 17

23. Park C.C., Nguyen P., Hernandez C., Bettencourt R., Ramirez K., Fortney L., Hooker J., Sy E., Savides M.T., Alquiraish M.H., et al. Magnetic Resonance Elastography vs Transient Elastography in Detection of Fibrosis and Noninvasive Measurement of Steatosis in Patients With Biopsy-Proven Nonalcoholic Fatty Liver Disease. Gastroenterology 2017, 152, 598–607. [CrossRef] [PubMed]

24. Yu C., Xu C., Xu L., Yu J., Miao M., Li Y. Serum proteomic analysis revealed diagnostic value of hemoglobin for nonalcoholic fatty liver disease. J. Hepatol. 2012, 56, 241–247. [Cross Ref]

25. Bell L.N., Theodorakis J.L., Vuppalanchi R., Saxena R., Bemis K.G., Wang M., Chalasani N. Serum proteomics and biomarker discovery across the spectrum of nonalcoholic fatty liver disease. Hepatology 2010, 51, 111–120. [CrossRef] [PubMed]

26. Kalhan S.C., Guo L., Edmison J., Dasarathy S., McCullough A.J., Hanson R.W., Milburn M. Plasma metabolomic profile in nonalcoholic fatty liver disease. metab . Clin. Exp. 2011, 60, 404–413. [CrossRef] [PubMed]

27. Oresic M., Hyotylainen T., Kotronen A., Gopalacharyulu P., Nygren H., Arola J., Castillo S., Mattila I., Hakkarainen A., Borra R.J., et al. Prediction of non-alcoholic fatty-liver disease and liver fat content by serum molecular lipids. Diabetologia 2013, 56, 2266–2274. [Cross Ref]

28. Mayo R., Crespo J., Martinez-Arranz I., Banales J.M., Arias M., Minchole I., Aller de la Fuente R., Jimenez-Aguero R., Alonso C., deLuis D.A., et al. Metabolomic-based noninvasive serum test to diagnose nonalcoholic steatohepatitis: Results from discovery and validation cohorts. Hepatol. commun. 2018, 2, 807–820. [Cross Ref]

29. Ekstedt M., Hagstrom H., Nasr P., Fredrickson M., Stal P., Kechagias S., Hultcrantz R. Fibrosis stage is the strongest predictor for disease-specific mortality in NAFLD after up to 33 years of follow-up. Hepatology 2015, 61, 1547–1554. [CrossRef] [PubMed]

30. Galiero R., Caturano A., Vetrano E., Cesaro A., Rinaldi L., Salvatore, T., Marfella R., Sardu C., Moscarella E., Gragnano F., et al. Pathophysiological mechanisms and clinical evidence of relationship between Nonalcoholic fatty liver disease (NAFLD) and cardiovascular disease. Rev. Cardiovasc. Med. 2021, 22, 755–768. [Cross Ref]

31. Ratziu V., Giral P., Charlotte F., Bruckert E., Thibault V., Theodorou I., Khalil L., Turpin G., Opolon P., Poynard T. Liver fibrosis in overweight patients. Gastroenterology 2000, 118, 1117–1123. [CrossRef] [PubMed]

32 . Angulo P. Long-term mortality in nonalcoholic fatty liver disease: Is liver histology of any prognostic significance? Hepatology 2010, 51, 373–375. [CrossRef] [PubMed]

33. Zhu H., Fan G.C. Extracellular/circulating microRNAs and their potential role in cardiovascular disease. Am. J. Cardiovasc Dis. 2011, 1, 138–149.

34. Pos O., Biro O., Szemes T., Nagy B. Circulating cell-free nucleic acids: Characteristics and applications. Eur. J. Hum. Genet. 2018, 26, 937–945. [CrossRef] [PubMed]

35. Turchinovich A., Baranova A., Drapkina O., Tonevitsky A. Cell-Free Circulating Nucleic Acids as Early Biomarkers for NAFLD and NAFLD-Associated Disorders. front. physiol. 2018, 9, 1256. [CrossRef] [PubMed]

36. Velu V.K., Ramesh R., Srinivasan A.R. Circulating MicroRNAs as Biomarkers in Health and Disease. J.Clin. Diagn. Res. 2012, 6, 1791–1795 [CrossRef] [PubMed]

37. Akuta N., Kawamura Y., Suzuki F., Saitoh S., Arase Y., Fujiyama S., Sezaki H., Hosaka T., Kobayashi M., Suzuki Y., et al. Analysis of association between circulating miR-122 and histopathological features of nonalcoholic fatty liver disease in patients free of hepatocellular carcinoma. BMC Gastroenterol. 2016, 16, 141. [CrossRef]

38. Sun C., Huang F., Liu X., Xiao X., Yang M., Hu G., Liu H., Liao L. miR-21 regulates triglyceride and cholesterol metabolism in non-alcoholic fatty liver disease by targeting HMGCR. Int. J. Mol. Med. 2015, 35, 847–853. [Cross Ref]

39. Yamada H., Suzuki K., Ichino N., Ando Y., Sawada A., Osakabe K., Sugimoto K., Ohashi K., Teradaira R., Inoue T. et al. Associations between circulating microRNAs (miR-21, miR-34a, miR-122 and miR-451) and non-alcoholic fatty liver. Clin. Chim . Acta 2013, 424, 99–103. [CrossRef] [PubMed]

40. Tan Y., Ge G., Pan T., Wen D., Gan J. A pilot study of serum microRNAs panel as potential biomarkers for the diagnosis of nonalcoholic fatty liver disease. PLoS ONE 2014, 9, e105192. [Cross Ref]

41. Raitoharju E., Seppala I., Lyytikainen L.P., Viikari J., Ala- Korpela M., Soininen P. Kangas A.J., Waldenberger M., Klopp N., Illig T., et al. Blood hsa-miR-122-5p and hsa-miR-885-5p levels associate with fatty liver and related lipoprotein metabolism-The Young Finns Study. sci. Rep. 2016, 6, 38262. [CrossRef]

Central Asian Journal of Medicine

COMPREHENSIVE APPROACH TO IMPROVING AUTOIMMUNE THROMBOCYTOPENIC PURPURA TREATMENT RESULTS

Gaybulla I.Mustafakulov[1], Farhod D. Ortiqboyev[2]

1 Associate Professor of the Department of General Surgery No. 2. Tashkent Medical Academy, Tashkent, Uzbekistan

2 Assistant of the Department of General Surgery No. 2. Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

This article presents the experience of leading 224 patients with autoimmune thrombocytopenic purpura (ATP). Comparative data of results of inhalation and traditional methods of treatment with glucocorticoid hormones and operative method of treatment - splenectomy (SE) are given. It has been established that the use of glucorticosteroids (GCS) Cold metered inhalation hormones proved to be most effective in 87.2% of patients (compared to the conventional treatment method - 75.7%) and accelerated remission by 6.3 days. EC implemented by the in the early postoperative period was more effective in 96.9% of cases.

Key words: thrombocytopenia, glucocorticoids, splenectomy, complications, prevention, hormone inhalation.

INTRODUCTION

Background. Among hemorrhagic diates, one of the common forms is autoimmune thrombocytopenic purpura (ATP). [1.5-10]

The most common and pathogenetically based treatment for ATP is the use of glucocorticoid hormones. However, the use of hormones, especially their taking per os is often the cause of complications from the gastrointestinal tract. [2,3]

With prolonged use of corticosteroids, especially when taken through the mouth, given the pronounced side effects, are looking for other ways to inject corticosteroids to reduce or prevent complications of glucorticosteroid (GCS) therapy [9,13,15]. Consequently, the improvement of both conservative and operative ATP treatment is undoubtedly has great scientific and practical interest for modern hematology and surgery. [4,11-16]

The aim of the present work is to compare the effectiveness of inhalation and traditional treatment with glucorticoid hormones in a complex with splenectomy (SE) in patients with ATP.

Material and methods of research. In the paper the results of conservative and operational treatment of 224 patients diagnosed with ATP. Patients with chronic form of ATP was - 187, with acute form - 37. Males - 88, females - 136. Hormonal treatment. A total of 95 (42.4 per cent) patients received: 48 (men 18 (37.5 per cent) of whom received traditional treatment; Females 30 (62.5 per cent), hormone inhalation 47 patients (of whom 22 (46.8 per cent) were men, 25 (53.2 per cent) - women). SE is performed in 129 (57.6 per cent) patients with chronic ATP (of whom 40 (31.1 per cent) are men, women - 89 (68.9%). The traditional method of SE is performed in 65 (50.4%) patients, suggested by us method in 64 (49.6%).

The following are used for verification of ATP criteria (except complaints, historical and objective inspection):

1. Thrombocytopenia (platelets<150x109/l) In the absence of other abnormalities in the calculation of the blood cells.

2. No clinical and laboratory signs illness in next of kin.

3. Normal or increased number of megakaryocytes bone marrow.

4. No other diseases or factors capable of causing thrombocytopenia in patients.

5. The effect of corticosteroid therapy.

During SE, the amount of blood loss is determined by weighing surgical dressings - napkins, before and after surgery, and blood loss after operation from a drainage tube, infusion into the dishes with a mark. In addition, patients with ATP were given ultrasound examinations for internal organs, electrocardiography, endoscopic examination of the gastrointestinal tract.

Patients complained of hemorrhagic syndrome: petechiae and ecchymosis on the skin, nasal, uterine bleeding, bleeding from gums and gastrointestinal tract, which were more common at platelet levels <20.5 30.0 x 109/l. The age of the disease at the time of the first inpatient visit was from 3 days to 5 months for acute ATP. In the history of duration The disease ranged from 6 months to 20 years with chronic ATP and during this time patients received hormones in tablets from 2 to 10 times.

GCGs were prescribed with traditional treatment of 2-2.5mg/kg in acute form, 1-1.5mg/kg in chronic form ATP per os and parenteral. Inhalation (prednisolone and dexamethasone solution) was performed on nebulizer inhaler apparatus «Boreal», (Italian production) at a dose of 1-2.0mg/kg. Patients also received

fibrinolysis inhibitors, vascular wall protectors, biological membrane stabilizers and topical treatment in the case of nasal and gum bleeding. Patients with a severe degree of anemia were transfused erythrocyte mass.

Complications detected in 50 (52.6%) patients with ATP on the side of the digestive tract; gastroduodenitis in 21, stomach ulcer in 6, Ulcer 12 of the rectum in 5, colitis in 2, GI discomfort in 11, stomach pain in 5.

SE performed 129 patients with ATP. 64 patients of the experimental group of splenectomy was performed in the way we suggested - when auditing the spleen was evaluated her mobility and contact with the circle, detached the back its surface from parenteral peritoneal hemostasis in the direction of the leg and back of the stomach. Then the spleen was easily dislocated into the wound, starting with the lower the poles thereof were released from ligaments and bound before; two clamps were placed over the ligature, then cut between the clamps and the stump sewn. The 0.5 x 0.5 cm window was then opened in the anterior leaf of the peritoneum from the upper brisket pole and the gastro-splenic ligament was ligated by the above method. If the width of the foot is large, more tissue is taken when the poles are isolated. The front leaf of the peritoneum in the leg area is not opened, this preserves the integrity tissue and hemostasis. The next stage of the operation - preliminary ligation of the leg of the spleen with catgut over the capsule pancreas, under control of the posterior surface, so as not to damage the tail of the pancreas the glands. In this case, all the elements of the leg of the spleen are gathered in a single stem with a straight axle, which is much improves subsequent clipping over the ligature. This in turn is preventing bleeding. Subsequently, the ligature is superimposed 2-3 clamp, and the spleen is removed. The stump is bandaged and sewn. This SE prevents damage to the tail of the pancreas, creates a reliable hemostasis, and preserves the integrity of adjacent tissues.

Results of the study. Inhalation at a dose of 1.0 to 2mg/kg per day. Of 18 patients with acute ATP Clinical hematology (CGE) for 13 (72.2%) patients, on average for 6.5 bed days, clinical effect (CE) in 2 (11.1%) patients, on average for 5.5 bed days. Clinical and clinical hematological effect (C and CGE) 15 (83.3 per cent) patients, average in 6.3 bed-days. 3 (16.7%) patients suffering from the effect of treatment there was no. In patients with acute ATP receiving inhalation therapy of hormones GCS hemorrhagic syndrome began to disappear for 3-4 days, the number of platelets became rise from 5-6 days of treatment.

19 patients (adults - 9, children - 10) with acute ATP, from the first or second day of receipt together with other GC hormones (prednisolone and dexamethasone) in tablets and injections at a dose of 1.5-2.0mg/kg per day. The results of

traditional hormonal therapy in adults and children with CATI showed that 13 (68.4%) patients received CGE, with an average of 9.8 bed days. KE is obtained from 2 (10.5%) patients with an average of 16.5 bed days. K and CGE are obtained in 15 (78.9%) patients, on average in 10.7 bed days. In 4 (21.1%) patients the effect of hormonal therapy is not obtained. The hormone treatment he received was ineffective for more than three to four weeks.

Results of inhalation therapy of sick children and adults chronic form ATP (HACT). Inhalation was carried out at a dose of up to 2mg/kg per day. Of 29 patients, CGE - for 13 (44.8 per cent) patients, on average for 5.8 bed days, CE also in 13 (44.8%) Patients received an average of 7.2 bed days, 3 (10.4 per cent) - no effect. Twenty-six (89.7 per cent) patients received K and CGE treatment, with an average of 6.5 bed days. Starting from 2 and 4 days, all patients with hemorrhagic syndrome are suppressed.

29 patients with HACT (9 children, 20 adults) received traditional treatment, including as pathogenetic therapy of HC hormones at a dose of 1.0-1.5mg/kg per day. From traditional GC hormone treatment to sick children and adults HACT received CGE 6 (20.7 per cent) of patients, with an average of 9.3 bed-days. Clinical remission (KR) in 15 (51.7%) patients, on average for 11.2 bed-days. K and KSR received in 21 (72.4 per cent) patients with an average of 10.7 bed days, 8 (27.6 per cent) patients were without effect with the persistence of hemorrhagic syndrome. Hemorrhagic syndromes began to disappear from 3-5 days in patients with remission. Thus: 47 Patients; APTA and HACT received dosed cold GCS hormone inhalation, with CT and CGR patients receiving 83.3% on average in 6.3 days, compared to 78.9% for traditional treatments and 10.7 days. In patients, HACT K and CGR received from 89.7% of patients, at 6.5 days, as opposed to 72.4% and 10.7 days. Of the 47 patients who received inhalation treatment, 26 (55.3%) had inhalation therapy, on average 6.1% bed days received by the CGE, 15 (31.9%), average 7.0 bed days or 41 (87.2%) patients, average K and CGE received in 6.3 bed-days. 6 (12.8%) patients have no effect, they have left skin hemorrhagic diseases manifested in the form of ecchymosis.

Results of splenectomy at ATP. For 2000-2002. 65 (50.4 per cent) patients with HITP were operated on in the usual way: children - 37 (56.9 per cent), adults – 28 (43.1%). Total blood loss was 7980 ml or one patient 122.8 ml. During the operation, only 5590 ml of STD and 9715 ml of erythrocyte mass were transfused. Total blood components transfused 15305 ml or per one patient 235.5 ml. Such complication as damage to the pancreas during surgery was observed in 12 (18.5%) patients. After surgery on the 1st and 2nd day 4 (6.2%). Fever increased to 380 and in 3 (4.6%) patients had complaints on the 2nd day after the operation pain

in the left abdomen and lumbar region. From the drainage tube, hemorrhagic discharge was in the 1st and 2nd days up to 100.0 ml or more. In 50% of patients drainage tube removed on the 1st day after surgery. Relaparotomy about internal bleeding after SE was conducted in 2 (3.1%) patients. The nearest postoperative results in patients with chronic ATP K and CGD accounted for 91.6% of patients. The proposed method is performed SE 64 patients with chronic ATP by current. Total blood loss is 4915 ml or per patient 76.8 ml. During surgery y 3 (4.7 per cent) The caudal portion of the pancreas was damaged in the catgut ligature, but no pancreatitis clinic was observed in the postoperative period. After hemorrhagic excretion operations from the drainage tube were up to 30 ml. The nearest postoperative results in ATP patients with chronic K and CGD 96.9% of patients had drainage tubes removed in 90% of cases on the 1st day after the operation. There were no complications during and after the operation.

Outcome discussion

Thus, inhalation method of administration of hormones in dosed cold form on nebulizer apparatus «Boreal» patients with acute and chronic current ATP results are as good as traditional treatment with oral and parenteral HC and has such benefits as; no complications from inhalation, good tolerance procedure, especially, children; prevention of neurosis, hysteria, pain syndrome associated with manipulation of GCS hormones in children; absence of withdrawal syndrome; prevention of hit parenteral infection; economic efficiency by reducing the amount of GC hormones, blood components, other drugs and reducing the number of bed days. In comparative terms with traditional treatment, acute ATP at 4.4, chronic ATP at 4.2 he’s been in remission for days.

The proposed method - allows preserving the integrity of adjacent tissues prevents damage to the tail of the pancreas and prevents bleeding during and after surgery. This being the case reduces the duration of surgery by 10-15 minutes, bleeding during surgery is reduced by 45.7 ml in one patient, and after surgery 2-3 times. Postoperative pancreatitis, relaparotomy and lethal results are not observed. Saves red blood mass, blood components and other drugs.

Findings.

1. Inhalation of hormones in dosed cold form on nebulizer apparatus «Boreal» patients with acute and chronic forms of ATP - an alternative to the existing traditional method of conservative treatment. From inhalation of HC, in comparison with traditional acute treatment ATP form at 4.4, with chronic ATP form at 4.2 beds earlier received remission. It warns against a number of complications of GPS therapy and transmission of parenteral blood transmissive infection.

2. Inhalation of GHS hormones in case of illness ATP is shown especially in children and people with gastrointestinal disease. Contraindicated in patients with a severe general condition on the background the main disease and their intolerance to inhalation of GHS.

3. The improved splenectomy method is less traumatic, with a lighter postoperative flow, less blood loss and a minimal number of complications.

4. The proposed procedure reduces pancreatic damage by more than 4 times and thus prevents the development of postoperative pancreatitis. Reduces surgery time by 10-15 minutes. A good result in the immediate postoperative period, after splenectomy, was 96.9% (with traditional treatment 91.6%).

REFERENCES

1. Altybaev U.A. Trombocitopenicheskaya purpura v Uzbekskoj SSR: Avtoref. dis. … kand. med. nauk. — M., 1984. — 25 s. Altybaev U.A. Thrombocytopenic purpura in the Uzbek SSR: Abstract of the thesis. dis. … cand. Med. Sciences. - M., 1984. - 25 p.

2. Cines D.B., Cuker A., Semple J.W. Pathogenesis of immune thrombocytopenia. PresseMed. 2014; 43 (4 Pt2): e49–59. doi:10.1016/j. lpm. 2014.01.010.

3. Ergashev U.Y. et al. Treatment of idiopathic thrombocytopenic purpura: prevention of hormonal complications in the stomach and duodenum // Central Asian Journal of Medicine. — 2020. — T. 2020. — №. 2. — C. 5–28.

4. Ergashev U. Y., Abdusalomov B. A., Minavarkhojayev R. R., Ortiqboyev F.D., & Malikov N. M. (2023). Evaluation of the pathomorphology of regeneration in diabetic foot syndrome and determination of its dependence on biochemical processes. World Bulletin of Public Health, 19, 66-78.

5. Grzhimolovskij A.V. Laparoskopicheskaya splenektomiya u gematologicheskih bol'nyh: Avtoref. dis… kand. med. nauk. — M., 2004. –25 s. Grjimolovsky A.V. Laparoscopic splenectomy in hematological patients: Abstract of the thesis. dis... cand. med. Sciences. - M., 2004. -25 p.

6. Hand-assisted laparoscopic splenectomy: indications and technique /Bermas H., Fenoglio M.E., Haun W., Moore J.T. //JSLS. — 2004. — vol. 8910. — P. 69–71.

7. Ismoilov F.M. DIAGNOSTIKA I LECHENIE BOL'NYH S OSTROJ KISHECHNOJ NEPROHODIMOST'YU. Zbiór artykułów naukowych recenzowanych., 69.

8. Kato A. Disorders associated with autoimmune thrombocytopenic purpura // Nippon Rinsho. — 2003. — vol. 61. —P. 604–608.

9. Mustafakulov G. I., Atahodzhaeva F. A., & Ergashev U. YU. (2020). Idiopaticheskaya trombocitopenicheskaya purpura pri beremennosti.

10. Mustafakulov G. I., Ergashev U. Y., Atakhodjaeva F. A., & Anvarhodjaeva S. G. (2022). Simultaneous surgeries in chronic immune thrombocytopenia.

11. Mustafakulov G.I. et al. Splenectomy for hairy cell leukemia //Central Asian Journal of Medicine. — 2021. — T. 2021. — №. 4. — C. 160–167.

12. Raimkulova N. R., & Usmonbekova G. U. (2017). Nefroprotektivnoe dejstvie statinov u bol'nyh s hronicheskim glomerulonefritom. Molodoj uchenyj, (8), 131-133.

13. Splenektomiya transtorakal'nym dostupom / SHavlohov V.S., Karagyulyan S.R., Efimov I.V. i dr. // Gematologiya i transfuziologiya. — 2007. t. 52, №5. — S. 50–54.

14. Vorob'ev A.I. Rukovodstvo po gematologii. — Moskva izd-vo «N'yudiamed», 2005. –31–35 s.

15. Vybor sposoba splenektomii pri zabolevaniyah sistemy krovi /Karagyulyan S. R., Grzhimolovskij A. V., Danishyan K.I., SHavlohov V.S. i dr. // Gematologiya i transfuziologiya. — 2007. — t. 52, №1. — S. 3–10.

16. Yusufjanovich E. U. (2023). Management of Patients with Acute Arterial Ischemia of the Lower Limb. International Journal of Scientific Trends, 2(2), 43-48.

Central Asian Journal of Medicine

DERMATOMYCOSES AND METHODS OF LABORATORY DIAGNOSIS

Egamberdi E. Eshboev[1], Otabek S. Imamov[2], Normurod D. Djumaev[3], Indira N. Abduvakhitova[3], Gayrat Sh. Toxtayev[4]

1 Professor, Republican Specialized Scientific-Practical Medical Center of Dermatology and Cosmetology, Tashkent, Uzbekistan

2 Associate Professor, Department of Dermatovenereology and Cosmetology, Tashkent Medical Academy, Uzbekistan

3 Department Head, Republican Specialized Scientific-Practical Medical Center of Dermatology and Cosmetology, Tashkent region branch, Uzbekistan

4 Assistant, Department of Dermatovenereology and Cosmetology, Tashkent Medical Academy, Uzbekistan
E-mail: gayrat.uz@mail.ru

ABSTRACT

The purpose of the study: preparation of a cheap and high-quality fresh medium, the basis of which is made up of local ingredients for the growth of pathogenic fungi. Materials and research methods: in the process of carrying out scientific research work, pathological material from 400 patients (skin scraping, damaged hair fiber, and nail plates) was studied in the Saburo food environment, which is applicable to the causative agents of fungal diseases of the skin, and in the proposed food environment. The results: cheap and high-effective medium was created for use in the daily practice of bacteriological laboratories under all treatment (dispensaries of venereal diseases, private laboratories) institutions located in the territory of the Republic.

Key words: dermatomycosis, fungi, Saburo, laboratory, medium.

INTRODUCTION

By the 21st century, fungal infections have caused a variety of diseases among humans, including, within the animal world. According to data provided by the World Health Organization, one in five of the inhabitants of the globe suffers from one type of fungal disease (4,21). Especially their development against the background of secondary processes in other diseases, primary diseases with

various Genesis, has severe consequences. An example of this is AIDS, and COVID-19 diseases (1,17). Fungi are the main cause of death of patients with severe pathologies – diseases accompanied by cancer, autoimmune, and immunodeficiency (8). It is worth saying that in conditions of immunodeficiency of conditionally pathogenic fungi, their pathogenic properties are increasing. New nosological forms are emerging, in addition, the resistance of fungi to antimycotic drugs is increasing. It should not be forgotten that the products of the life-activity of fungi, for example, mycogenic allergies, and mycotoxicoses, have a huge impact on human health.

Dermatomycoses in the English-language scientific literature ringworm or tinea (English "ring" – round or ring–shaped; "worm" – worm, snake); ringworm – contagious lesions of the skin with pathogenic fungi in a ring-shaped form; Latin "tinea" is a fungal disease of the skin, especially the head-haired part. This is the case when humans and animals are damaged by fungal infections of keratin-retaining tissues (skin, fine hairs, hair, and nails) (5). The pathogens of dermatomycosis damage the keratin-retaining tissues of humans and animals at the expense of the activity of its keratinase enzyme. Dermatomycoses are considered fungi-Cosmopolitan and are distributed in all regions of the globe. They are pathogenic to humans, infecting all domestic and wild animals and fish, and birds (14). Pathogenic species of fungi constitute a large group of disease-causing microorganisms in humans and animals. In general, more than a hundred species of all fungi are pathogenic, and the bulk of the rest is conditionally pathogenic. They belong to the genus of simple plants in terms of structure and are distinguished from plants by the absence of the substance chlorophyll in their composition. Fungi are common in nature and are found mainly in moist soil, watershed areas, in the air, in the bodies of plants, and trees, in the animal world, and finally among humans (20).

Most types of pathogenic fungi are found in an anaerobic environment, that is, they prefer conditions with little oxygen. For their survival, nitrogen, carbohydrates, and minerals are necessary, favorable environmental conditions for them are pH=6.0-6.4, and a moderate temperature is 220 -370 C. Fungi have round, oblong, tubular, horny forms, the length of their bodies, that is, their mycelium, is from 4-5 μm to 60-70 μm. (3). For fungi to live, reproduce, and function, they are required to have conditions, such as relatively low temperatures, darkness, humidity, an oxygen-free environment, and high levels of carbohydrates. On the contrary, dry temperatures, light, oxygen-rich conditions, and high heat levels are considered unfavorable. Fungi reproduce mainly by division or budding.

They have the characteristics of forming colonies that are specific in artificial planting areas, that is, in nutrient environments (12).

It is worth saying that medical mycology has long been overshadowed by the science of bacteriology and virology and is considered a secondary level to it. But changes in immunology, dermatology, endocrinology and infectious diseases require a new look at medical mycology. Particular concerns are the reproduction of conditionally pathogenic systemic fungi that occur against the background of underlying diseases and further complicate their course. Global problems are increasing the number of invasive fungi, and the collaborative arrival of fungi among people infected with HIV or COVID-19 is increasing their role. (7,9,18) It is noteworthy that in Endocrinology, organ transplantation, onco-hematology, and neonatology, the range of negative effects of pathogenic fungi increases. It is worth saying again that skin diseases caused by pathogenic fungi – with dermatomycoses (greek "derma" – skin, "mycosis" - fungi) (leg paw mycosis, rubromycosis, onychomycosis, trichophyty, microsporia, etc.) The number of patients is increasing in arithmetic progression (2).

The process of formation of dermatomycoses depends on the degree of disease initiation of fungi and the immunobiological characteristics of the microorganism, the age, and gender of patients, and the state of their endocrine glands. An important role in this is played by the increased absorption properties of the epidermis and dermal layer, profuse sweating, and the specific chemical composition of the skin (15).

The condition of occurrence of fungal diseases among children, especially in school-age children is because of insufficient levels of keratin in the structure of the skin epidermis and hair cells, the transition of the skin's water-oil-chemical environment to an alkaline or moderate state leads to the activation of fungi and an increase in the level of virulence. Dermatomycoses are more common, especially in patients with chronic and infectious diseases and debilitated. The source of the disease is a sick person or infected animals, from which the disease to healthy people occurs directly as a result of household contacts or indirectly, that is, items that are in the consumption by patients (clothes, dishes, toys, etc.). Is transmitted through. After the disease is transmitted, its clinical signs are manifested and develop on the skin, hair, nails, and mucous membranes (6).

Medical mycology faces serious problems in the following years, a number of antimycotic drugs have been developed and put into practice in order to properly treat the disease. But the need to improve laboratory examination methods is increasing from year to year. Because insufficient laboratory data often leads to a late receipt or incorrect execution of the examination results, ultimately this

condition complicates the treatment work and leads to a chronic course of the disease (10,11).

Timely early diagnosis significantly increases the likelihood of successful recovery, therefore, from the very beginning, it is necessary to carry out Mycological examinations of the patient, assuming the presence of a fungal infection. The identification of the causative agents of dermatomycosis of fungi from the affected skin or its excess provides the necessary opportunity for an accurate diagnosis. The development of molecular-genetic, biochemical, and immunological technologies began to be widely used in the laboratory diagnosis of fungal infections. But in order to fully study the morphobiological antimycotic properties of the etiological factor, it is necessary to isolate the culture of pathogens in food environments, in addition to the indication of mycotoxins, mycotoxicosis, and toxicoinfections of fungi. And for this, of course, it is necessary to introduce fungicides (22,25).

Various nutrient media have been proposed by a number of authors to obtain a pure culture of dermatomycosis pathogens (17,23). Their main components are peptone, agar-agar, and products such as various amino acids. But, due to the extremely high cost of the ingredients that make up the composition of these food media, as well as its deficiency and the growth of disease pathogens in these food environments in the long term (21-28 days), treatment was practically not used in the mycological laboratories of preventive institutions. So the problem remains open.

Taking into account the above points of view and feedback, as well as the relevance of the work, we aimed to prepare an inexpensive and high-quality new food environment, the basis of which is composed of local ingredients, in order to extract the causative agents of dermatomycosis and extract its pure culture.

It is known that the microscopic diagnosis of dermatomycoses does not allow for to the determination of the type of disease pathogens (21). The correct diagnosis of the patient can be made by determining the type of pathogens of diseases by absorbing the causative agents of fungal diseases of the skin in a cultural style, that is, in special nutrient media. At the same time, it is possible to determine the state of susceptibility to antimycotic drugs to the identified causative agent of the disease.

In the cultural diagnosis of dermatophytes, frequent interruptions in supply due to the fact that the food media used in today's practice are imported from foreign countries, and the high cost of the food environment causes a number of disadvantages. Alternatively, in these food environments, the pure culture of dermatophyte pathogens is isolated in the long term (21-28 days), while the level

of reproduction of fungal fungi in most cases does not exceed 40% in the practice of reputable Mycological laboratories (13.24).

It is known that in the Saburo food environment, the level of isolation of the pure culture of fungi remains low. In the Russian Federation, the level of isolation of the pure culture of fungi in the cultural investigations carried out in Saburo food environments in subsequent years did not exceed 36% (16).

This figure was 30-32% in the research carried out in the Republic on the examination of fungi by planting them in the Saburo food environment.

After planting in the nutrient medium, the growth of bacteria begins from 2-3 days, the growth of yeast and mold fungi from 4-5 days, and the growth of fungi begins from 6-7 days. Secondly, the causative agents of dermatomycosis (trichophytia, microsporia, epidermophytia) have high nutritional needs. In order for most types of dermatophytes to grow in their nutrient medium, a complete set of vitamins and proteins of animal origin is initially required. Therefore, the remoteness of the identification days of dermatophyte pathogens planted in the current Saburo food environment (19) once again requires conducting scientific and practical research in this regard.

The objective of this research is to produce a new nutrient medium to extract pure cultures of fungi from clinical materials that satisfy the efficacy criteria necessary to ensure the accurate and objective results required for the reliable results of any clinical mycological examination.

The composition of the proposed new nutrient medium consists of the following components (g/l): distilled water – 1 L, mycological peptone – 10.0, bacteriological agar-agar – 18.0-20.0, keratin hydrolysate – from 10.0 to 20.0, apricot extract – 80.0, vitamin V1 (thiamine chloride) – 1.0, ciprofloxacin – 5.0, cycloheximide – 0.001.

Microbiological peptone-proteins, carbohydrates, vitamins, as well as various minerals, are necessary for the nutrition of fungi. Most dermatophytes grow well in peptone food environments with added carbohydrates. The proper combination of carbohydrates and peptone added to the food environment is one of the important factors in the formation of the culture of dermatophytes. The presence of a sufficient amount of peptone reduces cases of pleomorphic changes, layering, twisting, and crater-shaped formation in the colony of dermatophytes.

The study of the assimilation of dermatophytes of proteins and peptones was explained by the fact that these substances can be sources of carbon and nitrogen.

Bacteriological agar – agar is a plant substitute for gelatin in the form of a powder or plate obtained from a mixture of agaropectin and agarose polysaccharides. Agar-agar does not contain fats at all, consisting of 5% protein

and 95% carbohydrates, while being a product rich in minerals necessary for the absorption of dermatophytes such as magnesium, iron, calcium, and iodine.

Keratin hydrolysate is a natural protein obtained from the horns of sheep and goat wool and poultry feathers of small and large horned animals. It consists of peptides, polypeptides, and amino acids.

Keratin is a natural protein, the skin and its derivatives are the main components of fine hairs, hair, and nails. Does not melt in a natural state. Through hydrolysis, large molecules of keratin are transferred to the state of a water-soluble substance. Keratin hydrolysate is a product rich in amino acids that dermatophytes need to grow.

The use of keratin tissue for growing dermatophytes in artificial food environments occurs in the practice of mycological examinations. With a gradual dissolution of the keratin substance in the structure of keratin-holding tissues under the influence of dermatophytes, changes in the skin, including hair, the appearance of wounds on the surface of the skin are associated with the assimilation of keratin by dermatophytes, the main mass of the skin horn layer.

By adding keratin hydrolyzate in sufficient quantities to the food environment, the need for dermatophytes for amino acids is compensated, which in turn ensures that fungi grow faster in the food environment of their aggressors.

Dermatophytes synthesize proteins necessary for cell structure from simple amino acids. The growth of dermatophytes in the nutrient medium is due to the fact that it digests a mixture containing a mixture of several natural amino acids, in such conditions amino acids are absorbed directly, so the need for them for the formation of proteins in cells is less. Many amino acids are lightly assimilated by most dermatophytes.

Apricot extract is an inexpensive, natural, local product added to the food environment and is very rich in carbohydrates, amino acids, and minerals necessary for the growth of dermatophytes. Apricot extract contains amino acids such as arginine, glycine, lysine, tryptophan, isoleucine, and tyrosine. 100 grams of apricot extract contains 65 gr. there are minerals carbohydrates, 1162 mg potassium, 55 mg calcium, 27 mg iron, and 10 mg sodium.

The addition of apricot extract, a complex of carbohydrates that are natural in their origin in the food environment, is important for the nutrition of many dermatophytes. In addition to the fact that apricot extract is extremely rich in carbohydrates, the saturation of dermatophytes with the minerals necessary for its nutrition further enriches the effectiveness of the nutrient medium.

The addition of the antibiotic **ciprofloxacin** to the nutrient medium was used to suppress the growth of the bacterial flora and thereby eliminate the antagonistic effect on dermatophytes.

Cycloheximide- inhibits the growth of yeast and mold fungi in the food environment.

New food environment preparation techniques: Based on the information given above, all the required components are prepared in advance. Initially, 18.0-20.0 gr of bacteriological agar-agar is poured into a glass flask, 900.0 ml of distilled water is poured over it, and the mixture is heated until agar-agar dissolves. 10.0 gr of Mycological peptone ,10.0 gr to 20.0 gr of keratin hydrolysate are added to the dissolved mixture, the amount of the mixture is brought to 1 liter by adding distilled water, and the product is thoroughly mixed. The resulting mixture is shaken. After that, the nutrient medium is poured into glass containers. The mouth of the jars is closed with a cotton gauze stopper and sterilized in an autoclave at 1 atm (1200 C) for 20 minutes.

After sterilization, the nutrient medium is cooled, and before solidification, 80.0 g of apricot extract, 1.0 g of vitamin V1(thiamine hydrochloride), 5.0 g of ciprofloxacin, 0.001 gr – cycloheximide are added to it. Its environment is then equated to 6.5.

Preparation of apricot extract. To do this, 1 kg of dried sorrel of apricot is taken and first thoroughly washed in warm water. Then it is crushed in a sharp knife to the same size (0.3 – 0.5 cm), placed in 2.5-3.0 liters of distilled water, and boiled in an enameled container on a gas stove for 30-35 minutes over the same fire. When the required time is up, the decoction is cooled and passed through a cotton-gauze filter. The resulting clean solution is placed in glass jars, and their mouth is closed with cotton gauze plugs. Then sterilized in an autoclave at 1 ATM (1200 C) for 15 minutes. Sterile apricot extract from an autoclave can be safely stored in a cool laboratory place for up to a year.

The nutrient medium prepared according to the instructions described above is poured into sterile Petri Bowls in a volume of not less than 3 mm (10.0 ml) thick. The nutrient medium can also be poured into branded test tubes (3.0 ml) and used freely. It is better to keep Petri bowls and test tubes in sterile boxing conditions, in which the nutrient medium is poured.

Recommended "nutrient medium for growing dermatophytes" (invention patent No. JAP 07071.22-08-2022 y) the effectiveness of the current Saburo was carried out by model experiments with the nutrient medium and by the method of comparative analysis of the growth of fungodermatomycetes in clinical materials.

In the experiments carried out, the growth rate and character of the colonies, as well as the morphological characteristics of dermatomycetes, were studied.

For the study, materials from damaged smooth skin, hair, and nail plates of 400 patients (184 children under 14 years old, 107 men and 109 women) were planted parallel to the surface of the standard Saburo dense nutrient medium, and the proposed nutrient media at one time and incubated at a thermostat at 260-370s. In addition to it, the damage of the two nutrient media by bacterial, yeast, and mold fungi has been studied in a comparative way.

From the practice of mycological examinations, it is known that in cultural diagnosis, the negative effect of secondary bacterial infections, yeast, and mold fungi infestation of food media is great. Our experiments have shown that in the Saburo food environment, the infestation with bacterial, yeast, and mold fungi was 19-21% in the case, and in the proposed food environment 11-13%.

In our model research work, cultures of three species of fungi (Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum) were studied, the most common among dermophytes. These types of dermatomycoses are fungi that can be isolated from most patients. Strains of skin-venereal diseases of the Tashkent region from the collection of therapeutic and pathogenic cultures of the Mycology Laboratory and pure cultures extracted from pathological materials obtained from patients diagnosed with mycosis were also used.

The growth dynamics of dermatophyte colonies were as follows. On the first day of observation, an increase in both environments did not occur, on the second day, the first 0.1-0.3 cm increase in Trichophyton rubrum began to be observed in the proposed food environment. On days 4-5-6, in Saburo and the proposed environments, the fungal colonies reached from 0.2 cm to 3.0-3.8 cm. But it is worth saying that by the 6-7 days of observation, the size of the colonies in the proposed food environment (6.1-6.5 cm) became almost twice as large as in the Saburo food environment (3.5-3.8 cm.

In the same way, a comparison was studied of the features of the formation of a colony of fungi of four species (Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum, Trichophyton verrucosum) in parallel at one time. From our research, it is known that in the proposed food environment, the flourishing and colony formation of all fungi was two times less (from 7-8 days to 11-12 days) than in the controlled ones.

Identification of colonies of fungi-dermatophytes in the food environment plays a key role in the accurate diagnosis of dermatomycoses. In this part of the study, studies were carried out on the identification of the colonies of fungi-dermatophytes belonging to four species (Trichophyton rubrum, Microsporum

canis, Epidermophyton floccosum, Trichophyton verrucosum). From the research, it turned out that Trichophyton verrucosum from research cultures was formed in 11-12 days, and Epidermophyton floccosum and Trichophyton rubrum in 9-11 days at the level of identification (pigment formation, mycelium, and the appearance of spores, etc.) in the short term and made it possible to fulfill the task of effective collection.

On the contrary, it was noted that fungi of four species, planted in the Saburo food environment, grow for 18-26 days. Hence, in relation to the proposed nutrient medium, the growth time of dermatomycetes was two times longer.

Recommendations and conclusions:

- In the practice of Mycological laboratories of the Republic, it was shown that the rate of absorption of the pure culture of dermatophytes of the food environment used is 30-32%, and the growth period is 18-21 days;

- For the first time, a quality new nutrient medium was prepared and recommended for the collection of dermatophytes, the basis of which is made up of local ingredients;

- It has been proven that the newly prepared food environment is effective from the environment used in practice, including the growth rate has been reduced from 6-7 days to 2-5 Days, and the identification period has been reduced from 18-21 days to 8-12 days;

- Secondary bacterial, yeast, and mold fungal infestation in the proposed food environment was reduced from 19.0% -21.0% to 11.0% -13.0% compared to the standard Saburo food environment;

-All technical requirements and guidelines of the proposed food environment were developed and recommended by standards.

REFERENCES

1. Adaskevich V.P. Skin manifestations in patients with coronavirus infection covid-19 and features of the work of a dermatovenereologist during a pandemic CONSILIUM MEDICUM 2020 | volume 22 | №7 / page 13.

2. Abidova Z.M., Nurmatov U.V., Tulyaganov A.R. Species composition of dermatophyte pathogens for 6 years (1995-2000) according to the data of the of the Ministry of Health of the Russian Federation. In the book Theses of the VIII All-Russian Congress of Dermatovenerologists M. -2001, -part I, -p. 154-5.

3. Allaberganova Z. S. Cultivation of yeast-like fungi of the genus CANDIDA on different nutrient media and their biological properties, abstract dissertation Candidate of Biological Sciences, Tashkent, 2006

4. Antonova S. B. MODERN CLINICAL AND EPIDEMIOLOGICAL FEATURES OF THE INCIDENCE OF DERMATOMYCOSIS IN CHILDREN. OPTIMIZATION OF DIAGNOSTIC, MEDICAL, AND PREVENTIVE TECHNOLOGIES Dissertation for the degree of Candidate of Medical Sciences, Yekaterinburg, 2019, pp. 4-5.

5. Arifav S.S., Eshboev E.X. skin and venereal diseases, Tashkent, 1997.

6. Arifov S.S. Clinical dermatology and venereology, Atlas, Tashkent, 2008.

7. Dvoryankova E.V., Korsunskaya I.M., Slavyanskaya T.A. Skin manifestations of COVID 19 Bulletin of the RUDN. Series: MEDICINE 2021;25(1): pp. 13-14

8. Report on the global HIV epidemic/AIDS. Global Report. 10th. UNAIDS 2020.

9. Zykov K.A., Stadnikova A.S., Tamrazova O.B., Sinitsyn E.A. Skin manifestations in COVID-19. Clinical dermatology and venereology. 2021;20(4):50 54.

10. Imamov O.S., Correction of connective tissue metabolism in patients with mycoses of the feet of elderly and senile age: abstract. dis. Candidate of Medical Sciences, Tashkent, 2011.

11. Karabaeva I.T. Development of methods of treatment of zooanthroponosis microsporia on the basis of clinical and immunobiochemical research, abstract of the dissertation of Doctor of Philosophy (Ph.D.), Tashkent, 2019.

12. Kochneva E.V. Determination of pathogenicity factors of Candida albicans fungi and their role in the development of the infectious process. Topical issues of modern medicine: Collection of scientific tr. Yekaterinburg, 2014: 110-113.

13. Podkhomutnikova O.V., Vorobyeva O.N., Konyakhina I.G., Lazareva G.A., Tipikina L.M. Method of isolation of dermatophytes from clinical material. RF Patent 2181144 (10.04.2002). 7 From 12 N 1/14, From 12 Q 1/04.

14. Raznatovsky K.I., Rodionov A.N., Kotrekhova L.P. Dermatomycoses: A guide for doctors. - St. Petersburg: Publishing House, 2003, p. 158.

15. Sadikov A.A., Tokhtaev G.Sh., COMPARATIVE ANALYSIS OF THE STATE OF THE SKIN MICROBIOME IN ATHLETES OF VARIOUS SPECIALIZATIONS DURING TRAINING PERIODS, Dermatovenerology and reproductive health 2020 No. 3-4, ISSN 2091-5969., 109 p.

16. Sergeev A.Yu., Sergeev Yu.V. Fungal infections. A guide for doctors. – Moscow:, 2008. – 480 p.

17. Tashkenbayeva U.A., Klebleeva G.D. Features of trace element and immunological status in patients with dermatological manifestations after COVID-

19 infection COLLECTION OF ABSTRACTS OF THE SCIENTIFIC AND PRACTICAL CONFERENCE "DERMATOVENEROLOGY AND COSMETOLOGY: ACHIEVEMENTS OF SCIENCE IN PRACTICE" 2022 Page 51.

18. Tilovberdiev Sh.A. Deep Mycoses in immunocompromentive patients: clinic, diagnosis, treatment, and Prevention; abstract of the dissertation of Doctor of Medical Sciences, Tashkent, 2020.

19. Khismatullina Z.R., Mukhamadeeva O.R. Sposob videlenia dermatofitov. Vestn dermatol 2006; 2: 25-27.

20. Eshbaev E.X., Babajanov X.R., 2019 M. Khudoynazarov S.Q infectious and parasitic diseases of the skin and their laboratory diagnostics, Tashkent, 2021.

21. Eshbaev E.X., Mirsaidova M.A. Laboratory diagnosis of the diagnosis of dermatovenerological diseases. Educational guide, Tashkent 2022.

22. Yakshibaeva L.A., Knyazeva O.A. DERMATOMYCOSES: FEATURES OF DIAGNOSTICS AND THERAPY // European Journal of Natural History. – 2021. – No. 2. – p.51.

23. Garg J., Tilak R., Garg A., et al. Rapid detection of dermatophytes from skin and hair. BMC Research Notes 2009; 2:60- 66.

24. Kwon-Chung K.J., Bennett J.E. Medical Mycology. Lea & Febiger. Philadelphia – London, 1992.- 866 p.

25. Rippon J.W. Medical mycology. In The Pathogenic Fungi and the Pathogenic Actinomycetes 3rd edition. Philadelphia: WB Saunders; 1988. 14.

Central Asian Journal of Medicine

EFFECTIVENESS OF COMPLEX TREATMENT OF PATIENTS WITH ACUTE PERITONITIS

Mahmuda N. Agzamova[1], Farhod D. Ortiqboyev[2]

1 Associate Professor of the Department of General Surgery, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

2 Assistant of the Department of General Surgery No. 2, Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

In our research, we tested the effectiveness of complex treatment of patients with acute peritonitis with lymphotropic therapy with antibiotics and thymalin according to our method.

Key words: peritonitis, lymphotropic drug administration, acute peritonitis, thymolin.

INTRODUCTION

Acute peritonitis-acute inflammation parietal. and visceral leaflets of the peritoneum. [1] Typically, peritonitis endangers the life of the patient and requires urgent medical attention. Untimely and inadequate treatment of acute peritonitis can lead to lethal outcome. [3,5] In the field of surgery, acute peritonitis a common disease. The reason can be called that most acute surgical diseases and abdominal injuries are often complicated by peritonitis.

Research objective

The purpose of this study was to assess the effectiveness of the use of a solution of furacilin on a hypertonic salt basis, lymphotropic administration of antibiotics and thymalin in patients with acute peritonitis.

Patients and methods

The study included acute peritonitis patients in the surgical department I - Clinics Tashkent. Patients were divided into 3 groups. The first group included 103 patients treated with traditional methods. The second group consisted of 89 patients who were treated after the operation abdominal flushing with a 10% hypertonic chloride solution solution (1:5000) sodium at a ratio of 2:1, antibiotics

injected lymphotropic. In the third group there were 106 patients in which Thymalinelymphotropic therapy has been included in our comprehensive treatment.

Results

Group 1 patients had local peritonitis in 42 (40.8%) diffuse in 36 (34.9%), spilled in 25 (24.3%) patients. Reactive - 44.7%, toxic - 44.7 47.9% and the terminal stage at 7.44%. 46.1% of the operated general condition was severe and very severe. 23.1% of patients had various concomitant diseases. The main clinical and laboratory indicators for teams examined prior to the intervention, are shown in table 1.

Table 1

Peritonitis indicators	**Peritonitis prevalence**	**1 group**	**2 group**	**3 group**
Tachycardia (in 1 min)	Local	102,8±8,61	96,9±7,1	101,4±9,3
	Diffuse	113,2±10,9	119,1±8,6	121,9±6,7
	Spilled	128,3±5,7	131,2±3,9	127,8±11,3
Body temperature (in degrees)	Local	37,6±0,7	36,9±1,01	37,3±1,2
	Diffuse	37,7±0,8	37,8±0,7	38,8±0,8
	Spilled	38,6±0,5	38,3±0,9	38,1±0,91
Breathing rate (in 1 min)	Local	25,1±1,8	27,2±2,6	24,3±1.9
	Diffuse	29,3±2,1	31,5±2,4	30,6±2,7
	Spilled	31,4±3,2	34,1±3,9	34,9±3,06
White blood cells (thousands)	Local	10,9±1,9	11,1±1,09	10,2±1,0
	Diffuse	14,1±1,1	16,6±1,51	18,8±2,2
	Spilled	20,3±1.7	19,7±1,8	22,9±1.9
Lymphopenia (in %)	Local	21,3±0,85	22,2±0,96	19,7±1,01
	Diffuse	17,4±1,1	15,5±0,9	14,7±1,2
	Spilled	12,03±0,91	11,8±0,77	10,1±0,8
ESR (mm/h)	Local	12,7±1,02	14,3±2,1	17,8±1,9
	Diffuse	29,3±2,7	30,2±1,9	32,5±2,7
	Spilled	45,8±4.1	39,7±2,3	52,16±4,8
LII (in unit)	Local	8,1±0,12	8,7±0,2	8,9±0,21
	Diffuse	11,1±0,7	12,8±0,3	13,1±0,11
	Spilled	13,4±0,9	13,3±0,05	14,4±0,9

With serous and serous hemorrhagic inflammatory exudate surgical wound stitched tight and installed microirrigators for intraperitoneal administration of

antibiotics. Abdominal vent was vented with pus cavities with tubular drains for exudate outflow, antibiotic therapy and washing.

With serous and serous hemorrhagic inflammatory exudate, surgical wound stitched tight and installed microirrigators for intraperitoneal administration of antibiotics. Abdominal vent was vented with pus cavities with tubular drains for exudate outflow, antibiotic therapy and washing.

Patients with local peritonitis in the postoperative period received traditional antibiotic therapy and intravenous infusion therapy. Lethal there were no outcomes.

Patients with severe diffuse and spilled peritonitis received complex intensive therapy: barbus, antibacterial therapy, correction metabolic disorders, hypovolemia and paralytic intestinal obstruction. Despite treatment, 10 patients died in this group - 4 patients (3.45%) diffuse, 6 (8.57%) spilled. Basic cause of death was acute cardiovascular insufficiency caused by the development of multi-organ deficiency as a result of severe endotoxicosis.

In the second group, local peritonitis was 40 (41.7%), diffuse in 37 (38.5%), spread in 19 (19.8%) patients. Reactive in 46 (46.9%), toxic - 43 (43.9%), terminal stage in 9 (9.2%). This patient after rapid intervention was washed abdominal concoction of a furacilin solution (1:5000) with 10% hypertonic sodium chloride solution in a 2:1 ratio, antibiotics injected lymphotropically.

Deaths in patients with local peritonitis no. Average stay decreased by 3 days, which is significantly less than the I group. Lethality at 1% diffuse, 5.7% diffuse.

In the third group, local peritonitis was 30 (30.3%), diffuse in 43 (43.4%) and diffuse in 26 (26.3) patients. Reactive in 49 (46.2%), toxic in 48 (45.2%) and in 9 (8.4%). In these patients lymphotropicthymalin therapy. [2,4]

The average hospital stay was less than 2 days compared to 2 days of group and 5 days of compared to 1 group. Treatment time reduced to 1.5 and 2 times compared to I and II group.

No deaths at local peritonitis. Diffuse peritonitis lethality was 0.34%, when spilled 2.9%.

As a result of the therapy received, there is a pronounced curative effect, reduced pulse rate, stabilization of AD, reduction of CD, reduction of intoxication, increase percent of lymphocytes and other improvements homeostasis.

REFERENCES

1. Agzamova M. N., & Usmonbekova G. U. (2018). Effektivnost' kompleksnogo lecheniya bol'nyh ostrym peritonitom. Molodoj uchenyj, (18), 135-137.

2. Ismoilov F. M. DIAGNOSTIKA I LECHENIE BOL'NYH S OSTROJ KISHECHNOJ NEPROHODIMOST'YU. Zbiór artykułów naukowych recenzowanych., 69.

3. Mustafakulov G. I., Ergashev U. Y., Atakhodjaeva F. A., & Anvarhodjaeva S. G. (2022). Simultaneous surgeries in chronic immune thrombocytopenia.

4. Teshaev O., Holov H., Babazhonov A., & Ortiқboev F. (2022). PRIMENENIE SETCHATYH IMPLANTOV PRI DIAFRAGMAL'NOJ GRYZHI PISHCHEVODNOGO OTVERSTIYA (OBZOR LITERATURY). Eurasian Journal of Medical and Natural Sciences, 2(6), 257-264.

5. Yusufjanovich E. U. (2023). Management of Patients with Acute Arterial Ischemia of the Lower Limb. International Journal of Scientific Trends, 2(2), 43-48.

Central Asian Journal of Medicine

CLINICAL FEATURES AND BLOOD CYTOKINE SPECTRUM IN PATIENTS WITH VARIOUS FORMS OF SKIN LEISHMANIASIS

Guli A.Ismailova[1], Zura M.Abidova[2], Farrux F. Umurov[3]

1 Doctor of Medicine, professor of the Department of Dermatovenereology and cosmetology of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: guliismailova555@gmail.com

2 Doctor of Medicine, dermatovenereologist of the Department UZ OOO Akfa Medline, Tashkent, Uzbekistan

3 Assistant of the Department of Dermatovenereology of the Bukhara Medical Institute, Bukhara, Uzbekistan
E-mail: hmx93@mail.ru

ABSTRACT

The purpose of the study: to study the features of the clinic and the cytokine spectrum of peripheral blood in patients with various forms of cutaneous leishmaniasis.

Materials and methods: clinical methods (clinic and course of cutaneous leishmaniasis in the endemic region of the Bukhara region, the Republic of Uzbekistan) were used; microbiological (detection of the pathogen - Borowski's bodies), immunological (IL-4, IL-6, IL-8, TNF-α, IFN - α and IFN -γ, relative and absolute number of B-lymphocytes (CD20+), markers of lymphocyte activation (CD25+, CD95+), statistical methods of investigation were used. The object of the study was 214 patients of both sexes with various clinical forms of cutaneous leishmaniasis aged from 1 to 68 years and 20 healthy individuals.

Results: according to the clinical forms of cutaneous leishmaniasis - tuberculous form was in 92 (43%), ulcerated leishmaniomas - in 68 (31.8%), ulcerated leishmaniomas with seeding tubercles with lymphangitis - in 53 (24.7%) and metaleishmaniasis - in 1 (0.5%) patient. Microbiological examination of lesions revealed in 190 (88.7%) of 214 patients Borovsky's body, in 161 (75.2%) cases zoonotic, in 53 (24.8%) cases - anthroponotic cutaneous leishmaniasis.

Conclusions: significant deviations of IL-6, IL-8 and TNF-α were found in all patients, while the most significant activation of pro-inflammatory cytokines was observed in patients at the stage of complications, lymphangitis, lymphadenitis and progression of the inflammatory process. In patients with ulcerated leishmaniomas with seeding tubercles and with lymphangitis, a deficiency of IL-4 and IFN-γ was recorded, as well as a decrease in the activity of markers of early activation of CD25+. The most pronounced expression of CD95+ receptors was recorded in patients with a protracted course and the development of complications, a less pronounced

form was noted in the tuberculous form of the disease. The results obtained made it possible to determine the main criteria for the progression of an immunodeficiency state in various clinical forms of cutaneous leishmaniasis.

Key words: leishmaniasis, clinic, cytokine spectrum.

INTRODUCTION

Cutaneous leishmaniasis (Leishmaniosi cutis), or Borovsky's disease (synonyms: Old World cutaneous leishmaniasis - Borovsky's disease; New World cutaneous leishmaniasis - American cutaneous leishmaniasis; visceral leishmaniasis - kala-azar) is a transmissible, protozoal disease with endemic distribution in countries with hot, tropical and subtropical climate [8,9,11]. The disease is accompanied by skin lesions, mainly ulcers, on exposed areas of the body, can leave permanent scars, cause severe disability and lead to stigmatization of people who have suffered from the disease. In the early 1990s, WHO estimates that leishmaniasis affects about 12 million people in 88 countries. About 95% of cases of cutaneous leishmaniasis occur in the Americas, the Mediterranean basin, the Middle East and Central Asia. The annual number of new cases of this form of the disease is estimated to range from 600,000 to 1 million, but only about 200,000 cases are reported to WHO. In Central Asia, the main endemic zones are located in Uzbekistan and Turkmenistan [5,6,13].

Cutaneous leishmaniasis (CL) in Uzbekistan is also a fairly common pathology among natural focal diseases. In the endemic regions of Uzbekistan (Bukhara, Surkhandarya, Kashkadarya, Jizzakh, Karakalpakstan), there is a rather high prevalence of zoonotic cutaneous leishmaniasis, where dozens of new cases of this disease are recorded annually. [6,7,12].

Leishmaniasis, depending on the region of distribution, causes damage to the skin, mucous membranes and internal organs. In the foci of this disease, large outbreaks often occur with the defeat of 60-90% of non-immunized people.

Affecting people of predominantly working age, CL deprives them of the ability to work, sometimes for a long time, which in turn brings great economic damage to the state. [5,7,11].

Currently, the existing methods of combating CL, including the extermination of reservoirs of the pathogen and carriers, are laborious and do not always give a significant result. Due to the increase in morbidity, registration of complications and atypical forms, insufficient preventive measures and pathogenetically substantiated methods of not only outpatient, but also inpatient treatment, make the problem of CL extremely relevant [1,2,4,10,13,14].

An important link in the immunopathogenesis of CL, which determines the outcome of the disease, is the state of immune reactivity. Moreover, the clinical

course of the disease largely depends not only on the form or stage of the disease, but also on the state of imbalance in the system of cytokines and their receptors with pro- and anti-inflammatory functions, which largely determines the mechanisms of dysregulation of cellular and humoral immunity and the development of the disease [3,9,12,15].

Therefore, the study of various issues regarding the clinical course, immunopathogenetic aspects and the development of effective methods of CL therapy on this basis has particular relevance.

Purpose of the study

To study the features of the clinical course and the cytokine spectrum of peripheral blood in patients with various course of cutaneous leishmaniasis.

Material and methods

Clinical methods (clinic and course of cutaneous leishmaniasis in the endemic region of the Bukhara region, the Republic of Uzbekistan) were used; microbiological (detection of the pathogen - Borowski's bodies), immunological (IL-4, IL-6, IL-8, TNF-α, IFN - α and IFN -γ, relative and absolute number of B-lymphocytes (CD20+), markers of lymphocyte activation (CD25+, CD95+), statistical methods of investigation were used. The object of the study was 214 patients of both sexes with various clinical forms of cutaneous leishmaniasis aged from 1 to 68 years and 20 healthy individuals.

Results and discussion

The 214 patients with CL under observation were aged from 1 to 68 years. There were 98 (45.8%) men and 116 (54.2%) women. There were 53 (24.8%) urban residents and 161 (75.2%) rural residents.

There were 115 (53.7%) patients under the age of 14 years, 32 (14.9%) at the age of 15-30 years, 12 (5.6%) at the age of 31-40 years and over 40 years of age. - 55 (25.8%) patients. The vast majority were rural residents (78.6%), and among the patients, children under the age of 14 years (53.7%) predominated among those surveyed.

The duration of the disease ranged from 15 days to 3 years, including up to 2 months in 117 (54.6%), from 3 to 4 months in 75 (35.1%), from 5 to 6 months in 20 (9.3%), from 7 months - up to 1 year in 1 (0.5%) patient, and over 1 year - in 1 (0.5%) patient.

According to the clinical forms of CL - tuberculous form was diagnosed in 92 (43%), ulcerated leishmaniomas - in 68 (31.8%), ulcerated leishmaniomas with tubercles of seeding with lymphangitis - in 53 (24.7%) and metaleishmaniasis - in 1 (0.5%) of the patient. Microbiological examination of lesions revealed in 190 (88.7%) of 214 patients with Borovsky's body positive.

As can be seen from the observations, zoonotic CL was detected in 161 (75.2%) cases, anthroponotic CL in 53 (24.8%) cases. Infection occurred at the place of residence of patients, and in most cases through blood-sucking insects - mosquitoes. The largest number of cases lived in the Romitan, Jondor, Peshku and Olot regions of the Bukhara.

Clinical observations showed that among patients with anthroponotic form of cutaneous leishmaniasis (53 patients), 27 had a tuberculous stage of the disease, the remaining 26 patients had a tuberculous-ulcerative stage of leishmaniasis. It should be noted that only 12 out of 53 patients with anthroponotic form of cutaneous leishmaniasis had specific lymphangitis or lymphadenitis. The number of foci varied from 1 to a maximum of 3, which is typical for anthroponotic leishmaniasis. In all patients with rural type of cutaneous leishmaniasis, rashes were represented by ulcerative and complicated forms of the disease. In one case, a complicated form of CL was found - metaleishmaniasis (tuberculoid type, the patient has been suffering from leishmaniasis for 9 years) with manifestations of new tubercle elements around the old scar.

An analysis of the clinical course showed that, lesions were more often localized in open areas of the body, mainly on the skin of the face, in the area of the nose, cheeks, and were presented in the form of tuberculous elements with an inflammatory infiltrate around in children. The skin was distinguished by a bright red color, and in the center of the tubercles there was a serous-bloody crust in the affected area.

In addition to tuberculous elements, there were also ulcerative rashes in adult patients, mainly located on the upper (shoulders, forearms, elbows, hands) and lower extremities (thighs, shins, feet) and on the trunk.

Zoonotic and anthroponotic types of CL had a typical clinical picture. In the anthroponotic form of CL, tubercular leishmanioma was manifested by a barely noticeable papule-tubercle with a diameter of up to 2-3 mm, the color of normal skin, which slightly rose above the level of the surrounding healthy skin, without visible inflammatory changes. The skin above it was tense, shiny and had a reddish-brown color. In the center of some tubercles there was a small crater-like depression with horny scales on the bottom or a rounded ulcer with a smooth or wrinkled bottom, covered with a purulent coating. At the same time, the edges of the ulcer were uneven, steep, the bottom was slightly granular with scanty serous-purulent discharge, as well as areas of necrotization. A roller-like infiltrate was formed around the ulcerative elements. As a rule, the number of ulcers did not exceed 1-3 and they were localized mainly on open areas of the skin accessible to mosquitoes (face, hands).

There was a red, acutely inflammatory, cone-shaped tubercle up to 2-4 mm in diameter in patients with zoonotic CL. The tubercles reached up to 15-20 mm in diameter in some patients. There was an inflammatory edema of the skin around the tubercles. Ulcerative elements with abrupt edges and necrotic bottom reached from 2-4 mm to 4-5 cm in diameter. A wide infiltrate and inflammatory edema with seeding tubercles around could be seen along the periphery of the ulcers. The ulcers were uneven with undermined edges, the bottom of which was filled with necrotic masses or copious serous-purulent discharge. In part of the ulcers, the edges were even, undermined, and an infiltrate rose up around it in the form of a roller.

Along with tuberculous and ulcerative elements, some patients had foci with growing granulations in the form of papillae, resembling a "fish caviar symptom". In some patients, the pathological process proceeded with complications in the form of lymphangitis, lymphadenitis and successive leishmania. There were swelling of the legs and feet due to lymphostasis on the lower extremities with complications of lymphadenitis. In 1 (0.5%) patient, metalishmaniasis was diagnosed, where the pathological process was represented by yellowish-brown small tubercles up to 2-3 mm in diameter. In place of the former tubercles and ulcerations, there were ulcerated old tubercles and the formation of scars was clearly visible, and new, fresh tubercles continued to appear along the edges of the infiltrate.

In some cases, an abortive course of CL, accompanied by a long-term preservation of small tubercular elements without the formation of an open ulcer was observed.

Elements of rashes in 121 (56.5%) patients were localized in the face (eyebrows, nose, cheeks, bridge of the nose, corner of the mouth, chin), in 26 (12.1%) - on the upper limbs (shoulders, forearms, elbows, hands).), in 20 (9.4%) - on the lower extremities (thighs, shins, feet), in 16 (7.5%) - on the trunk, upper and lower extremities, in 15 (7.0%) - on the face and upper limbs, in 9 (4.2%) patients in the upper and lower limbs, and in 5 (3.3%) patients in the chest and trunk.

In patients, the number of existing ulcers in the lesions varied from 1 to more than 10 pieces. Thus, 113 (52.8) patients had 1 ulcer, 73 (34.1%) - 2-3, 19 (8.9%) - 4-5, 5 (2.3%) - 6-7, in 4 (1.9%) - 8-9 ulcerative elements.

Subjective sensations against the background of inflammation in the form of itching were accompanied in 78 patients, pain in 54, 82 patients did not complain. Moreover, 18 patients had pain and itching at the same time.

The cytokine network is the most important regulatory mechanism of intercellular interactions. An imbalance in the production of cytokines is important in the immunopathogenesis of chronicity and disease progression. We have studied the content of anti- and pro-inflammatory cytokines in patients depending on the clinical forms of CL (IL-4, IL-6, IL-8, TNF-α and IFN-γ).

It was necessary to establish the features of cytokine-mediated mechanisms of dysregulation of the immune system and to characterize changes in the subpopulation composition of lymphocytes in patients with CL.

Blood sera of 96 patients with various clinical manifestations of CL were selected for the study. The control group consisted of data from 20 practically healthy individuals comparable by sex and age.

Studies have shown the highest values of pro-inflammatory cytokines IL-6, IL-8, TNF-α in patients with ulcerated leishmaniomas with seeding tubercles with lymphangitis ($p<0.001$). (Fig. 1) A less pronounced reaction from IL-8 was found in patients with ulcerated leishmaniomas, although within reliable limits. All patients with CL had significantly high levels of TNF-α, the highest values were obtained in the group with complicated forms. A different picture was observed in the level of IL-4. Relatively low values were determined only in patients with ulcerated leishmaniomas and ulcerated leishmaniomas with tubercles of seeding and with lymphangitis. The same dynamics was observed in relation to immune IFN-γ, the concentration of which in low limits was also characteristic of patients with complicated forms of CL.

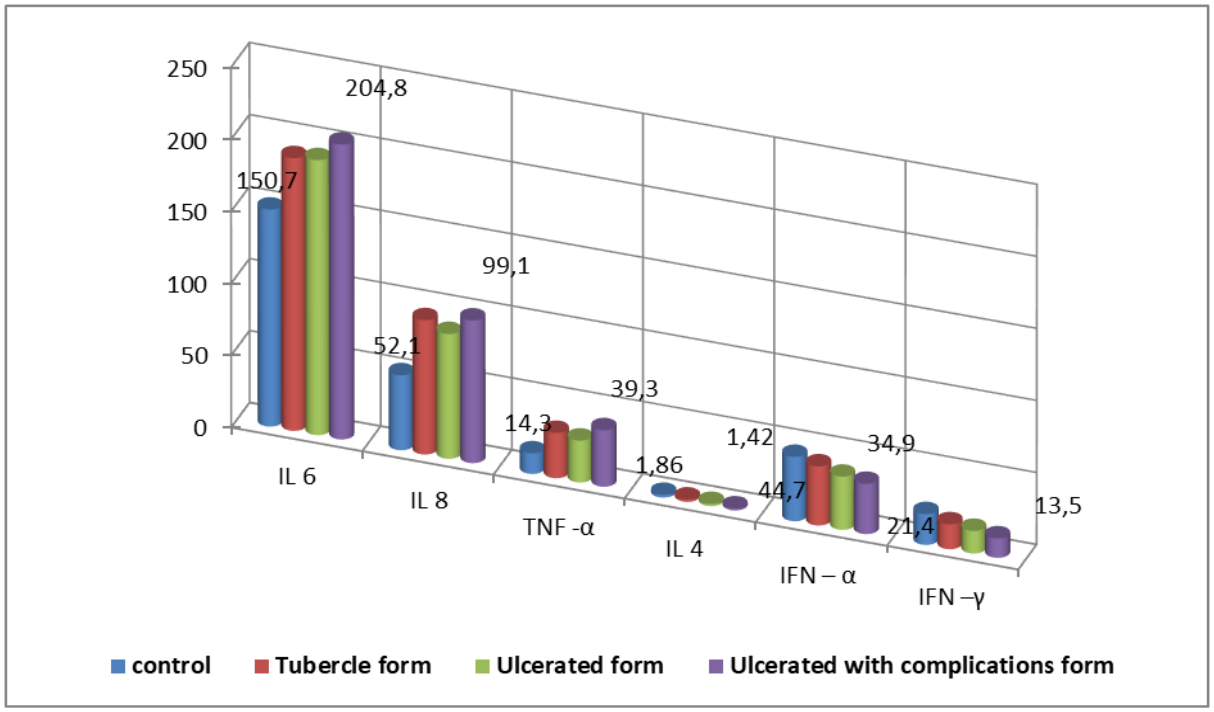

Fig. 1. Indicators of blood cytokines in patients with various clinical forms of cutaneous leishmaniasis.

Thus, the analysis of the obtained data shows that changes in the content of cytokines are detected in CL, which is expressed by a deficiency in the blood serum of the concentration of the anti-inflammatory cytokine IL-4, as well as IFN-γ, and an increase in the content of pro-inflammatory cytokines IL-6, IL-8 and TNF-α, which are directly dependent on the clinical form of the disease.

The analysis of the content of lymphocytes in the blood of patients expressing activation antigens showed a significant increase in the relative and absolute number of CD20+ cells in all patients with CL compared with the control, which suggests activation of the B-cell component of the immune system as a whole. A significant decrease in the absolute number of cells with the CD25+ marker was noted in patients with all clinical forms of CL, however, the absolute value was reduced in patients with ulcerated leishmaniomas with seeding tubercles and with lymphangitis. Increased expression of CD95+ receptors indicates an imbalance in activation signals, which leads to the development of an immune response through apoptosis. At the same time, in the tubercular stage, increased expression of CD95+ was less pronounced than in other clinical forms.

Conclusions

Thus, clinical and epidemiological studies have shown that CL mainly affects children under 14 years of age (53.7%), women (54.2%), with the duration of the process in most cases from 2 to 6 months. The tuberculous form was diagnosed in 92 (43%), ulcerated leishmaniomas - in 68 (31.8%), ulcerated leishmaniomas with tubercles of seeding and with lymphangitis - in 53 (24.7%) and metaleishmaniasis - in 1 (0.5%) of the patient. In 161 (75.2%) cases, zoonotic CL was detected, in 53 (24.8%) cases - anthroponotic CL. In children, ulcers were more often localized in open areas of the body, mainly on the skin of the face, in the area of the nose, cheeks, and in adults - on the skin of the lower and upper extremities. The number of lesions in the form of ulcers ranged from 1 to more than 10. Clinical observations made it possible to identify the features of the course and characterize the skin-pathological process of CL in the conditions of the Bukhara region and the city of Bukhara.

A comparative analysis of the studied immunological parameters in patients with CL made it possible to establish their pronounced changes. Significant deviations of IL-6, IL-8 and TNF-α were noted in all patients with CL, the most significant activation of pro-inflammatory cytokines was observed in patients at the stage of development of complications, lymphangitis, lymphadenitis and progression of the inflammatory processAt the same time, against the background of IL-4 and IFN-γ deficiency, a pronounced activation of B-lymphocytes with the

CD20+ phenotype was observed, which was inherent in all patients with various forms of CL. In addition, a decrease in the activity of markers of early activation of CD25+ was recorded in patients with ulcerated leishmaniomas with seeding tubercles and with lymphangitis. The most pronounced expression of CD95+ receptors was recorded in patients with a protracted course and the development of complications, less pronounced in patients with tuberculous form of CL.

The obtained results made it possible to determine the main criteria for the progression of an immunodeficiency state in various clinical forms of CL, and, on this basis, to develop approaches to therapy.

REFERENCES

1. Akovbyan A. A., Muhamedov S. M. Treatment of acute necrotizing cutaneous leishmaniasis with monomycin // Vestn. dermatol. - 1968. - №1. - S. 74-76.

2. Alyavi S. F. Clinical and experimental substantiation of the use of ointment "Leishmycin" in zoonotic cutaneous leishmaniasis.: Avtoref. diss. … kand. med. nauk. – Tashkent, 2000. – 24 s.

3. Arustamyan T. A. On the persistence and duration of immunity in cutaneous leishmaniasis // Vestn. dermatol. - 1965. - №5. - S. 66-68.

4. Vaisov A. SH. The use of laser therapy in the complex therapy of zoonotic cutaneous leishmaniasis // Novosti dermatologii i venerologii. – 2009. - №2. - S. 13-14.

5. Danilov S.I., Nechaev V.V. Topical skin infectious diseases of the tropics. – SPb: SPb GMA im. Mechnikova, 2001. S. 34-53.

6. Zoonoznyj kozhnyj lejshmanioz v Uzbekistane i ego profilaktika / SHaripov M. K., Razzakov SH. A., Krasnonos L. N. i dr. // Med. parazitol. i parazitar. bolezni. - 1987. - №1. - S. 39-45.

7. Zoonotic cutaneous leishmaniasis and prospects for its prevention in the Uzbek SSR / Krasnonos L. N., Ulematov A. I., Abdullaev I. V. i dr. // Med. zhurnal Uzbekistana. - 1978. - №10. - S. 12-15.

8. Kapkaev R.A., Skripkin YU.K.Borisenko K.K. i dr. Handbook of a dermatovenereologist. – Tashkent: Ibn Siny, 1992. S. 179-182.

9. Skripkin YU.K., Butov YU.S. Clinical dermatovenereology.-Moskva: GEOTAR-Media, Tom 1, 2009. S. 350-372.

10. A case of atypical course of cutaneous leishmaniasis in an HIV-associated complex / Ismailova G.A., Azizov B.S., Artykova N.S.,F.H.Nabiev. // Novosti dermatovenerol. i reprodukt. zdorov'ya. -2009.-№3.-S.59-62.

11. Ficpatrik T., Dzhonson R., Vulf K., Polano M., Syurmond D. Dermatology. Atlas-reference book.. McGraw-Hill. Praktika- 1999. S. 870-877.

12. Efficiency of complex treatment for cutaneous leishmaniasis/ G.A.Ismailova,F.F. Umurov, Z.M. Abidova// EADV Symposium 2022.- Ljubljana, 12-14 may. P.555.

13. Koff A. B., Rosen T. Treatment of cutaneous Leishmaniasis // J. Amer. Acad. Dermatol. - 1994. - Vol. 31. - P. 693-708.

14. Van der Snoek E., Robinson D., van Hellemond J. A review of photodynamic therapy in cutaneous leishmaniasis // J. Eur. Acad. Dermatol. Venerol. - 2008. - Vol. 14. - P. 87-89.

15. Shahbasi F., Shababi S., Kasemi B./ Evalution of PCR assay in diagnosis and identification of cutaneous leishmaniasis: a comparison with the parasitological methods // Parasitol. Res. - 2008. - Vol. 103. - P. 1159-1162.

Central Asian Journal of Medicine

PATHOGENETIC APPROACH IN TREATMENT BRONCHIAL ASTHMA IN CHILDREN

Barno T. Khalmatova[1], Gulnoza A. Tashmatova[2]

1 DSc, professor, head of Department of Children's diseases of Tashkent Medical Academy, Uzbekistan
E-mail: khalbar@mail.ru

2 PhD, senior teacher of Department of Children's diseases of Tashkent Medical Academy, Uzbekistan
E-mail tashmatovagulnoza@gmail.com

ABSTRACT

The article presents data on the clinical trials of local production of Montelukast (Republic of Uzbekistan). The purpose of the study is to assess the clinical efficacy and tolerability of montelukast preparations produced in Uzbekistan, in comparison with the drug Singlon, produced by Gedeon Richter JSC (Hungary). Methods. The clinical study was limited, comparative, open, controlled, randomized with four parallel groups. Studies were conducted in patients who are hospitalized in the pulmonology and allergology departments of the clinic of the Tashkent Medical Academy. The study involved 150 children aged 2 to 14 years with a diagnosis of intermittent, mild and moderate persistent bronchial asthma. Results: The clinical efficacy of the drugs was assessed in points for the improvement of clinical and laboratory data. The study showed a positive dynamics of clinical and laboratory parameters in all children who received Montelukast drugs. Conclusion. Studies have shown that local production montelukast is not inferior in its properties to foreign analogues and leads to a decrease in the level of cys-LT, IgE in children with asthma.

Key words: allergy, atopy, leukotriene receptors, bronchial asthma, children, montelukast.

INTRODUCTION

All over the world, including in Uzbekistan, bronchial asthma (BA) in children is an allergic disease that requires special attention. Epidemiological studies show that almost 1/3 of affected children experience 3 or more episodes of wheezing per year (which is considered the equivalent of an adult attack). Currently, there is a fairly wide range of effective drugs with a good safety profile and an affordable price for patients with this disease. Despite this, a large

proportion of patients receive inadequate treatment, which leads to a decrease in the quality of life, the formation of fixed bronchial obstruction, and even death [1,5]. Cysteinyl leukotrienes (LTC4, LTD4, LTE4) are potent anti-inflammatory eicosanoids released from various cells, including mast cells and eosinophils. These important pro-asthmatic mediators bind to cysteinyl leukotriene receptors (CysLT). CysLT type-1 (CysLT1) receptors are found in the airways (including airway smooth muscle cells and macrophages) and on other pro-inflammatory cells (including eosinophils and certain myeloid stem cells) [2,11,12]. CysLTs are associated with the pathophysiology of asthma and allergic rhinitis. In asthma, leukotriene-mediated effects include bronchospasm, mucosal secretion, vascular permeability, and recruitment of eosinophils. In allergic rhinitis, CysLTs are released from the nasal mucosa after exposure to the allergen during the early and late phase of the reaction, and are also associated with symptoms of allergic rhinitis. An intranasal test with CysLTs demonstrated an increase in nasal airway resistance and symptoms of nasal congestion[1,7,10].

Montelukast is an active substance that, when administered orally, binds with high affinity and selectivity to CysLT1 receptors. In clinical studies, montelukast inhibited bronchospasm induced by inhaled LTD4 at a dose of 5 mg. Bronchodilation occurred within 2 hours after oral administration. The bronchodilatory effect caused by β-agonists was complemented by the effect of montelukast. Treatment with montelukast inhibits both the early and late phases of bronchoconstriction due to antigenic stimulation. Montelukast, compared with placebo, reduces the level of eosinophils in the peripheral blood in adults and children. In a separate study, treatment with montelukast significantly reduced the number of eosinophils in the airways (determined by sputum analysis) and in peripheral blood, and improved clinical control of asthma [3,5,8,14].

In adult studies, montelukast 10 mg once daily, compared with placebo, showed a significant improvement in morning FEV1 (10.4% change from baseline compared to 2.7%), morning maximum expiratory flow rate (MOV) (24.5 L/min change from baseline vs. 3.3 L/min) and a significant decrease in total β-agonist use (change from baseline: -26.1% vs. -4.6%). Relief of daytime and nighttime asthma symptoms was reported by patients to be significantly better than placebo.

A clinical study was conducted to evaluate the use of montelukast for the symptomatic treatment of seasonal allergic rhinitis in patients aged 15 years and older with asthma and concomitant seasonal allergic rhinitis. In this study, montelukast (10 mg tablets, once daily) demonstrated a statistically significant improvement in daily rhinitis symptom scores compared to placebo. The 24-hour rhinitis symptom score is the average of the daytime (mean scores for nasal

congestion, rhinorrhea, sneezing, itchy nose) and nighttime (mean scores for nasal congestion on awakening, difficulty falling asleep, nocturnal awakenings) scores for rhinitis symptoms. Patients' and physicians' overall assessments of drug efficacy in allergic rhinitis were statistically better than placebo. Evaluation of efficacy in asthma was not the primary goal of this study [2,4,6,9,13].

In an 8-week study in children aged 6 to 14 years, montelukast 5 mg once daily compared to placebo significantly improved respiratory function (FEV1 8.71% vs. 4.16% change from baseline) indicator; change from baseline in morning MORV of 27.9 L/min vs. 8.2%.

A significant decrease in the measure of exercise-related bronchospasm (EIB) was observed at week 12 of the study in adults (maximum decrease in FEV1 22.33% for montelukast compared with 32.40% for placebo; time to recovery within 5% from baseline FEV1 44.22 minutes compared to 60.64 minutes). This effect was consistent throughout the 12-week study period. A reduction in ERF was also demonstrated in a short study in children aged 6 to 14 years (maximum reduction in FEV1 18.27% versus 26.11%; time to recovery within 5% of baseline FEV1 17.76 minutes versus from 27.98 minutes). The effect in both studies was demonstrated by the end of the drug dosing interval (1 time per day).

In aspirin-sensitive patients receiving concomitant inhaled and/or oral corticosteroids, montelukast treatment compared with placebo resulted in a significant improvement in asthma control (change from baseline in FEV1 8.55% versus -1.74% and change from baseline in reducing the total use of β-agonist -27.78% compared with 2.09%).

At the pharmaceutical market of the Republic of Uzbekistan today there are several names of montelukast preparations (Singlon, Gedeon Rixter, Hungary; Montular, Kusum, India; Miteka, India; Brizezi, India, etc.). The government of the republic pays great attention to the development of locally produced medicines. In the arsenal of pediatricians in Uzbekistan for the treatment of asthma, there are such drugs as Montexa (Nika Pharm, Uzbekistan), Neoclast (OOO Nobel, Uzbekistan), Astanol (Remedy Group, Uzbekistan).

PURPOSE OF THE STUDY

Evaluation of the clinical efficacy and tolerability of montelukast preparations manufactured in Uzbekistan, in comparison with the Singlon preparation, manufactured by Gedeon Richter JSC (Hungary).

MATERIALS AND METHODS

The study was conducted in accordance with the Declaration of Helsinki, adopted in June 1964 (Helsinki, Finland), revised in October 2000 (Edinburgh, Scotland) and in accordance with the Law of the Republic of Uzbekistan "On

Medicines and Pharmaceutical Activities" , "The National Standard of Uzbekistan - GSR - Good Clinical Practice", taking into account the GSR rules used in international practice, the Regulations "On the procedure for conducting clinical trials and examination of materials for clinical trials of pharmacological and medicinal products" (Appendix 1 to the Order of the Ministry of Health of the Republic of Uzbekistan No. 40 dated 26 January 2021). Informed consent was obtained from the parents of the patients.

The clinical trial was limited, comparative, open, controlled, randomized with four parallel groups. The studies were carried out in patients undergoing inpatient treatment in the departments of pulmonology and allergology of the clinic of the Tashkent medical academy.

The study involved 150 children aged 2 to 14 years with a diagnosis of intermittent and mild persistent asthma. All children were divided into 4 groups: 1st group - children who received Astanol (Remedy Group, Uzbekistan) n=30; group 2 - children who received Neoclast (OOO Nobel) n=30; group 3, children who received Montexa (Nika Pharm, Uzbekistan) n=30; Group 4 (control) children who received the drug Singlon (Gedeon Rixter, Hungary) n=60. The average age of children was 6.8±2.1 years. The number of boys and girls included in the study was comparable. Children from 2 to 5 years of age were prescribed montelukast at a dose of 4 mg (chewable tablets), children from 6 to 14 years of age 5 mg (chewable tablets) once a day, at night, for 1 month.

All children underwent general clinical (collection of an allergic history, examination), physical examination, complete blood count, determination of total IgE, determination of the level of cys-LT in the urine, chest X-ray, peak flowmetry before and after the study.

Urine samples for the determination of cys-LT in the amount of 5 ml were collected in the morning. Quantitative determination of the final metabolite cys-LT (LTC4/D4/E4) in urine (reagent from Neogen, Ukraine) was performed by enzyme immunoassay. Measurement range: 0.04-8 ng/ml. Sensitivity: 0.04 ng/ml.

Statistical processing of the results was performed using the Statistica 10.0 software package. The data are presented as arithmetic mean values with an error of the mean. The difference in values was considered significant at $p<0.05$.

RESULTS AND DISCUSSION

The inclusion criteria for the trial were:

- patients of both sexes aged 2 to 14 years;

- diagnosis - intermittent, mild bronchial asthma;

- availability of informed written consent of the patient's parents (guardians) for the child's participation in a clinical trial

The criteria for exclusion from the trial were:
- the age of patients younger than 2 years and older than 14 years;
- the presence of contraindications to the appointment of Montelukast;
- severe bronchial asthma of a constant course (because monotherapy is not recommended)
- participation of the patient in other clinical studies within the last 30 days;
- lack of informed written consent of the patient to participate in the clinical trial.
The effectiveness of drugs was evaluated according to the following criteria:
- clinical improvement of the patient's condition (taking into account the dynamics of characteristic manifestations);
- reduction of manifestations and intensity of shortness of breath, cough, sputum.
- improvement of laboratory research data.
Evaluation of the effectiveness of the study drug was carried out on the basis of the above criteria in points according to the following scale:

Tolerability of drugs was assessed based on subjective symptoms and sensations, which the patient or his parents reported to the doctor, and taking into account objective data obtained by the doctor. The study took into account the dynamics of laboratory parameters. The tolerance of the study drugs was assessed in points on a scale from 0 to 4 points.

For the distribution of subjects into groups, the method of simple randomization was used. The initial table of distribution of patients by groups was formed on the basis of random numbers obtained using the MS Excel random number generation function.

After the patient was included in the study and assigned a serial number, the envelope corresponding to this number was opened, and the treatment contained in this envelope was administered.

Starting point of patient participation in the study: day of first administration of study drug or comparator

Treatment was described in detail in all patients included in the study.

Any therapy associated with comorbidities was recorded in the medical history and individual registration form.

All patient examination data were entered into the medical history, outpatient card and individual patient registration form.

Table 1

Dynamics of clinical manifestations of allergy in patients

Symptoms	Group 1 n =30		Group 2 n =30		Group 3 n =30		Group 4 n =60	
	before	after	before	after	before	after	before	after
Cough	2,76±0,02	0,73±0,03	2,23±0,04	0,4±0,01	2,83±0,03	0,5±0,01	2,9±0,04	0,1±0,01
Dyspnea	3.0±0,07	0,7±0,09	3,0±0,05	0,5±0,08	2.8±0,07	0,2±0,05	2,9±0,09	0,3±0,04
asthma attacks	2.1±0,07	0,1±0,005	2,1±0,08	0,08±0,003	2.1±0,05	0,06±0,002	2,7±0,09	0,04±0,001
p	*<0,001*		*<0,001*		*<0,001*		*<0,001*	

The severity of symptoms was noted in points:

0 - no sign *2 - moderately pronounced*

1 - weakly expressed *3 – expressed*

Table 2 shows that after the use of montelukast preparations, both domestically produced and in the comparison group, the number of eosinophils in peripheral blood decreased by 50% or more at the 4th week of therapy.

Table 2

Dynamics of the content of eosinophils in the blood (in %)

Preparations	**General blood analysis**	
	Eosinophils%	
	before	after
Group 1 (n =30)	5,6±0,20	3,1±0,12
Group 2 (n =30)	6,1±0,20	2,9±0,3
Group 3 (n =30)	5,9±0,20	2,3±0,2
Group 4 (n =60)	6,2±0,20	2,1±0,2

The study of the content of IgE in the blood of patients, as the main indicator of the allergological profile, also revealed a significant improvement in the results of the treatment with the tested drugs (p<0,001)

Table 3

Dynamics of the level of total immunoglobulin E in the blood (M±m)

Preparations	**IgE (ed/l)**	**IgE(ed/l)**
Group 1 (n =30)	381.6±4.5	236.4±4,07
Group 2 (n =30)	512.2±5.8	196.4±3,7
Group 3 (n =30)	481.2±5,5	245.3±4,11
Group 4 (n =60)	502.7±5,6	185,7±3,09

As can be seen from the data in Table 3, all children showed a decrease in the level of total IgE in the blood one month after taking the drugs. The greatest decrease was noted in children, groups 2 and 4 (p<0,001).

Numerous clinical studies indicate the key role of cys-LT in the pathogenesis of bronchial obstruction in bronchial asthma. Patients with bronchial asthma showed statistically significantly higher levels of cys-LT in the urine compared with healthy children.

During the study, we studied the state of the level of cys-LT in the urine in 52 patients.

Table 4

Dynamics of the level of cys-LT in urine (nm/l)

Preparations	$C_4D_4E_4$	$C_4D_4E_4$
Group 3 (n =30)	4.15±0.18	2.89±0.09
Group 4 (n =22)	4.23±0.2	1.92±0.06

Studies have shown that taking montelukast leads to a decrease in the level of cys-LT in the urine. At the same time, in children of the 4th group, a more significant decrease in the level of cys-LT was noted than in children of the 3rd group (p<0.05).

In children older than 5 years of age, a study of the peak expiratory flow rate was performed by performing peakflowmetry. The study of the PSV1 index (in %) did not reveal any significant changes during the entire study in all Groups. However, it should be noted that all children had positive changes in the value of this indicator. (Table 5).

Table 5

Dynamics of changes in PSV1 (in %) in children 5 years and older

Preparations	PFM1 baseline	PFM1 after treatment
Group 1 n =12	65,2±1,12	73,7±1,01
Group 2 n =17	64,3±1,01	75,1±1,03
Group 3 n =14	60,2±1,06	79,1±1,11
Group 4 n =22	58,2±1,12	77,7±1,09

Summing up the results of the studies, and after analyzing them, the values of the indicators of the effectiveness and tolerability of the drugs were derived, which indicate the equivalence of their action on the examined patients.

Table 6

Evaluation of the effectiveness and tolerability of drugs in points

Drug/Indicator	Efficiency	Portability
Group 1	2,9±0,01	3,9±0,06
Group 2	2,8±0,05	4,0±0
Group 3	2,8±0,1	4,0±0
Group 4	3,0±0,00	4,0±0

Conclusions. In accordance with the results of clinical trials and recommendations of international documents (GINA, 2015, 2018) [7,8], montelukast is recommended for use in mild BA as an alternative to ICS and in moderate BA in combination with ICS. The use of montelukast in pediatric practice will ensure the stability of the condition of children with bronchial asthma.

The data obtained allow us to conclude that Preparations montelukast produced in Uzbekistan (Montexa, Astanol, Neoclast) are effective drugs for the treatment of mild bronchial asthma in children from 2 to 5 years of age.

REFERENCES

1. Choi J. W. et al. The prevalence of symptoms of allergic diseasesin children residing in industrialregions of Uzbekistan //International Journal of Psychosocial Rehabilitation. – 2020. – T. 24. – №. 4. – C. 2105-2115.

2. de Weck A., Sanz M.L., Gamboa P. New pathophysiological concepts on aspirin hypersensitivity (Widal syndrome); diagnostic and therapeutic consequences// Bulletin de l'Académie nationale de médecine. – 2015. - № 189(6). – p. 1201–1218.

3. Erbagci Z. The leukotriene receptor antagonist montelukast in the treatment of chronic idiopathic urticaria: A single-blind, placebo-controlled, crossover clinical study// J Allergy Clin Immunol. - 2002. - № 124(3). – p.484-492.GINA 2018. www.ginasthma.org.

4. Gex G., Nendaz M., Janssens J.P. Leukotriene-modifiers in asthma treatment// Revue médicale suisse. – 2006. - № 2(77). – p. 1997-2006.

5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention (GINA). - National Institutes of Health; National Heart, Lung, and Blood Institute [accessed June 8, 2018; updated 2022].

6. Khalmatova B. T., Tashmatova G. A. ESTIMATION OF THE EFFICIENCY OF THE DOMESTIC PREPARATION MONTELUKAST IN THE COMPLEX THERAPY OF BRONCHIAL ASTHMA IN CHILDREN. – 2021.

7. Micheletto C., Tognella S., Visconti M., et al. Changes in urinary LTE4 and nasal functions following nasal provocation test with ASA in ASA-tolerant and -intolerant asthmatics// Respiratory medicine. – 2006. - № 100(12). – p. 2144-2150.

8. Mirrahimova M. H. BRONCHIAL ASTHMA IN CHILDREN: A MODERN VIEW OF THE PROBLEM //Central Asian Journal of Medicine. – 2019. – T. 2019. – №. 1. – C. 74-80.

9. Mirrahimova M. H., Khalmatova B. T., Tashmatova G. A. Learning efficiency and possibility of anti-leukotriene preparations for children with a

bronchial asthma in Uzbekistan conditions //Problems and perspectives in pharmaceutics and drug discovery. – 2018. – T. 4. – №. 1. – C. 85-89.

10. Nedelskaya S.N., Pakholchuk O.P., Raskina E.V. The place of leukotriene receptor antagonists in the treatment of bronchial asthma in children // Asthma and allergy. - 2011. - No. 1. - P.59-61.

11. O'Byrne P.M., Gauvreau G.M., Murphy D.M. Efficacy of leukotriene receptor antagonists and synthesis inhibitors in asthma// J Allergy Clin Immunol/ - 2009. - № 110(3). - p. 397-403.

12. Orlova E.A., Kostina E.M. Experience in the use of montelukast in the treatment of allergic diseases // Bulletin of the Ural Medical Academic Science. - 2012. - No. 4 (41). - p.210.

13. Tintinger G.R., Feldman C., Theron A.J. et al. Montelukast: more than a cysteinyl leukotriene receptor antagonist?// TheScientificWorldJournal [electronic resource]. – 2010. - № 10. – p. 2403-2413.

14. Wenzel S.E. The role of leukotrienes in asthma// Prostaglandins, leukotrienes, and essential fatty acids. – 2003. - № 69(2-3). – p. 145-155.

Central Asian Journal of Medicine

CAUSES OF DEVELOPMENT AND CLINICAL-LABORATORY MANIFESTATIONS OF URATE NEPHROPATHY IN CHILDREN

Barnokhon N. Karimova[1], Ilkhom O. Otajonov[2], Nargiza F. Nurmatova[3]

1 Senior teacher of the Department of "Family Medicine and Children's Diseases" of the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: barnoshakbn@gmail.com

2 DSc, Associate professor of the Department of Hygiene of Children, Adolescents and Nutrition, Tashkent Medical Academy, Uzbekistan
E-mail: ilhom1802@mail.ru

3 DSc, Associate professor of the Department of Propedeutics of children's diseases, Tashkent Medical Academy, Uzbekistan
E-mail: nargiza-nurmatova78@yandex.ru

ABSTRACT

Urate nephropathy in children is based on increased production of uric acid and, as a result, an increase in its concentration in the released urine and blood. According to various authors, this violation is recorded in 2-15% of the examined persons. Violation of purine metabolism is quite widespread, and, according to various researchers, is recorded in 5-12% of the examined persons. Currently, there is a certain tendency to increase this type of metabolic disorders, primarily due to the increased influence of environmental factors, such as the accumulation of excess lead in the body, as well as an increase in alcohol consumption, which can lead to the spread of urate dysmetabolism, which is population-based. The aim of the study is to identify urate nephropathy in children in the early stages.

Materials and methods. An analytical study of 700 medical histories and outpatient maps (form 112-U) of children aged 4-10 years performed, with selection of study subjects from 42 patients with recurrent uraturia. Of these, 28 are girls, 14 are boys. We divided these children into two groups: 1-group 20 children from 4-6 years old, 2- group 22 children from 7-10 years old. Conclusion: It was established that the main risk factors for urate nephropathy are: aggravation of hereditary history in the maternal and paternal pathology of metabolism, early artificial feeding, violation of the water and salt regime.

Key words: Urate nephropathy, nitrogemia, renal microanomalia, Zimnitsky sample, urine pH, dysuric disorders.

INTRODUCTION

Urate nephropathy in children is based on increased production of uric acid and, as a result, an increase in its concentration in the released urine and blood. According to various authors, this violation is recorded in 2-15% of the examined persons. Environmental factors, urbanization, nutritional patterns can lead to the spread of such disturbances in the purine exchange. As you know, urate nephropathy often proceeds covertly and it is detected by chance. Often, this pathology is diagnosed in the stage of nephrosclerosis with slowly progressing nitrogemia and pronounced arterial hypertension [1, 6], as well as in climatically unfavourable seasons of the year when adapted. Such variants of dysmetabolic nephropathies are called econephropathy [1].

Violation of purine metabolism is quite widespread, and, according to various researchers, is recorded in 5-12% of the examined persons. Currently, there is a certain tendency to increase this type of metabolic disorders, primarily due to the increased influence of environmental factors, such as the accumulation of excess lead in the body, as well as an increase in alcohol consumption, which can lead to the spread of urate dysmetabolism, which is population-based. In this regard, the problem of early diagnosis of this type of metabolic disorders, especially often manifested by kidney damage, becomes urgent. Early detection of urate nephropathy allows stopping its progression, development of nephrosclerosis and terminal renal failure [1, 2, 4].

Urate nephropathy, depending on the stage of progression, can be transformed into urate interstitial nephritis, urolithiasis, glomerulonephritis, CPN. In secondary urate nephropathy on the basis of purinosis, differential significance is given to the presence of gout in the pedigree of the patient, urolithiasis, essential arterial hypertension, "metabolic syndrome," obesity, type 2 diabetes mellitus, idiopathic CKD, attacks of "acetonemic vomiting," etc. Many transformations of urate nephropathy, namely: urate interstitial nephritis, urolithiasis (urate), glomerulonephritis (more often against the background of gout), CPN (more often against the background of gout, interstitial nephritis), can be determined by other conditions, for example, immune factor, renal microanomalia, renal blood flow condition and In practice, there are difficulties in diagnosing situations where metabolic and morphological changes in the kidneys, in some cases, are a clinical manifestation of purinosis, in others - a consequence of renal tubulopathy. In these patients, the correction of metabolic disorders should follow the pathogenetic principle and the definition of diagnosis, as urate nephropathy will not contradict the essence of clinicomorphological changes. Clinically, urate nephropathy (UN) is often quite modest [3, 5]. Urinary syndrome is detected accidentally and

manifested by isolated crystalluria (urate) or in combination with microproteinuria (sometimes moderate), microleucocyturia and microhematuria [5]. The urine persistent abrupt reaction is pH 4.5-5.5, at a rate of 7.4-7.5. In the blood - hyperuricemia of varying degrees of severity. There may be manifestations of disuria, pollakiuria, urinary rhesi (phenomena of urate cystitis). In some cases, especially in young children, orange crystals of uric acid, or an orange rim on the walls of a night pot, can be visually detected in settled urine. In cases where, along with the above-described urinary syndrome, partial disorders of nephron function appear in the form of a violation of osmodiuresis, titrated acidity of urine, hypoisostenuria, the development of metabolic (urate) interstitial nephritis [1, 2, 4, 6] is not excluded.

In this regard, an urgent problem is the early diagnosis of this type of disorder, which will stop its progression, the development of nephrosclerosis and terminal renal failure.

The aim of the study is to identify urate nephropathy in children in the early stages.

Materials and methods. An analytical study of 700 medical histories and outpatient maps (form 112-U) of children aged 4-10 years performed, with selection of study subjects from 42 patients with recurrent uraturia. Of these, 28 are girls, 14 are boys. We divided these children into two groups: 1-group 20 children from 4-6 years old, 2- group 22 children from 7-10 years old. The control group was 20 children who, according to medical records, had a first or second health group with no urinary system pathology. In parallel, 20 mothers with family history burdened by disease were examined and observed. The work done at the Tashkent Medical Academy. The examination of patients carried out based on the nephrology department and polyclinic. A genealogical history was analyzed with the identification of leading risk factors, a history of the course of pregnancy, childbirth, the incidence and nature of feeding children in the first year of life, the nature of nutrition and water-salt regime during life in the families surveyed, suffered and comorbid diseases, as well as the peculiarities of the clinical picture. All children underwent a comprehensive clinical-laboratory and instrumental examination, biochemical blood analysis, urine pH. The functional state of the kidneys assessed according to the results of a Zimnitsky sample, a dry-eating sample, clearance of endogenous creatinine, and serum urea levels. All patients underwent ultrasound examination of the gastrointestinal tract, kidneys and bladder. Study results and discussion. It established that in children from families with a history aggravated by diseases of impaired metabolism, urate nephropathy occurs in 90.1% of cases. The incidence of kidney disease in relatives is generally

higher than in the control group, with maternal kidney and urinary tract diseases occurring 2 times more frequently than in the father. A survey of 20 mothers revealed that half of them had an increase in blood pressure (60%). 50% of women were diagnosed with chronic gastroduodenitis, 10% with chronic cholecystitis, and according to the results of ultrasound, 5% of them first showed bile stone disease, in 5% of mothers - urolithiasis.

We have determined that disruption of salt metabolism in the form of an increase in uric acid in the blood and its increased excretion with urine in a number of children is associated with their early transfer to artificial and mixed feeding. Risk of hyperuricosuria in children on artificial feeding increases by 2.5 times

With the age of children, the nature of nutrition in the families surveyed also changes. There is an abuse of food rich in preservatives, which increases the risk of urate nephropathy by 10 times.

The clinical picture of preschool children dominated by complaints of pastosity of the eyelids, dysuric disorders (70%), precipitation of salts in the urine (65%), increased sweating, increased nervous excitability (35%), sleep disturbance in the form of difficult falling asleep, night fears (20%). Arthralgia, mainly at night, were recorded in 25%, myalgia in 15% of children, acetonemic vomiting in 5% of children.

With age, the number of complaints among children 7-10 years old decreases. The most common complaints were of abdominal and lumbar pain (59%). Increased nervous excitability, emotional lability (45.4%), sleep disturbance (31.8%), decreased appetite (59%) were detected. For the first time, an increase in blood pressure recorded in 9% of the patients examined.

In general blood tests, eosinophilia was significantly more common in the children examined than in the comparison group. The main and most significant symptom of urate nephropathy in children is hyperuricosuria. Most of the children tested (83%) showed an increase in urinary uric acid levels from 800 to 1000 mg/day. Combined urate-oxalate crystalluria was significantly more common in children aged 4-6 years. On average, 80% of children showed a sharply acidic urine reaction in general analyses. During crystallographic examination, urates (67.2%) and sodium urates (47.1%) were most often detected in an open drop of urine, mainly large crystals, uric acid crystals (25.2%) of various sizes prevailed.In 69.9% of children, protein was traced as a thin rim along the edge.

Conclusion: It was established that the main risk factors for urate nephropathy are: aggravation of hereditary history in the maternal and paternal pathology of metabolism, early artificial feeding, violation of the water and salt regime. New risk factors have been identified: abuse of food rich in preservatives.

Lowering urine pH less than < 5.75 is an independent risk factor for developing urate nephropathy in children.

REFERENCES:

1. Ignatova M.S., Lengn V.V. Hereditary kidney diseases occurring with hematuria. Russian Journal of Perinatology and Pediatrics 2019; 3: 59: 82–90.

2. Length V.V., Ignatova M.S., Osmanov I.M. and others. Dysmetabolic nephropathies in children. Russian Journal of Perinatology and Pediatrics 2018; 58: 5: 36–45.

3. Novikova N., Kovalchuk M., Stepina N. et al. Distinct effect of xenobiotics on the metal-binding properties of protein molecules. J Synchrotron Rad 2015: 22: 1: 1001–1007.

4. Parish L.S., Length V.V., Ignatova M.S. Glomerulonephritis primary. Pediatric nephrology. Ed. M.S. Ignatov. M.: Honey. Heart attack. Agency, 2011; 263–297.

5. Yurieva E.A. Suhorukov V., Tsaregorodtsev A.D., etc. Alteration of protein molecules in endogenous body intoxication as a risk factor for chronic metabolic diseases. Molecular Medicine 2018; 3: 45–52

6. Yurieva E.A., Yablonskaya M.I., Raba G.P. and others. Pathogenetic aspects of urinary (purine) diathesis in children. Russian Journal of Perinatology and Pediatrics 2017; 58:4:40–46

Central Asian Journal of Medicine

THE VALUES OF FREE FATTY ACIDS IN THE BLOOD IN WOMEN WITH METABOLIC SYNDROME IN THE POSTMENOPAUSAL PERIOD

Nurkhan Kh. Mukhamedova

DSc, associate professor of the department of medical and biological-chemistry of the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: nurhon6969@mail.ru

ABSTRACT

Metabolic syndrome (MS), which includes a number of systemic clinical and biochemical processes (insulin resistance, abdominal obesity, dyslipidemia, arterial hypertension), attracts close attention of general practitioners. The risk factors and pathological processes leading to the development of this syndrome remain controversial. Several hypotheses for the development of MS have been proposed, of which the theory of insulin resistance is the leading one. To date, all possible causes and mechanisms for the development of MS have not been finally disclosed. Non-esterified fatty acids play an important role in the development of MS.

Key words: metabolic syndrome, insulin resistance, fatty acids, blood, glucose.

INTRODUCTION

It is known that insulin resistance stimulates increased hypolysis and the release of large amounts of free fatty acids, which, in combination with elevated blood glucose levels, provides an additional amount of substrate for the synthesis of triglycerols in the liver [1, 2, 3, 4]. Hyperinsulinemia, which occurs due to inhibition of insulin degradation in the liver, further enhances peripheral insulin resistance. The proposed and known mechanisms of the relationship between MS and free fatty acids predetermine the need to study the role of free fatty acids in the formation of MS in postmenopausal women [6, 7].

Purpose of the research

To study the level of free fatty acids in the blood of women with MS in the postmenopausal period.

Material and Methods

We examined 54 women with MS in the postmenopausal period, the duration of postmenopausal ranged from 2 to 14 years (average 8.4-1.53 years, the average age of the examined was 55.2+4.73 years).

The following exclusion criteria were used for inclusion in the main group: cardiovascular diseases, bronchial asthma, oncopathology, viral hepatitis, blood and kidney diseases.

The control group consisted of 14 postmenopausal women without manifestations of MS.

Metabolic syndrome in the examined women was diagnosed according to the criteria proposed by the experts of the US National Cholesterol Education Program (2004). The criteria for MS were waist circumference greater than 88 cm, blood pressure 130/85 mm Hg. and above, the content of triglyceride in the blood serum is 1.7 mMool / l or more, HDL cholesterol (high-density lipoprotein cholesterol) is less than 1.3 mmol / l, the level of glucose in the blood plasma on an empty stomach is 6.1 mmol / l or more.

For the study of carbohydrate metabolism, the determination of the content of fasting glucose in the blood serum was used, and 2 hours after the oral glucose load, the level of insulin by the enzyme immunoassay method, using the kits of the DRG-Diagnostics form, the HOMA index was calculated. Hyperinsulinemia was diagnosed when the fasting insulin level was above 12.5 μU/mm, and when the HOMA index was above 2.77, patients were considered insulin resistant.

The content of free fatty acids in the blood serum was determined using the NEFAFS test system from Diasys (Germany), the determination of C-reactive protein in the blood serum was carried out using the BioChemMac test kits (Russia). The analyzers of the firms "MINDRAY" and "HUMAN" were used in the studies.

Statistical data processing was carried out by the method of variation statistics using Student's t-test. The results were processed using the Statistica software package.

Results and Discussion

The analysis of the results of the studies presented in the table showed the presence of significant changes in the studied biochemical parameters of the blood of the examined postmenopausal women with MS. In patients with elevated levels of triglyceride in the blood, dyslipidemia was observed, which exceeded that of healthy individuals by an average of 3 times ($P<0.05$).

Table 1

Biochemical parameters of blood in women with metabolic syndrome in the postmenopausal period (M + m).

Index	**Healthy women *n=14***	**Women with MS PM and PP *n=54***
Blood glucose mmol/l (on an empty stomach)	4,01± 0,24	5,28 +0,21*
Blood glucose mmol/l	4,43+0,27	6,74+0,63*
Blood glucose mmol/l in 2 hours	7,89+1,04	19,6+1,64*
Insulin in blood μU/ml	1,43+0,14	4,33+0,24*
HOMA index	0,54+0,05	1,81+0,19*
Glycerin in the blood mmol / l	0,33+0,02	0,79+0,16*
Free fatty acids in the blood	0,013+0,001	0,12+0,01*

***Note:* ***-significance of differences P<0.05 when compared with healthy individuals

Along with an increase in the level of triglyceride, an increase in the concentration of free fatty acids in the blood of the examined persons was noted on average by 2.4 times (P<0.05).

According to Titov V.N., an increase in free fatty acids in the blood disrupts the functional state of insulin receptors and the uptake of glucose by cells, which leads to an increase in blood glucose levels [5]. As can be seen from the data obtained in the examined patients, the level of glucose in the blood on an empty stomach and after 2 hours, respectively, showed an excess of the initial values by 1.3 and 1.5 times (P<0.05). The state of hyperglycemia and hyperlipidemia in postmenopausal women with MS contributed to a 2.5-fold increase in blood insulin levels, thus indicating the effect of lip toxicity.

Violation of the receptor-mediated transport of fatty acids and glucose against the background of insulin resistance and hyperinsulinemia leads to disruption of the structure of cell membranes and metabolic processes occurring in liver hepatocytes.

It has been shown that oxidative stress and increased formation of oxygen free radicals play an important role in the destruction of hepatocyte membranes. At the same time, the main generator of reactive oxygen species are mitochondria, in which up to 1-2% of reactive oxygen species from the total amount of molecular oxygen is formed. Moreover, when observing the process occurring in the mitochondria, it was found that the process is accelerated by increasing the level of free fatty acids, since the oxidation of fatty acids further increases oxygen

consumption. Active oxygen, or free radicals, promote oxidation of LDL (low density lipoprotein), and thereby induce inflammation, which is also confirmed by an average increase in C-reactive protein by 10 times ($P<0.05$).

Conclusion

Thus, metabolic disorders that occur during MS in postmenopausal women are manifested by a state of insulin resistance and an increase in the level of free fatty acids, lead to inhibition of the process of glycolysis and activation of gluconeogenesis in hepatocytes of the liver, inflammation in the vessels, all this indicates involvement in the pathological process of the liver and of cardio-vascular system.

REFERENCES

1. Alexandrov O.V. Alekhina R.M. et al. Metabolic syndrome, etiology and pathogenesis // Ross.med. magazine-2016-№6-pp.50-55

2. Carcaillon L, Brailly-Tabard S High plasma estradiol interacts with diabetes on risk of dementia in older postmenopausal women.//Neurology. 2018 Feb 11;82(6):504-11.

3. Metabolic syndrome. Report of the National Heart, Lung and Blood Institute of the American Heart Association // Clinical Pharmacology and Therapy -2019-No. 13-pp.66-68

4. Titov V.N. Atherosclerosis as a pathology of polyunsaturated fatty acids. Biological foundations of the theory of atherosclerosis-M.2018

5. Titov V.N. Combined disorders of essential fatty acids and endothelium-dependent vasodilation in the pathogenesis of arterial hypertension and atherosclerosis //Clin. laboratory diagnostics -2018-№10-pp.3-13

6. Titov V.N. The unity of the physicochemical and biological action of glycerol and cholesterol alcohols in the absorption of fatty acids by cells. Features of the pathogenesis of "metabolic pandemics" // Klin and lab diagnostics -2015.-No. 1.-pp.23-28.

7. Endakova E.A. Novgorodtseva T.P. Modification of the composition of blood fatty acids in cardiovascular diseases - Vladivostok, 2017.

Central Asian Journal of Medicine

SURGICAL TREATMENT METHODS OF ACUTE LOWER LIMB ARTERIAL THROMBOSIS ON PATIENTS AFTER CORONAVIRUS INFECTION

Uktamkhon A. Asrarov[1] , Jakhongir K. Matmuradov[2]

1 DSc, assistant of department of faculty and hospital surgery № 1 of Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: uka-han@mail.ru

2 Assistant of department of faculty and hospital surgery № 1 of Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: jakhongir.kamilovich@gmail.com

ABSTRACT

This article reflects the result of different types of surgical interventions on patients with lower limb arterial thromboses, who had had coronavirus infection. 43 patients were divided into 2 groups: the 1st group underwent to thrombectomies, whereas 2nd group – catheter thrombolysis and thrombaspiration. The results demonstrates applying of catheter thrombolysis instead of thrombectomy significantly decreases frequency of complications, rethromboses and mortality.

Key words: lower limb arterial thrombosis, acute ischemia, thrombectomy, catheter thrombolysis, coronavirus infection.

INTRODUCTION

Information regarding the incidence of acute lower limb ischemia is scarce, but several national registries and regional surveys give figures of 140,000,000 per year. According to I. N. Bokarev, one case of acute ischemia occurs annually per 6,000 people [1, 6, 5]. The incidence of acute ischemia associated with embolism has decreased in recent years, probably because of a decrease in rheumatic valvular heart disease, improved monitoring of such patients, and progress in the treatment of patients with cardiac arrhythmias. On the contrary, cases of acute thrombotic ischemia have become more common [3, 4].

The most common cause of acute thrombosis is atherosclerosis, in which thrombosis can develop as a primary thrombosis against the background of an asymptomatic ulcerated plaque, or as a secondary one against the background of a long-term occlusive-stenotic process [2]. Primary acute thrombosis (up to 42% of the total number of cases of acute thrombosis) clinically differs little from arterial embolism - a sudden onset is characteristic. Coronavirus affected pandemic significantly had spread the frequency both arterial and venous thrombosis. Identification of acute arterial thrombosis due to the coronavirus-associated coagulopathy and it's further complications, their possible ways of managing and recovering still has their actuality and in demand.

Purpose of study. Improvement the results of treatment of patients with lower limbs arterial thrombosis, who have had coronavirus infection, by optimizing the diagnosis and treatment tactics.

Materials and methods. For the period from September 2020 to January 2022, 43 patients with acute lower limbs' arterial thrombosis were treated at the Emergency Surgery Department of the Multidisciplinary Clinic of the Tashkent Medical Academy. The average age was 61.3±0.6 years. 27 (62.8%) of them were male, 16 (37.2%) female. Patients were divided into 2 groups depending on the applied treatment tactics: the main group - 15 (34.8%) and control - 28 (65.2%) patients. All of patient, underwent to the research had anamnesis of coronavirus infection. An average duration of recovering from COVID-19 was 2 months.

Diagnosis included standard clinical laboratory and instrumental examinations, supplemented by ultrasound dopplerography (USDG), ultrasound duplex scanning of the lower limbs vessels, multisliced CT and contrasting angiography of the lower limbs arteries. Confirmation of positive coronavirus infection anamnesis included enzyme-linked immunosorbent assay technique.

All patients had standard preoperative preparation, including double anticoagulant, infusion therapy, improving of blood circulation in the microvasculature.

Results and discussion. The degree of ischemia was determined according to A.S. Saveliev's classification; and there were 4 (26.67%) patients in the main group, whom were diagnosed with acute ischemia II-a degree to; 8 (53.33%) — II-b; 3 (20%) — III-a. In the control group, the distribution according to the degree of acute ischemia was: 8 (28.57%) patients — II-a degree; 13 (46.43%) — II-b; 7 (25%) - III-a. According to the level of arterial damage: in the main group, 5 (33.33%) patients had thrombosis of the iliac-femoral segment, 7 (46.67%) patients had thrombosis of the femoral-popliteal segment; 3 (20%) - popliteal-tibial segment. In the control group: 10 (35.71%) patients had thrombosis of the iliac-

femoral segment, 12 (42.86%) patients had thrombosis of the femoral-popliteal segment; 6 (21.43%) - popliteal-tibial segment. According to the ratio of concomitant diseases, a significant preponderance of a certain nosology was not determined in any of the researched groups.

Surgical interventions on patients were performed within 24 hours after admission to the hospital. Patients in the control group underwent thrombectomy from the affected arterial segment and fasciotomy (according to indications), while patients in the main group underwent endovascular thrombolysis and thrombaspiration. In cases where it was impossible to puncture the femoral artery on the affected limb, access performed through the contralateral lower limb. Urokinase used as a thrombolytic drug. The effectiveness of the method was determined based on a number of subjective and objective criteria. Changes in clinical dynamics were considered as subjective criteria: limb warming, skin color change, improvement in motor and sensory functions, and the appearance of pulsation distal to thrombosis. The objective criteria included changes in USDG parameters in the form of an improvement in the ankle-brachial index (ABI), changes in speed indicators and visual sonographic control of thrombus lysis. However, the main objective criterion for thrombus lysis was angiography data during and after the procedure.

After performed thrombectomies on patients of the control group, regression of ischemia was estimated in 24 (55.81%) patients. In 2 (4.65%) cases, rethrombosis was noted within 12 hours after the surgical intervention and therefore these patients underwent thrombectomy repeatedly. In addition, in 2 (4.65%) cases, after thrombectomy, there was no regression of ischemia, and a following secondary high amputation of the lower limb was performed. Lethality in the comparison group was not observed. In all 7 (16.27%) patients with acute grade 3 ischemia, thrombectomy was mandatory supplemented with anterior and posterior fasciotomy. Thrombectomy was performed in all cases with an incision along the Ken line.

In the patients of the main group, who underwent catheter thrombolysis and thromboaspiration, no episodes of retrombosis were observed. However, in 1 (2.32%) case, a partial regression of ischemia was detected with irreversible necrotic changes, limited in the foot by a demarcation line, which was subsequently disarticulated. To perform catheter thrombolysis and thrombaspiration, femoral angiography was performed by antegrade puncture of the femoral artery with the installation of a catheter for subsequent lysis.

Due to selective administration, in most cases it was possible to obtain positive results with a lower dose of fibrinolytics than with systemic use. The dose

of urokinase ranged from 300,000 to 900,000 IU. After completion of thrombolysis, the catheter was not removed, but an intra-arterial infusion of anticoagulants, antiplatelet agents, and antispasmodics was performed. The catheter was removed after the normalization of the parameters of the blood coagulation system (on the 3rd day after the procedure).

Despite the advantage of regional thrombolysis in peripheral thrombosis, not all patients managed to completely lyse thrombi. However, even with successful thrombolysis, the causative factors of thrombosis were not eliminated. Therefore, peroral anticoagulant medicament for prolonged taking was prescribed for 3 (6.97%) patients.

To determine the correlation between the incidence of complications, the blood coagulation system was assessed every 48 hours after the interventions (Tables 1, 2).

Table 1.

Blood clotting time by the groups

	BCT start time in the main group	BCT start time in the comparison group	BCT finish time in the main group	BCT finish in the comparison group
1 day	270± 2	250± 3	290± 1	265± 3
3 days	250± 3	223± 1	268± 2	240± 2
5 days	230± 2	197 ± 2	255± 3	233± 1
7 days	225± 1	190± 1	263± 2	227± 2

Despite the fact that the treatment of this category of patients is an extremely difficult problem, nevertheless, certain prospects are associated with the optimization of the diagnostic algorithm and the differentiated choice of one or another method of surgical intervention. According to the results of our research, indirect thrombectomy is an unpromising method, since in many cases it is insufficient to free the arterial lumen from atherothrombotic masses, especially in medium and small caliber vessels. After thrombectomy, 2 (4.65%) patients underwent amputation, while no complications were observed in patients with thrombolysis.

Table 2.

PTI and APTT by the groups

Day	Main group PTI	PTI comparison group	Main group APTT	Comparison group APTT
1 day	65± 1	70± 2	28 ± 2	31 ± 1
3 days	71 ± 2	78± 1	32 ± 1	35± 2
5 days	75± 2	89 ± 1	35 ± 3	38 ± 2
7 day	82 ± 2	98 ± 2	37 ± 1	40± 3

Somewhat better results were obtained during various reconstructive operations. But the possibility of their implementation is limited in patients who do not have a peripheral blood flow. In this group of patients, the only method of revascularization is the regional thrombolysis. The effect achieved in the process of lysis, as well as in case of unsuccessful lysis, can be supplemented with a subsequent operation.

Traditionally performed thrombectomy with further anticoagulant therapy in the postoperative period has been standard for many years. Reperfusion syndrome after revascularization and reconstruction of the affected arterial segments proceeds more aggressively, which is the cause of more frequent complications. For patients who underwent endovascular thrombolysis and thromboaspiration, the approach to the use of a fibrinolytic drug and its advancement in the distal direction up to the microvasculature is promising.

Conclusions

1. In the course of diagnostic measures, thrombosis was detected against the background of an atherosclerotic process in combination with a passable tibial segment; primary reconstructive surgery is indicated for such patients.

2. Indirect thrombectomy is indicated for thrombosis of the main arteries without significant atheromatous lesions or emboli.

3. Indications for endovascular thrombolytic therapy are peripheral forms of thrombosis or long-standing thrombosis against the background of a pronounced atherosclerotic lesion with an unsatisfactory peripheral vascular bed, i.e. when indirect thrombectomy is unfavorable prognostically, and reconstructive surgery cannot be performed.

REFERENCES

1. Bokarev I.N., Popova L.V. Sovremeenye problem trombozov arteriy I ven // Prakticheskaya medicina, 2014, T.6, №9, C. 13-17.

2. Karimov Sh.I., Irnazarov A.A., Asrarov U.A. Prmenenie gibridnykh khirurgicheskikh vmeshatelstv u bolnykh s kriticheskoy ishemiey nizhnikh konechnostey pri multifokalnom ateroskleroze. Tibbiyot yangi kuni; 3(27)2019, 46-52.

3. Babunashvili, M.A., Glagolev V.E., Kartashov D.S. multi-stage endovascular treatment of multifocal atherosclerosis. Journal archive 2013; 53 (11): 90-95.12

4. Gavrilova N.E., Metelskaya V.A., Yarovaya E.B., Boytsov S.A. The Role of duplex scanning of the carotid arteries to identify coronary atherosclerosis and determining the degree of its severity. Rus Journal of Cardiology 2014; 4 (108): 108-112).6

5. Gozhenko A.I., Kovalevskaya L.A., Kotyuzhinskaya S.G. et al. Atherosclerosis: new achievements and failures. J Health Sci 2014; 04 (04): 101-114.7.

6. Oganov R.G. Cardiovascular comorbidity: common approaches to prevention and treatment. Rational pharmacotherapy in cardiology 2015; 11 (1): 4-7.3

Central Asian Journal of Medicine

CORRECTION OF INTESTINAL DISBACTERIOSIS IN CHILDREN WITH CHRONIC HEPATITIS B ASSOCIATED WITH LAMBLIASIS

Nargiza F. Nurmatova

DSc, Associate professor of the Department of Propedeutics of children's diseases,
Tashkent Medical Academy, Uzbekistan
E-mail: nargiza-nurmatova78@yandex.ru

ABSTRACT

Analysis and evaluation of the state of intestinal microbiocenosis in 85 children with chronic hepatitis B associated with lambliasis for the purpose of correction of disbiotic disorders in the intestine of children with individual approaches to the treatment choice.

Key words: Chronic hepatitis B, disbacteriosis, lambliasis, therapy, probiotics, children.

INTRODUCTION

The disbiotic events in the intestine are one of the pathogenic part in the development of pathological process and simultaneously unfavourable outcome of chronic viral hepatitis (CVH) in children [4,6,16]. Our previous studies of the state of intestinal microbiocenosis in children with chronic viral hepatitis confirmed that irrespective of the presence or absence of lambliasis the disturbances in the contents of the intestinal microflora were revealed in 99.7 % of cases [7,10,12,15]. Under the conditions of chronic viral persistence the disbiosis contributes to development of disturbances of secretory, motor and barrier functions of the intestine and all ways of the lamblia brining appear to be real. In turn, lamblia under conditions of intestinal disbacteriosis at CVH in children, in the aggressive environment excrete a plenty of toxins which promote generalization of the viral infection with the appropriate consequences - polysystem organ insufficiency, that results in inhibition of the macroorgan resistance and then under the conditions of associated viral-parasitary infection provide development of two parallel already mutually aggravating processes [2,3,5,13,17]. Now the question about a choice of an optimum biopreparation remains rather problematic, because of presence of a

huge arsenal of medicinal means in the pharmaceutical market used for correction of intestinal disbiosis. The results of our early performed investigations showed that the existing methods of treatment of disbalance in the intestinal microecology are not always effective (62.2 %). Taking into account this fact, and also recently registered characteristic development of microbiota resistance to the biological agents noted over the last time [1,9,14], a question arose for us about development of a method allowing in short terms (1-2 days), in comparison with bacteriological research (5-7 days) to carry out a choice of a biopreparation for treatment of disbacteriosis in the children with chronic viral hepatitis, ensuring the maximal effect from its application. In this connection the searches of means rendering influence on restoration of intestinal microecology are represented by the extremely urgent problem and, are rather perspective for maintenance of a choice of optimal preparation individually for each patient. The above-stated facts were the basis for more detailed study of a condition of microbiocenosis of the intestine and revealing more effective approach to correction of the damaged intestinal microbiocenosis in children with chronic hepatitis B (CHB) on the background of lambliasis invasion.

The purpose of research was the estimation of efficacy of application of a biological agent on the basis of a method of an individual estimation of lymphocyte sensitivity in the test in vitro in children with chronic hepatitis B on the background of lambliasis.

Materials and methods of research. Under supervision there were 85 children with CHB and intestinal lambliasis at the age of 3 to 14 years hospitalized to the hepatological center of the RSSPMC of Pediatrics of the MH of RUz. The distribution of the patients in dependence of activity of CHB showed that disease on the background of lambliasis developed in the progressing form. So, the overwhelming majority (80.0 %) of the patients had moderate (49.4 %) and marked (30.6 %) activity of illness. The duration of CHB was 4.1±0.2 years. The diagnosis of CHB was based on data of medical history of disease, clinical examination, biochemical and instrumental investigations. The verification of a HBV-infection was performed with use of methods IFA and PCR (HBsAg, HBsAb, HBeAg, HBeAb, HBcorAb, HBV-DNA). The intestinal microflora was studied according to the methodical recommendations offered by I.B.Ershova (2002). The study of intestinal microflora was carried out by technique of R.V.Epshtein-Litvak and F.L.Vilshanskaya (1977), the classification offered by B.M. Granitov was also used (2002). Lambliasis diagnosis was carried out by methods: immunofluorescence - definition of an antigen G. Lamblia in feces; PCR-

definition of DNA G. Lamblia in blood/feces and, three-multiple microscopic examination of residual components of the feces.

For definition of the lymphocyte sensitivity to biopreparations there was used method of an individual estimation of a choice of biopreparation based on definition of the functional activity of T-lymphocytes of the peripheral blood (Patent UZ IAP 04570 is used, 2012) [8]. In this method the performance of the "loading" test is proposed for the estimation of functional activity of the T-lymphocytes in the reaction of E-rosette formation in vitro in incubation with probiotics, that allowed taking into account of the body individual sensitivity in each concrete case to choose an effective biopreparation. As the control the contents of E-rosette-forming cells (E-RFC) was measured in the blood serum in the same patients without stimulation of preparations. The criteria for estimation were the results of E-RFC > 5 % to the control - hyperergic, E-RFC < 5 % - hypoergic and E-RFC without changes (Inoyatova F.I., 2012; IAP 04570). There were used bacterial preparations with various contents of biocultures: Bifilax-immuno - $10x10^9$ COE, L.paracasei CRL-431, B.animalis BB-12 in capsule (Pharmaxx International, Denmark), Lacto-G - $5x10^9$, L.acidophilus, B.longum, B.bifidum, B.infantis and fruitzooligosaccharides in capsule (GMP, Georgia) and Narimax-plus-,$2x10^8$ COE L.acidophilus, L.rhamnosus, B.bifidum, St.thermophilus, L.bulgaricus, L.salivarius in capsule (JSC-Vitamax-E, Yerevan).

At the comparative analysis of the test in vitro with addition of biopreparations used for restoration of the intestinal microflora we revealed positive result to the preparation Bifilax-immuno in 68.7 % of cases, Lacto-G – 38.7 % and Narimax-plus – 30.0 %. In this connection the basic group was made of 55 children who have received on a background of basic therapy chosen in test in vitro a high-sensitive biopreparation in age dependent doses. Other 30 children (control group) on the background of basic therapy have received dry bacterial preparations: bifidum- and lactobacteria in the standard dozes within one month. The eradication of lamblia was carried out with use of preparation Macmiror (nifurantel) in doze 15 mg/kg 2 times per day for 7 days, taking into account its small hepatotoxicity. The estimation of efficiency of used therapy was performed on the clinical, biochemical and bacteriological data.

The statistical processing was performed with use of a method of variational statistics with application of t-criterion Student test under the special program Excel-2000. The differences were considered to be reliable at values of $p < 0.05$.

Results and discussion. The study of the intestinal microbiocenosis has allowed us to establish prevalence (more than 3.5 times) of disbacteriosis (D) of more marked degrees in children, being ill with CHB on the basis of lambliasis,

D-IV (48.2 %) and D-III (35.3 %), respectively. It testifies about pathogenic influence of lamblia antigens and their toxins on the intestinal mucosa, aggravating not only already available inflammatory processes, but also immunological tolerance of the gastrointestinal tract, as a whole. The features of the type landscape of microorganisms in the intestine depended on the degree of disbacteriosis which were characterized by a phase of aggression of aerobic flora that is expressed by reduction of the number of anaerobes in relation to aerobes, presence of deficit of bifidobacteria and lactobacteria, or their full absence on the background of significant growth of the facultative flora and their toxic metabolites.

The use of individually chosen biopreparations showed significant effect on the dynamics of the main clinical symptoms in children with CHB on the basis of lambliasis. The comparative analysis of application of biopreparations has shown that use of individually chosen preparations had more effective influence on the development of CHB in comparison with multicomponent preparations. In particular, clinical response of 78.4 % of children (against 38.3 % in group of the control, $p < 0.05$) was positive, that was reflected in improvement of the state of health of children, reliably more rare the symptoms of asthenovegetative syndrome were registered as complaints on rapid weakness and fatigue as well as headaches, dizziness and sleep disturbances, ($p < 0.001$-0.05). The skin integuments were pale and dry in the third part of patients of group I (34.5±4.7 % and 30.9±6.3 %, respectively), that was 2,1 times less often in relation to the patients of group II, $p < 0,001$. Positive dynamics was noted in the symptoms of dyspeptic syndrome. (DS). Such symptoms as poor appetite and furred tongue were registered in 2.0 and 2.3 times less often, respectively, in children of the main group ($p < 0.05$ and $p < 0.001$ concerning the control). Dyspeptic syndrome was noted predominantly among the children from control group - 61.6 % of cases. Such symptom, as the nausea was observed in 4 patients of the main group (10.9±4.2 %), which was met in 2,7 times less often concerning group of the control (30.0±8.4 %), $p < 0.05$. The vomiting symptoms disappeared in the patients receiving polycomponent biopreparations, whereas this parameter at the patients of control group was registered in 13.3±6.2 % of the patients, $p < 0.05$. The symptoms of the dyspeptic syndrome as a pain in the abdomen, meteorism reduced in 2.3 and 2.6 times, respectively, collywobbles in the abdomen was more frequent than 2.7 times and stool desorders were registered in 13.3±6.2% of the patients, $p < 0.05$. Cholestatic syndrome (CS) was more characteristic for children from group of the control, thus subicteric skin integuments after treatment was found in 20.0±7.3 % of cases, while in the basic group this parameter decreased to 10.9±4.2 % ($p > 0.05$). There

were not revealed reliable differences in subicteric sclera in the both groups. The complaints on skin pruritus were reliably rare in the patients from the main group in 10,9±4,2 % of children, whereas, in control group this parameter was registered in 33,3±8,6 % of cases ($p < 0.05$). Hemorrhagic syndrome (HS) in form of nasal bleeding was noted after treatment reliably more rare – in 2.5 times in children of main group, ($p < 0.05$). The intensity of extrahepatic signs in CHB, as a capillary network and vascular asterisks in children of the main group decreased in 1.5 times ($p < 0.01$ concerning group of the control). It is necessary to note, that after the therapy carried out in children of the main group there were also revealed changes in the sizes of a liver and spleen. The increase in the sizes of a liver - hepatomegalia (GM) more than 3 cm was reliably revealed 2,0 times more rare in children of the main group, than in children of control group ($p < 0.05$). In the basic group splenomegalia (SM) was registered 1,8 times less often concerning group of the control ($p < 0.01$). Thus, after application of sensitive biopreparations on the background of basic therapy we reveal significant improvements of clinical syndromes of CHB in comparison with control group.

At the comparative analysis in the studied children on the background of the used therapy the changes of a number of biochemical parameters (Tab.1) were observed. Considering parameters of biochemical homeostasis it is necessary to note, that all studied parameters before treatment in children with CHB accompanying with lambliasis and disturbance of intestinal microbiocenosis considerably exceeded parameters of healthy children (corresponds to reliability from $p < 0.02$ to $p < 0.001$). The inclusion into therapy of the chosen polycomponent probiotics rendered positive influence on dynamics of parameters of the syndrome of cytolisis. So, the average parameter of AlAT decreased 2,5 times ($p < 0.001$ in relation to a parameter before treatment), reached normalization in 56.6 % of children. The same changes occurred with AsAT, which average level before treatment was 1.42±0.11mmol/l, after treatment – 0.40±0.08mmol/l ($p < 0.001$). After a course of basic therapy the level of AlAT decreased to 2.06±0.14 ммmol/l ($p < 0.05$), exceeding, however, parameters of norm in 5.2 times.

Table 1.

Dynamics of the biochemical parameters changes in children with CHB associated with lambliasis (%).

Parameter	Health	Before treatment n=85	After treatment		P
			Main group n=55	Control group n=30	
AlAT, mmol/l	0.49±0.03	2.30±0.20*	0.89±0.14*	2.06±0.14*	< 0.01
AsAT, mmol/l	0.34±0.02	1.42±0.11*	0.40±0.08	1,0±0.12*	< 0.01
Bilirubin, total					
Bilirubin, mcmol/l	14.85±0.57	26.9±2.9*	15.4±2.25	22.8±5.7	< 0.05
Protein total, g/l	71.32±0.86	55.3±2.78*	69.0±0.80	64.2±0.6*	> 0.05
Albumins, %	54.5±0.72	46.0±3.48*	49.3±0.64*	39.8±0.98*	< 0.01
Gamm-globulin, %	15.7±0.47	24.2±2.32*	18.2±0.66*	28.3±1.44*	< 0.001
Thymol test, Un/l	4.5 ± 0.28	8.8±0.41*	5.96±0.42	11.9±1.03*	< 0.001
PTI %	75.0±0.66	66.0±1.28*	74.2±0.78	66.8±1.73*	< 0.05
Finrinogen, g/l	3.01±0.09	2.42±0.07*	2.73±0.07*	2.25±0.09*	< 0.05
SMP, mmol/l	0.136±0.04	0.280±0.01*	0.230±0.01*	0.270±0.01*	< 0.01

Note: * - reliability of differences in relation to parameters of healthy children;
P- reliability of parameters between groups on the background of therapy.

Under action of the complex treatment the parameters of cholestatic syndrome changed. Thus, the reliable decrease was noted in the parameters of the total bilirubin, the level of which after treatment was 15.4±2.25 mcmol/l ($p < 0.05$). The average level of total and direct bilirubin in the patients of control group remained to be higher and accounted for 23.0±5.7 mcmol/l and 8.73±2.3 mcmol/l, respectively, ($p>0.05$). In the patients of the studied group the reliable (from $p < 0.01$ to $p < 0,001$) increase of average values of albumin (49.3±0.64%), prothrombin (to 74.2±0.78 %) and fibrinogen (to 2.73±0.07 g/l) indicated about increase in the synthetic function of the liver (hepatopril syndrome). The level of total protein in dynamics acquired the tendency to increase ($p> 0.05$). The effect of basic therapy with monocomponent biopreparation on the synthetic liver function we did not found. So, the contents of total protein, albumin, prothrombin and fibrinogen were within the limits of starting meanings. There were also no significant changes in the parameters of mesenchymal-inflammatory syndrome and endogenous system of detoxication ($p>0.05$). In the patients of the studied group in the parameters describing mesenchymal-inflammatory syndrome there was also noted marked normalizing effect of the biopreparations used that was expressed in the reduction of the level of gamma-globulin (to 18.2±0.66 %) and thymol probe (to 5.9±0.42), $p < 0,001$. The activation of systems of endogenous detoxication was confirmed by significant lowering of the level of middle molecules to 0.230±0.01mmol/l in the at the patients of the main group ($p < 0.01$ in relation to parameters before treatment and group of control). Thus, in children with CHB on the background of lambliasis with disturbance of intestinal microbiocenosis the use

of chosen in the test in vitro of highly-sensitive biopreparations additionally to basic therapy showed positive effect on a number of biochemical parameters of CHB.

At the comparative analysis of quantitative and qualitative changes in the contents of intestinal microflora (Tabl.2) in children with CHB associated with lambliasis after complex treatment the amount of normal contents of bifido- and lactobacteria in the limits 109-1010KOE/g was noted in 34.5±4.7 % and 30.9±6,3 %, respectively, that was 2.5 times more frequently in relation to the patients of control group – 13.3±6.2 % ($p < 0.01$; $p<0,001$, respectively).

Table 2.

Dynamics of the changes of the intestinal microflora representatives in children with CHB on the background of lambliasis (%).

The agents of the intestinal microflora	Main group n=55		Control group n=30		P
	Before treatment	After treatment	Before treatment	After treatment	
Bifidobacteria:					
norm. contents (10^9-10^{10}CFU/g)	3.7±2.5	34.5±4.7	3.3±3.3	13.3±6.2	<0.001
moderate reduction (10^6-10^5CFU/g)	21.8±5.6	49.1±6.8	20.0±7.3	23.3±7.7	<0.05
significant reduction (<10^5 CFU/g)	74.5±5.9	18.2±5.2	76.6±7.7	63.4±8.8	<0.001
Lactobacteria:					
norm. contents (10^9-10^{10}CFU/g)	3.6±2.5	30.9±6.3	6.7±4.5	13.3±6.2	<0.01
moderate reduction (10^6-10^5CFU/g)	29.1±6.2	50.9±6.8	30.0±8.4	33.3±8.6	>0.05
significant reduction (<10^5 CFU/g)	69.1±6.3	18.2±5.2	63.3±8.8	53.4±9.1	<0.001
E.coli typical:					
norm. contents (10^7-10^8CFU/g)	5.5±3.1	34.5±4.7	6.7±4.5	16.7±6.8	<0.01
amount decrease (<10^7CFU/g)	74.5±5.9	49.1±6.8	73.3±8.1	70.0±8.4	<0.02
amount increase (>10^8CFU/g)	20.0±5.4	18.2±5.2	20.0±7.3	13.3±6.2	>0.05
E.coli lactozonegative	30.9±6.3	18.2±5.2	33.3±8.6	26.7±8.0	>0.05
E.coli hemolytic	20.0±5.4	5.5±3.1	20.0±7.3	16.7±6.8	>0.05
Enterococci:					
norm. contents (10^7-10^8CFU/g)	7.3±3.5	50.9±6.8	10.0±5.5	16.7±6.8	<0.001
amount decrease (<10^7CFU/g)	74.5±5.9	49.1±6.8	73.3±8.1	70.0±8.4	<0.02
amount increase (>10^8CFU/g)	18.2±5.2	-	16.7±6.8	13.3±6.2	<0.05
Staphylococcus aureus	29.1±6.2	9.1±3.9	26.7±8.0	20.0±7.3	<0.05
Staphylococcus epidermidis	29.1±6.2	5.5±3.1	23.3±7.7	20.0±7.3	<0.05
Proteus	14.5±4.8	-	16.7±6.8	10.0±5.5	<0.02
Klebsiella	14.5±4.8	9.1±3.9	13.3±6.2	10.0±5.5	>0.05
Candida fungi	56.4±6.7	18.2±5.2	53.4±9.1	36.7±8.8	<0.02
Two-component associations of the opportunistic microorganisms	20.0±5.4	9.1±3.9	20.0±7.3	16.7±6.8	>0.05
Three-component associations of the opportunistic microorganisms	10.9±4.2	-	13.3±6.2	10.0±5.5	<0.02
Four-component associations of opportunistic microorganisms	5.5±3.1	-	6.7±4.5	3.3±3.3	>0.05

The note: P - statistically reliable distinctions of parameters on the background of therapy.

The amount of significant reductions of bifido- and lactobacteria (<10^5CFU(colony-forming units/g) in the patients of the main group were revealed 3.7 and 3.1 times less often accordingly to the parameter of control group (p<0,001). The detection of colon bacillus with normal fermentative activity was registered reliably more in the patients of the main group ($p < 0.01$ in comparison with the control). Reduction of quantity of the typical colon bacillus 107CFU/g in the patients of control group after treatment came to light almost 1,4 times more than in the patients of the main group, $p < 0.02$. There were also hemolytic E.coli 2,9 times less often in children of the main group ($p > 0.05$ in comparison with the control). The quantity of the normal contents of enterococci in limits 10^7-10^8CFU/g in the patients of the main group was registered almost in a half of patients (50.9±6.8 % against 16.7±6.8 %, $p < 0,001$). Reduction of quantity of enterococci to 10^7CFU/g was noted after therapy by chosen in the test in vitro of highly-sensitive biopreparations and was registered in 49.1±6.8% of cases, whereas in the patients of control group these results were revealed almost 1,4 times more often ($p < 0.02$). The increase of quantity of enterococci higher 10^8CFU/g in the patients of the main group after treatment was not found out, whereas in group of the control these figures were reached 13.3±6.2 % of cases ($p < 0.05$). From the representatives of opportunistic microflora (OM) - golden and epidermal staphylococci were revealed 2.3 and 3.5 times less often, respectively, in children of the main group after treatment (9.1±3.9 % and 5.5±3.1 % against 20.0±7.3 % of cases, respectively, $p < 0.05$). The determination of non-fermentative bacteria of a sort Proteus after the therapy performed in the patients of the main group was failed, however, in the children of the group of control these characteristics were not changed practically ($p < 0.05$). The yeast-like fungi of a sort Candida also decreased 2.1 times and the revealing of associations of opportunistic microorganisms decreased, and also there were absent three- and fourcomponent associations in children of main group ($p < 0,05$-$0,001$). The pair combinations of opportinustic microorganisms were met almost 2 times less often in children receiving polycomponent biopreparations, in which there were found combinations Candida+Staphylococcus aureus, $p > 0.05$.

Thus, the correction of the disbiotic disturbances in the intestinal microbiosis in children with CHB on the background of lambliasis resulted in improvement of the microecological status of the patients, at which representatives of the obligatory microflora increased while opportunistic microorganisms as well as their associations reduced. Totally, data received during this investigation indicated about real positive properties of therapy, which application led to improvement of the well being of the studied children, significant improvement of the state of the

intestinal microbiocenosis and as well as achievement of the normal levels of the majority of studied biochemical characteristics that provided for development of remission: by clinical signs – 76.5 % (against 23.8 % in group of the control), biochemical – 64.4 % (against 28.2 % in the control group) and microbiological parameters in 62.0 % of the patients (against 25.2 % concerning the control), $p<0.05$.

The conclusion. For the effective approach to the correction of the damaged intestinal microbiocenosis in children with CHB on the background of lamblia invasion and for providing of the choice of optimal biopreparation for each of patients it is recommended performance of the "loading" test in vitro before prescription of the probiotic agent. The choice of the individual treatment and evaluation of the efficacy of intestinal biocorrection from the first day of admission to the hospital will promote prolongation of the period of remission and favourable prognosis of the main disease.

REFERENCES

1. Bondarenko V.M., Matsulevich T.V. Intestinal disbacteriosis as clinical-laboratory syndrome: a modern condition of a problem // M.: Medicine, 2007. - P. 36-54.
2. Efficacy Of Macmiror® In The Therapy Of Giardiasis Invasion In Children With Chronic Hapatitis B. NF Nurmatova, FI Inoyatova, M Azadovna - European Journal of Molecular & Clinical Medicine, 2020.T7. Issue 03. P.3596-3607
3. Escobedo A.A., Alvares G., Gonzalez M.E. et al. The treatment of giardiasis in children: a single-dose tinidazole compared with 3 days of nitazoxanide. // Ann. Trop. Med. Parasitol.-2008.- 102 (3).- P. 199-207.
4. Fedosyina E.A., Jarkova M.S., Maevskaya M.V. Bacterial intestinal microflora and liver diseases // Russian Journal of Gastroenterology, hepatology and Colonoproctology. - 2009. - №6. – P. 73-81.
5. Inoyatova F.I., Nurmatova N.F., Abdumajidova Sh.U., Inogamova G.Z. et al.: Role giardiasis in chronic viral diseases in children. Improving diagnosis and treatment Metod. rekomend.—Tashkent.—2012.—27 s
6. Inoyatova F.I., Abdumadjidova Sh.U. Clinical-immunological features of the chronic hepatitis delta in children with intestinal disbacteriosis //Actual problem of diagnosis, treatment and medical rehabilitation in diseases of the internal organs //Materials of the V Congress of therapeutists of Uzbekistan.-Tashkent, 2008.-P.140-141.
7. Inoyatova F.I., Abdumadjidova Sh.U., Inogamova G.Z. et al. Role of lamblia invasion during chronic virus pathology in children. Improvement of diagnostics and treatment // Methodical recommendations, 2011.

8. Inoyatova F.I., Nurmatova N.F., Inogamova G.Z. et al. «Method for evaluation of efficacy of the bacteriotherapy of the intestinal disbacteriosis in children with chronic viral hepatitis B". Patent RUz N IAP 04570 of 10.08.2010 (date of reg. in the State reg. of 06.09.2012).

9. Konanihina S.Yu., Serduk O.A. Efficiency and prospects of nifuratel using in therapy of lambliasis in children // Voprosi sovremennoy pediatrii. - 2005.- 4 (5).- P. 2- 6.

10. Korovina N.A., Zakharova I.N., Zaidenvarg G.E., Korobova L.A. et al. Lambliasis in children: problems of diagnosis and choice of therapy // Russian Medical Journal -2006.- № 2- P. 36-48.

11. Mossman Sims R.J., Woodgate R.I. Managing chronic hepatitis B in children // J. Pediatr. Health Care. - 2008. - Vol.22, N6. - P. 360-367.

12. Muhsen K (1), Levine MM. A systematic review and meta-analysis of the association between Giardia lamblia and endemic pediatric diarrhea in developing countries. // Clin Infect Dis. 2012 Dec; 55 Suppl 4:S271-93.

13. Selivestrov P.V., Radchenko V.G., Safronenkova I.G., Sitkin S.I. Interrelations between liver and intestine on the background of disbalance of colon microflora // Gastroenterology of Saint-Petersburg.-2010.- № 2-3.-P.15-18.

14. Wallace B. Clinical use of probiotics in the pediatric population // Nutr. Clin. Pract.-2009. -vol.24, N1.- P. 5-50.

15. Rol' lyamblioznoy invazii v techenii khronicheskoy virusnoy patologii u detey. Uluchsheniye diagnostiki i lecheniya. Inoyatova F.I., Abdumadzhidova SHU, Inogamova G.Z. - Metodicheskiye rekomendatsii, 2011 g.. 15. The role of giardiasis invasion during chronic viral pathology in children. Improving diagnosis and treatment. FI Inoyatova, SHU Abdumadzhidova, GZ Inogamova - Guidelines, 2011

16. Sostoyaniye mikroflory kishechnika u detey s khronicheskim gepatitom V i lyambliozom. FI Inoyatova, NF Nurmatova, SHU Abdumadzhidova - Detskiye infektsii. 2012, T.11., №1.S.20-23. 16. State of intestinal microflora in children with chronic hepatitis B and giardiasis. FI Inoyatova, NF Nurmatova, SHU Abdumadzhidova - Children's infections. 2012, V.11., No.1.S.20-23

17. Funktsional'noye sostoyaniye pecheni u detey, bol'nykh khronicheskim gepatitom V i lyambliozom kishechnika. NF Nurmatova, FI Inoyatova - Children's Medicine of the North-West, 2021.T9. №1.S262-263. Functional state of the liver in children with chronic hepatitis B and intestinal giardiasis. NF Nurmatova, FI Inoyatova - Children's Medicine of the North-West, 2021.V9. No. 1.C262-263

Central Asian Journal of Medicine

STATISTICAL ANALYSIS OF PATHOLOGICAL ANATOMY OF THROMBOEMBOLIC COMPLICATIONS IN CORONAVIRUS INFECTION

Shokhrukh R. Omonov[1], Khasan Z. Tursunov[2], Khamza N. Babaev[3], Nigora Kh. Kholieva[4]

1 Assistant of the Department of Pathological anatomy of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: dr.shohruhomonov1990@gmail.com

2 Doctor of Medicine, professor of the Department of Pathological anatomy of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: tursunov.hasan@bk.ru

3 PhD, Associate professor of the Department of Pathological anatomy of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: khamzababaev@gmail.com

4 Assistant of the Department of Pathological anatomy of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: nigoraxalieva@mail.com

ABSTRACT

This article compares the scientific findings of world scientists aimed at elucidating the pathological anatomy of thromboembolic complications in the composition of coronavirus infection and statistical analysis of coronavirus infection in our country. Statistical analysis showed that complications of thromboembolism in the period from 2019 to 2021 as part of coronavirus infection in the world will be 37%, of which 14% will be pulmonary embolism. Thromboembolic complications in patients with coronavirus infection, including sinus thrombosis, are currently considered the most common cause of death from Covid infection.

Key words: pathological anatomy, coronavirus infections, sinus thrombosis, thromboembolism, thrombosis.

INTRODUCTION

Currently, during the pandemic, there are too many death cases due to thrombo-embolic complications of corona virus infection. Prevention and

treatment of thromboembolic complications is an urgent problem. Thromboembolism is an acute blockage (embolism) of a blood vessel with a blood clot that has broken off from its place of origin (heart, vessel wall) and entered the blood circulation. As a result of thromboembolism, blood flow in blood vessels stops, tissue ischemia occurs in the occlusive vascular basin, often leading to an ischemic infarction.

Etiology and pathogenesis: Thromboembolism is the most common type of vascular embolism. Thromboembolism is caused by damage to the endocardium (in endocarditis, myocardial infarction) or vascular endothelium (in aortic aneurysm, aortitis, thrombophlebitis, vasculitis, atherosclerosis, etc.) and formation of thrombosis. Medicines that slow down fibrinolysis and bleeding also increase blood clot formation. Cardiac arrhythmias, especially paroxysmal tachycardia and fibrillation, contribute to the formation and separation of thrombus in the cardiac cavities. The formation of blood clots in the right chambers of the heart, large veins often causes the risk of pulmonary embolism. (4). COVID-19 (2019 new coronavirus disease) continues to threaten the global health system. Epidemiological evidence shows that SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) is most susceptible to patients with metabolic and chronic diseases. In patients with severe acute respiratory syndrome associated with movement insufficiency contaminated with coronavirus-19, risk of venous thromboembolism increases when if dehydration occurs during self-isolation. Patients' hospitalization for the treatment of coronavirus disease (COVID-19) greatly increases the risk of developing pneumonia and thromboembolic complications. These thromboembolic events are the result of at least two distinct mechanisms. Pulmonary microvascular thrombosis (immunothrombosis) and hospital-associated venous thromboembolism.

Immunothrombosis – through the course of evolution, the blood coagulation system developed as a result of the immune response, with fibrin preventing the spread of pathogenic microbes into the body. When viruses such as SARS-CoV-2 enter the body, during acute viremia, cytokine production, activation of monocytes and macrophages, interleukin-6 production (IL-6) and potentially the initiation of the coagulation system are induced. The entry of SARS-CoV-2 into human cells is ensured by the effect on angiotensin enzyme-2 (ACE-2) receptors. These receptors are found in many tissues such as pneumocytes, heart, kidney, endothelium, macrophages and intestine. The main part of the cells expressing ACE-2 are alveolar epithelial type II cells of lungs (type-II pneumocytes). The abundance of ACE-2-expressing cells in the alveoli of the lungs and the large surface area of the lungs make it the main target organ for viruses. Extravascular fibrin develops in

the pathogenesis of acute lung injury in COVID-19. Immunothrombotic inflammatory response, combined with hypoxia and increased local tissue factor production develop in patients with SARS-CoV-2 infection. Monocyte activation and subsequent cytokine hyper-production can also lead to endothelial cell activation, which involves a change from an antithrombotic phenotype to a procoagulant phenotype.

Coronavirus disease 2019 (SARS-Cov-2) is a new viral infection causing acute respiratory distress syndrome (ARDS) that was first identified in December 2019 in Wuhan, China. This infectious disease quickly spread to almost all countries, causing the most dangerous pandemic since the Spanish flu of 1918-1920 [1]. One of the worst features of COVID-19 is the risk of thromboembolic complications and a severe coagulopathy called COVID-19-induced coagulopathy (CAC), with a venous thromboembolism (VTE) rate of about 25 percent. Damage to vascular endothelial cells infected with SARS-Cov-2 can lead to neutrophil collection and immune complex formation. Contemporary activation of coagulation, inflammation, and immune pathways is consistent with the concept of immunothrombosis [2]. These two processes are initially triggered by SARS-Cov-2-induced diffuse endothelial dysfunction through angiotensin-converting enzyme (APF-2) and transmembrane protease serine 2 (TMPRSS2) receptors, which are now recognized as specific entry sites of the virus into the vasculature. Rare autooptic studies of patients with COVID-19 show extensive areas of inflammatory infiltration associated with interstitial edema, thrombotic lesions, and changes in alveolar architecture, with characteristic vascular features consisting of severe endothelial damage and disrupt of cell membranes, termed intracellular virus-associated endotheliitis. Histological analysis of pulmonary vessels in patients with COVID-19 showed widespread thrombosis with microangiopathy, including the formation of hyaline membranes and infiltration of macrophages and monocytes [3,4,5].

Although these results were mainly observed in patients older than 65 years with a history of comorbidities, occasionally, pulmonary complications with extensive parenchymal damage requiring invasive ventilation were also observed in some younger patients. A recent European Society of Cardiology (ESC) article on Atherosclerosis and Vascular Biology focused on endothelial damage as a major target organ for thrombotic complications [6]. This complex scenario involves an altered immune and inflammatory response, oxidative stress, damage to the endothelial structure, and platelet activation. Histological markers are also mediated by both specific populations of lymphocytes associated with increased immunity and by pre-coagulation markers that predispose to intravascular

thrombosis. Thrombotic activity can increase in other vascular areas such as coronary and cerebral vessels, leading to acute coronary syndrome and stroke, respectively [7,8]. Although these common findings have been reported in the recent literature, which patients are at increased risk of developing immune and thromboembolic (TE) complications remains to be determined. Another point that remains to be determined is whether current clinical laboratory and diagnostic approaches applied to patients with COVID-19 are able to rapidly detect and ultimately prevent clinical deterioration. A better understanding of the mechanisms linking infectious diseases to embolic complications is a challenge for future research. Of note, the altered sign of the coagulation cascade and the specific investigation of molecular and protein signaling dysfunction may lead to treatment optimization.

This is a peer-reviewed review of thrombotic complications associated with SARS-Cov-2 infection, including randomized clinical trials, controlled trials, meta-analyses, and position papers published in the field. We excluded clinical cases and single center studies from our paper case reports. Searching terms and definitions for all articles published in Pub Med between December 2020 and March 2021 included taking the terms such as "risk factors," "thrombosis," "coagulation," "vascular complications," and "antithrombotic therapy."

Epidemiological studies have shown that elderly patients with a higher severity of comorbidity are more prone to develop adverse complications after infection with COVID-19. The presence of risk factors such as cardiovascular disease (CVD) or simply diabetes and heart disease in the medical history leads to the end of the disease with unpleasant consequences [9]. Accordingly, admission to the emergency department (ED) and the need for invasive ventilatory support are more common in patients with cardiovascular disease, whose mortality is 5-10 times higher than in patients without risk factors [10, 11]. Patients with a high severity of cardiovascular diseases and comorbidities are more likely to develop cardiac complications, mainly due to increased complications of TE and ARDS [12, 13]. These results were confirmed in 5,700 hospitalized patients in the New York area, showing that cardiovascular risk was independent of race and geographic region [14].

In a meta-analysis of 75,000 subjects, hypertension, cardiovascular disease, diabetes, smoking, chronic obstructive pulmonary disease, malignancy, and chronic kidney disease were the most common underlying medical conditions associated with hospitalization [12]. Of note, another analysis evaluating cardiac biomarkers found elevated levels of troponin (TnT), pro-V-type N-terminal natriuretic peptide (NT-proBNP), and C-reactive protein in patients with CVD. In-

hospital mortality was similarly associated with a history of cardiovascular disease and TnT level: patients without known cardiovascular disease with elevated TnT levels were relatively better, but patients with cardiovascular disease or elevated TnT levels (69 percent) was unacceptably many during hospitalization [13]. Available data suggest that myocardial injury is significantly associated with severe COVID-19 outcomes, and this trend is likely due to the presence of CVD. Studies have shown that TnT levels are significantly correlated with C-reactive protein (CRP) and NT-proBNP levels, providing further evidence linking myocardial injury to the severity of inflammation. Inflammation and the associated cytokine storm can affect the respiratory and cardiovascular systems; otherwise, it can cause myocarditis, cardiac arrhythmias, acute coronary syndrome, pulmonary embolism, and disseminated coagulopathy. Although these complications may be associated with a significant increase in TnT, its increase may simply be due to a violation of ventilation exchange and a decrease in oxygen delivery at the level of the myocardium. Today's elevated levels of TnT and natriuretic peptides increase the risk of death in ICU (Intensive Care Unit) with invasive ventilation, acute heart failure, compensatory hypertension and severe arrhythmic complications [11,12]. Clinical manifestations and cardiovascular complications may include a wide range of events related to the site of immunothrombosis; Although pulmonary complications are more common, other systems may also be involved in the spread of the virus. Organs that cause the disease are organs with increased blood perfusion, in which a high concentration of the virus can circulate. It should be noted that the coronary arteries and cardiac compartments, the cerebrovascular system and the kidneys are the areas where the virus can cause clinical complications due to direct poisoning or endothelial dysfunction, which are located in different areas, leading to thrombotic events and multi-organ failure [13, 14].

The purpose of the study. The purpose of this work is to study the causes and pathomorphology of thromboembolism in coronavirus infection according to the data of autopsy studies and statistical analysis of the pathological anatomy of complications.

Material and methods. The main cause of the disease based on autopsy results of 111 patients with thromboembolic complications caused by coronavirus infection, were analyzed retrospectively. The age of the dead patients ranged from 20 to 70 years old, including: 19 people with diabetes, 5 people with pregnancy, 31 people with ischemic heart disease, 24 people with COPD, 1 person with kidney disease, 26 people with heart disease, 1 person with cirrhosis of the liver and 4 patients with atherosclerosis.

The dead patients were divided into 5 groups according to gender and age: group 1 included patients aged 21 to 30 years: women (6 cases) men (2 cases); In 2-nd groups, women aged 31 to 40 years (10 cases) and men (14 cases); In 3-rd groups, women aged 41 to 50 years (10 cases) and men (13 cases); In 4-th group, women aged 51 to 60 years (11 cases) and men (15 cases), and in 5-th group women (12 cases) aged 61 to 70 years and men (18 cases). Autopsy was performed by Shor's method. All internal organs were taken for histological examination and their slices with a thickness of 0.5-1.0 cm and 1 cm2 were processed with 10 percent neutral formalin in a room temperature for 24-48 hours.

Results and discussion. 9 cases with pulmonary artery thromboembolism as the main cause of death were identified, which is 8.1 percent out of 111 cases.

There is a correlation of thrombosis level in relation to the sex and age of the deceased patients: thus, from 21 to 30 years old - 7.3 percent (8 cases); 31 to 40 years old - 21.6 percent (24 cases); 41 to 50 years old - 20.7 percent (23 cases); From 51 to 60 years old - 23.4 percent (26 cases) and from 61 to 70 years old - 27 percent (30 cases). The highest incidence rate of the disease is women and men aged 61 to 70 years, 12 cases in women and 18 cases in men. Because at this time, many other somatic diseases such as diabetes mellitus, IHD, etc. appeared together in women and men. The lowest point of incidence was between ages of 21 and 30, which was 6 in women and 2 in men.

Monitoring of patients in relation to gender; It was found that 44.1% (49 cases) in women infected with coronavirus infection and 55.9% (62 cases) of men died from complications of thrombosis. According to the occurrence of somatic diseases in patients who died from complications of thrombosis due to coronavirus infection: diabetes mellitus 17.1 percent (19 cases), pregnancy 4.5 percent (5 cases), ischemic heart disease 28.0 percent (31 cases), acute cerebral blood circulation disturbance 21,6 percent (24), kidney disease 0.9% (1), liver disease 23.4% (26), liver cirrhosis 0.9% (1) and atherosclerosis 3.6% (4) organized.

Ischemic heart disease took the first place among infectious diseases - 28.0 percent (31 cases). After that, hypertension disease - 23.4 percent (26 cases).

In our study, there were 3 cases of death due to complications of sinus thrombosis, morphologically, the combination of necrotic process in the nasal cavity with sinusitis in the upper respiratory tract, soft and hard palates.

Summary

1. Among the 111 patients who died from thromboembolic complications during the period from 2019 to 2021 as part of the coronavirus infection, 9 of them, i.e. 8.1%, have died from pulmonary artery thromboembolism.

2. The highest incidence rate of the disease in women and men aged 61 to 70 years, 12 cases in women and 18 in men. The lowest incidence point was between the ages of 21 and 30, cases - 6 for women and 2 for men.

3. By gender: 44.1 percent (49 cases) in women and 55.9 percent (62 cases) in men.

4. According to the occurrence of somatic diseases combined with infectious diseases: the first place was occupied by ischemic heart disease - 28.0 percent (31 cases). After that, hypertension disease took 23.4 percent (26 cases).

REFERENCES

1. Erkin N. Bilalov, Laziz N. Tuychiev, Shukhrat A. Baymuradov, Okil I. Oripov, Bakhodir E. Bilalov, Rajab Israilov, Azamat Yusupov, Akhmadjon Nozimov. CAVERNOUS SINUS THROMBOSIS ASSOCIATED WITH COVID-19. //Journal of Hunan University (Natural Sciences). October 2021. Vol. 48. No. 10

2. Zumrad Abduqayumovna Ergasheva, Rajabboy Israilovich Israilov, Alisher Kayumovich Shadmanov, Zukhriddin Salokhiddinovich Salokhiddinov, Mamazair Akhmedovich Khujamberdiev, Sardor Shakirov, Abdukhalim Khaliddin Ugli. Morfologicheskie osobennosti changes in the cardiovascular system during COVID-19. // Re-Health Journal #4 (12)-2021. 52-61.

3. Israilov R. PATHOMORPHOLOGY OF PULMONARY DISEASE WITH COVID-19. //A new day in medicine. – 2021. - #6(38). - pp. 186-194.

4. Pan A., Liu L., Wang C., Guo H., Hao X., Wang Q., Huang J., He N., Yu H., Lin X., et al. Association of Public Health Interventions with the Epidemiology of the COVID-19 Outbreak in Wuhan, China. JAMA. 2020;323:1915–1923. doi: 10.1001/jama.2020.6130. - DOI - PMC - PubMed

5. Frantzeskaki F. Immunothrombosis in acute respiratory distress syndrome: Cross talks between inflammation and coagulation. Respiration. 2017;93:212–225. doi: 10.1159/000453002.

6. Lopez-Castaneda S., García-Larragoiti N., Cano-Mendez A., Blancas-Ayala K., Damian-Vázquez G., Perez-Medina A.I., Chora-Hernández L.D., Arean-Martínez C., Viveros-Sandoval M.E. Inflammatory and Prothrombotic Biomarkers Associated with the Severity of COVID-19 Infection. Clin. Appl. Thromb. Hemost. 2021;27:1076029621999099. doi: 10.1177/1076029621999099.

7. Cui S., Chen S., Li X., Liu S., Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J. Thromb. Haemost. 2020;18:1421–1424. doi: 10.1111/jth.14830.

8. Bryce C., Grimes Z., Pujadas E., Ahuja S., Beasley M.B., Albrecht R., Hernandez T., Stock A., Zhao Z., AlRasheed M.R., et al. Pathophysiology of SARS-CoV-2: The Mount Sinai COVID-19 autopsy experience. Mod. Pathol. 2021;1:1–12. doi: 10.1038/s41379-021-00793-y.

9. Xu Z., Shi L., Wang Y., Zhang J., Huang L., Zhang C., Liu S., Zhao P., Liu H., Zhu L., et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir. Med. 2020;8:420–422. doi: 10.1016/S2213-2600(20)30076-X.

10. Pennisi M., Lanza G., Falzone L., Fisicaro F., Ferri R., Bella R. SARS-CoV-2 and the Nervous System: From Clinical Features to Molecular Mechanisms. Int. J. Mol. Sci. 2020;21:5475. doi: 10.3390/ijms21155475.

11. D'Ascenzo F., De Filippo O., Borin A., Barbieri L., Adamo M., Morici N., Giachet A.T., Iannaccone M., Crimi G., Gaido L., et al. Impact of COVID-19 pandemic and infection on in hospital survival for patients presenting with acute coronary syndromes: A multicenter registry. Int. J. Cardiol. 2021 doi: 10.1016/j.ijcard.2021.03.063. in press.

12. Evans P.C., Rainger G.E., Mason J.C., Guzik T.J., Osto E., Stamataki Z., Neil D., Hoefer I.E., Fragiadaki M., Waltenberger J., et al. Endothelial dysfunction in COVID-19: A position paper of the ESC Working Group for Atherosclerosis and Vascular Biology, and the ESC Council of Basic Cardiovascular Science. Cardiovasc. Res. 2020;116:2177–2184. doi: 10.1093/cvr/cvaa230.

13. Madewell Z.J., Yang Y., Longini I.M., Jr., Halloran M.E., Dean N.E. Household Transmission of SARS-CoV-2: A Systematic Review and Meta-analysis. JAMA Netw. Open. 2020;3:e2031756. doi: 10.1001/jamanetworkopen.2020.31756.

14. Liu P.P., Blet A., Smyth D., Li H. The Science Underlying COVID-19: Implications for the Cardiovascular System. Circulation. 2020;142:68–78. doi: 10.1161/CIRCULATIONAHA.120.047549.

Central Asian Journal of Medicine

INTERVENTIONAL CORRECTION OF EXTRAHEPATIC PORTAL HYPERTENSION IN PATIENT AFTER LIVER TRANSPLANT. THE FIRST CASE REPORT IN UZBEKISTAN

Konstantin Semash[1], Timur Djanbekov[2], Mirshavkat Akbarov[3], Azim Usmonov[4], Maksudjon Shermatov[5], Temurbek Gaybullaev[6]

1 MD, PhD, liver transplant surgeon, liver transplant program curator, V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery, Department of HPB surgery and Liver Transplantation #1, Tashkent, Uzbekistan
E-mail: mail@doctorsemash.com

2 MD, PhD, liver transplant surgeon, liver transplant program curator, V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery, Department of HPB surgery and Liver Transplantation #1, Tashkent, Uzbekistan
E-mail: djanbekov.md@gmail.com

3 professor, Doctor of Science, Head of Department of Hepatobiliary Surgery and Liver Transplant, V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery, Department of HPB surgery and Liver Transplantation #1, Tashkent, Uzbekistan
E-mail: mma1963@mail.ru

4 MD, surgeon, V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery, Department of HPB surgery and Liver Transplantation #1, Tashkent, Uzbekistan
E-mail: azimusmonovdr@gmail.com

5 MD, interventional surgeon, V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery, Department of interventional radiology, Tashkent, Uzbekistan
E-mail: 7005max@mail.ru

6 residency doctor, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: temursolo@gmail.com

ABSTRACT

Liver transplantation is a multi-component and complex type of operative treatment. Patients undergoing such a treatment sometimes are getting various complications. One of these complications is a portal hypertension associated with portal vein stenosis.

Materials and methods. In 8 months after the right lobe transplantation from living donor in an adult patient the signs of portal hypertension were observed. Stenosis of the portal vein was revealed. Due to this fact percutaneous transhepatic correction of portal vein stenosis was per formed.

Results. As a result of the correction of portal blood flow no more portal vein stenosis obtained. According to the laboratory and instrumental methods of examination the graft had a normal function, portal blood flow was adequate. In order to control the anastomosis patency Doppler ultrasound was performed in the 5-days and 21-days period. Due to these examinations the no stenosis was obtained, the rate of blood flow in the portal vein due to Doppler data has reached 60-70 cm/sec, and a decrease of the spleen size was noted.

Key words: portal hypertension, liver transplantation, portal vein stenosis, balloon angioplasty.

INTRODUCTION

Liver transplantation, to date, is the standard and the only one treatment for patients with end-stage diffuse and focal liver diseases [1]. In the Republic of Uzbekistan only living donor liver transplant (LDLT) is currently performed. This type of transplant care has a number of advantages over transplantation from a deceased donor: good graft quality, the ability to perform the surgery in the required time frame, and better tissue compatibility with the donor.

LDLT is a multicomponent, difficult method of surgical treatment. Patients undergoing this type of medical care may have various complications. One of these complications is a violation of blood flow in the portal vein as a result of the development of portal vein stenosis (PVS) [2,6,9-11]. Various disorders of the portal blood supply of the liver graft are formidable complications associated with a high incidence of its dysfunction and possible graft loss [3]. The progression of portal stenosis after liver transplantation inevitably leads to aggravation of the clinical manifestations of portal hypertension syndrome (splenomegaly, ascites, esophageal varicose veins, cytopenia) [6].

Doppler ultrasound is the main method for diagnosing post-transplant vascular complications, including portal vein stenosis [5]. Another informative method is computed tomography (CT) with intravenous contrast administration, which makes it possible to determine the severity and extent of PVS [4,22].

There are palliative and radical treatments for portal hypertension due to portal vein stenosis. Palliative methods include shunt operations on the portal system. The disadvantage of this method is the reduction in the volume of blood flow in the portal vein system, which can subsequently lead to aggravation of stenosis, in addition, encephalopathy as a traditional complication of bypass surgery. Radical methods include restoring the blood flow of the portal vein by its reconstructing by using artificial grafts or autografts, as well as endovascular

methods of treatment. The disadvantage of surgical reconstruction of the portal vein is the need for traumatic repeated surgical intervention in the area of the graft gate, access to which is difficult due to adhesions, as well as the risk of restenosis, so the expediency of the operation is determined to a greater extent by portal vein thrombosis with the impossibility of its correction by another method [20,21].

According to literature, endovascular correction techniques are the most preferable. One of the most effective and minimally invasive methods of treatment is endovascular angioplasty, including percutaneous transhepatic balloon angioplasty or stenting of the PVS [3,6-8,12,16-22].

After reviewing the Uzbekistan scientific literature, we did not find any works on the topic of interventional correction of portal vein stenoses in patients after liver transplantation. In view of this, we decided to demonstrate a clinical case of X-ray endovascular treatment of a patient with portal vein stenosis that occurred in the long-term period after liver transplantation.

Materials and methods.

Patient A., 48 years old, observed in the V. Vakhidov Republican Specialized Scientific and Practical Medical Center of Surgery since January 2022 with hepatitis C liver cirrhosis (MELD 22 points, Child-Pugh class C), portal hypertension (3rd degree esophageal varicose veins, splenomegaly, polyserositis, hypersplenism syndrome). Due to severe splenomegaly and severe pancytopenia, the patient underwent selective embolization of the splenic artery before liver transplantation. Also, patient had recurrent hydratoraxes, so pleural drainage was also carried out.

In May 2022, the patient underwent LDLT. The right lobe from her son was transplanted. The patient was discharged without complications in 21 days after surgery with good graft function. The immunosuppressive protocol was standard for our clinic: a two-component scheme using tacrolimus and methylprednisolone.

After discharge the observation performed on an outpatient basis, every 30 days laboratory control and ultrasound control of the graft were performed. Four months after transplant the patient complained of jaundice and itching. A comprehensive examination was performed, any data for the stricture of the biliary anastomosis was not obtained, signs of graft rejection were revealed (ALT 800 U/l AST 640 U/l, serum bilirubin 305 umol/l). The rejection crisis was stopped by pulse therapy with glucocorticosteroids (methylprednisolone 20 mg/kg of body weight), the immunosuppressive protocol was also corrected - mycophenolic acid was added. The patient was discharged with satisfactory graft function and normal blood tests.

The next appeal was in October 2022 with complaints of an increase in the size of the abdomen, tachycardia, feet, ankles and hips edema. The patient underwent a comprehensive examination. According to the ultrasound data, there was splenomegaly (Fig. 1), ascites, as well as an expansion of the intrahepatic portal vein branches up to 20 mm (Fig. 2). Due to the difficult visualization of the hepatoduodenal ligament during ultrasound examination, the patient underwent CT procedure with intravenous contrast admitting. Significant PVS in the area of the portal anastomosis was revealed (Fig. 3).

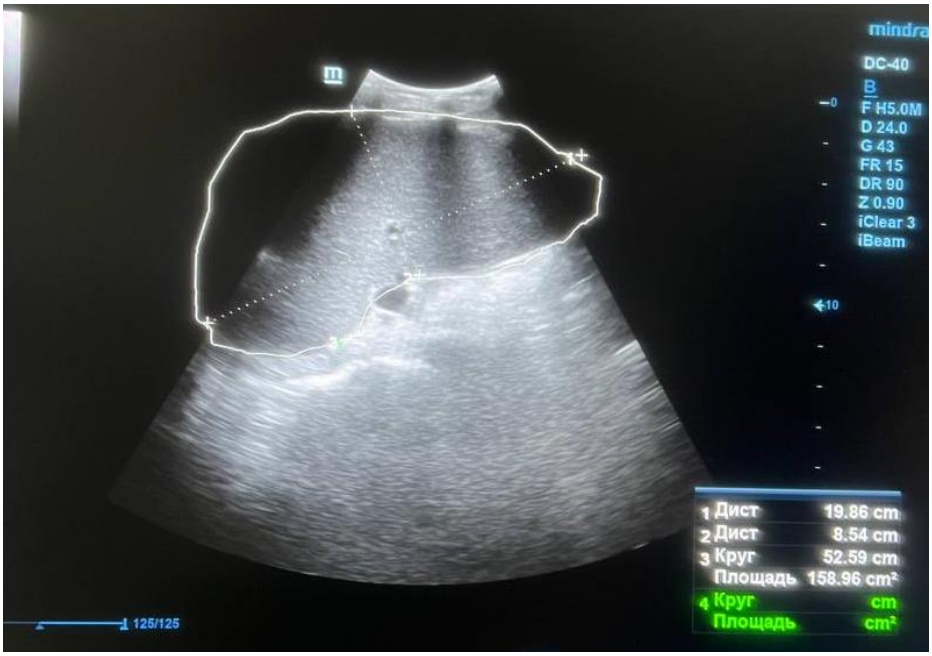

Figure 1. Ultrasound examination. Spleen size increased up to 159 sm^2.

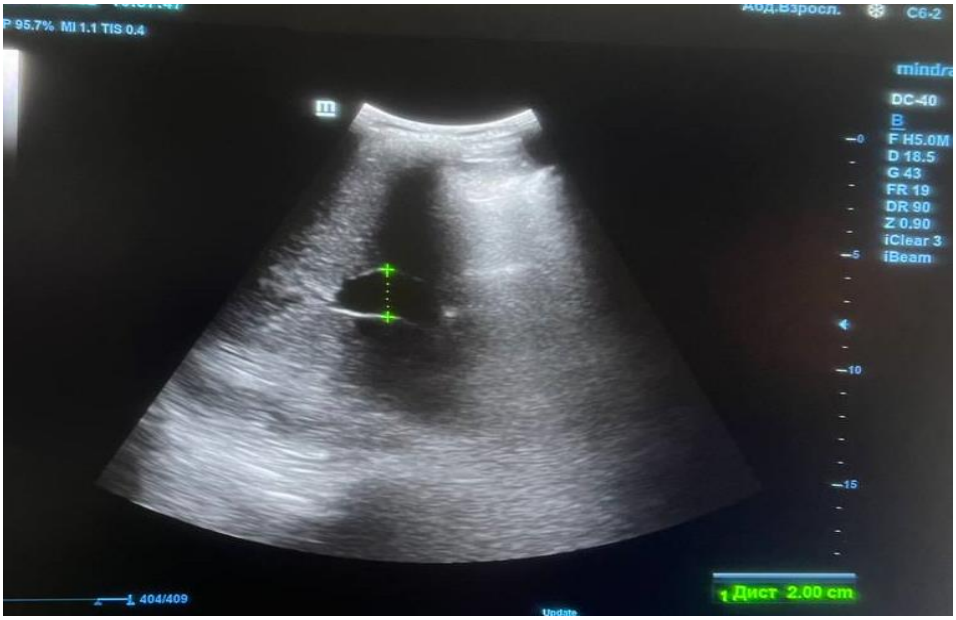

Figure 2. Ultrasound examination. Expansion of the intrahepatic portal vein branches up to 20 mm.

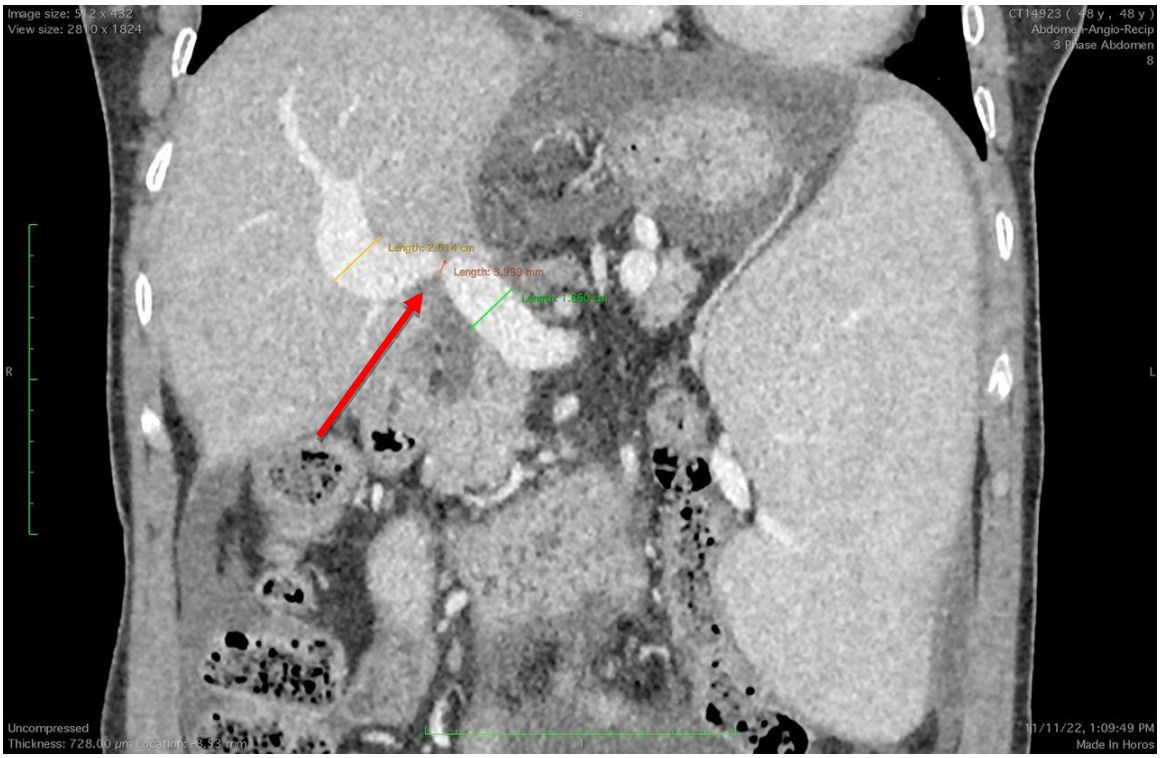

Figure 3. CT-angiography. The arrow indicates the site of portal vein stenosis. PVS diameter was 3.9 mm.

Considering the developed stenosis of the portal vein and the long period passed after liver transplantation, the traditional surgery of re-anastomosis is associated with huge surgical risks. Also, knowing the international experience of interventional correction of such complications [2,6,16-21], we decided to perform percutaneous-transhepatic balloon angioplasty of the PVS.

Surgery.

After local anesthesia with 1% lidocaine solution, using ultrasonic navigation, transhepatic puncture of a branch of the portal vein was performed using Chiba 20G needle. Plain angiography of the portal vein system was performed. A coronary guiding was passed through the puncture needle and installed into the splenic vein. An introducer installed using the guiding. An angulated EndoFlex-4 catheter was inserted into the splenic vein system. Angiography was performed and the site of portal vein stenosis was identified (Figure 4).

The catheter has been removed. The guiding was replaced with a more rigid one. A 12mm x 40mm Mustang-type balloon was inserted through the conductor, and balloon angioplasty of the stenosis was performed under a pressure of 16 ATM. Next, a similar plastic was performed with a 20x40 mm balloon under a pressure of 3 ATM. Control angiography showed a significant angiographic effect, there was no data for portal vein stenosis (Figure 5).

Guidewires and introducer removed. Control ultrasound showed no graft hematomas and signs of bleeding. The blood flow through the portal vein was adequate (linear blood flow 55 cm/sec).

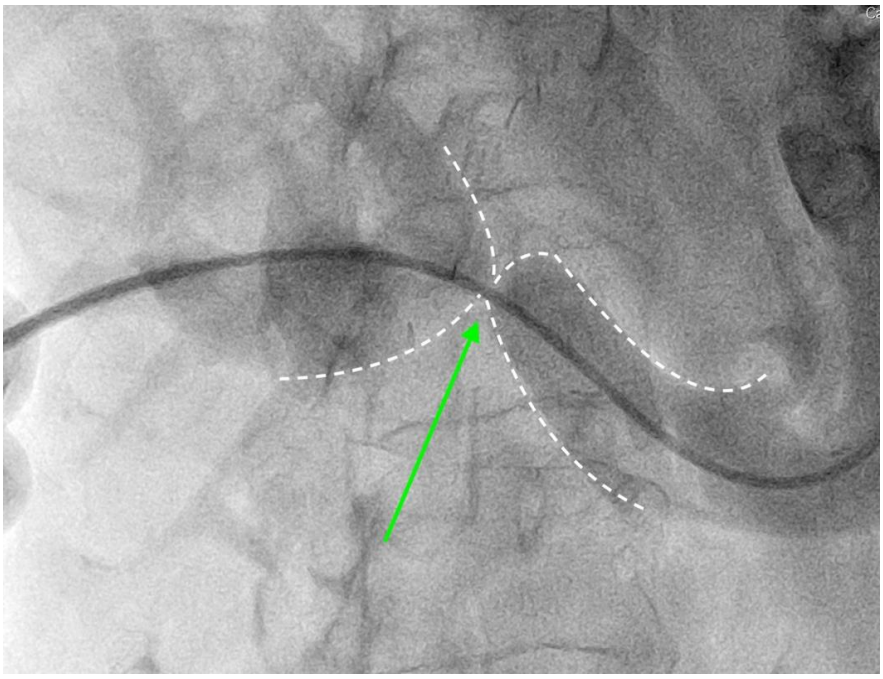

Figure 4. Percutaneous-transhepatic portography. The arrow indicates the site of portal vein stenosis.

.

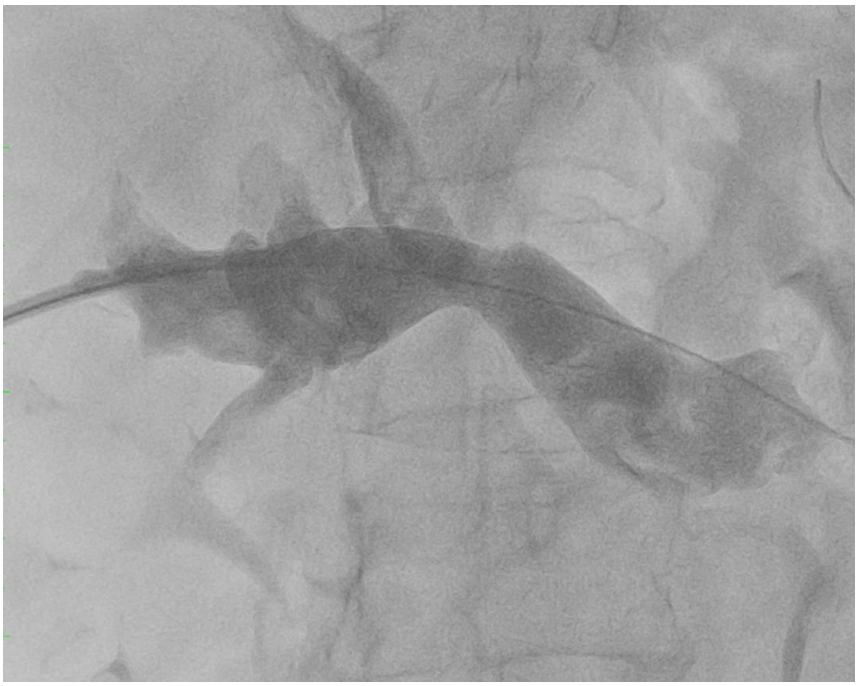

Figure 5. Percutaneous-transhepatic portography. Effect after PVS balloon angioplasty.

Results and follow up.

In the postoperative period the patient received infusion and antiplatelet therapy. Also, immunosuppressive therapy was carried out. In the dynamics during the control ultrasound examination, the ascites regressed completely, the spleen size with a significant decrease. According to laboratory data, no signs of graft dysfunction were observed. The patient was discharged on the 5th day after the procedure for further outpatient monitoring

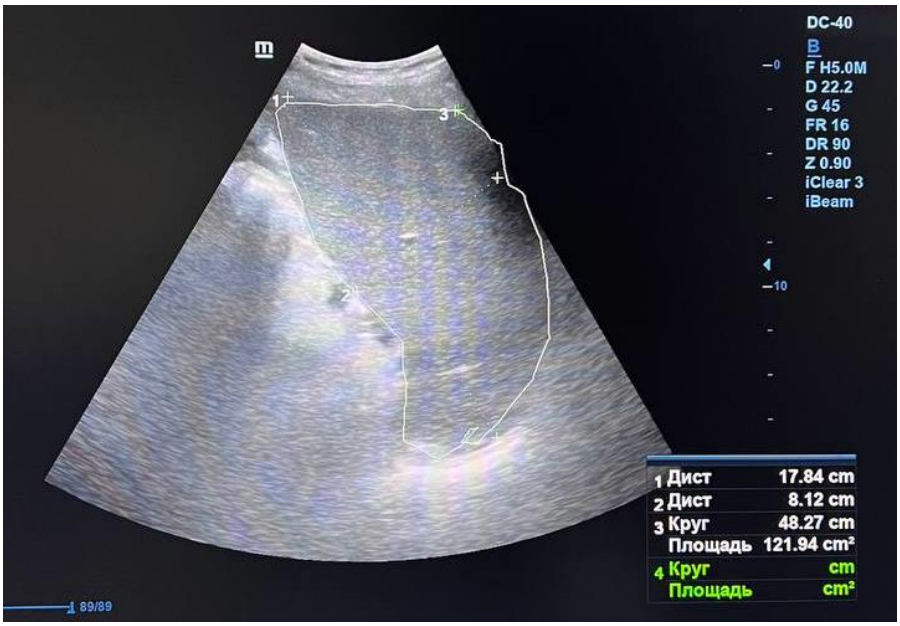

Figure 6. Reduction of the spleen size during dynamic ultrasound observation in 21 days after balloon angioplasty of the PVS.

Outpatient control was carried out 21 days after surgery. According to Doppler ultrasound data, 60-70 cm/sec laminar portal blood flow detected, there was no signs of PVS, splenomegaly with significant regression (Figure 6). According to laboratory data, no cytopenia was observed.

Discussion.

Vascular complications after LDLT require in-time diagnosis and treatment before the graft dysfunction appears [2–6]. In our case, the cause of early recurrent portal hypertension was stenosis of the portal vein in the area of the anastomosis with a partial violation of the outflow from the liver.

In our practice, portal vein stenosis is a rare complication after LDLT. Taking into account the fact that patients with portal vein stenosis have a risk of bleeding due to manifestations of portal hypertension and thrombocytopenia, as well as the presence of a pronounced adhesive process in the abdominal cavity, treatment in such patients should be performed as much as possible in minimally invasive ways. Thus, the percutaneous method has an advantage even over the method of

using a mini surgical access to cannulate a branch of the superior mesenteric or inferior mesenteric veins [6].

This case report demonstrates the high efficiency of percutaneous transhepatic access in the correction of extrahepatic portal hypertension in such patients. It is highly recommended to detect blood flow disorders in the portal vein as early as possible to prevent the development of portal hypertension syndrome in the post-transplant period. This requires regular ultrasound monitoring of liver graft blood flow characteristics [4,5].

Conclusion.

Diagnosis and timely detection of portal vein stenosis in patients after liver transplantation is very important for maintaining the function of the graft and preventing the development of portal hypertension. To do this, recipients need to carry out regular ultrasound control with duplex scanning of the graft blood flow, and in case of detection of signs of blood flow disorders in the portal vein system, CT angiography should be performed.

Percutaneous transhepatic balloon angioplasty of the portal vein stenosis is a minimally invasive and highly effective method for correcting portal hypertension in patients after liver transplantation.

REFERENCES

1. Gautier S.V, Konstantinov B.A, Cirul’nikova O.M. Transplantaciya pecheni. M.: Medicinskoe informacionnoe agentstvo, 2008.

2. Settmacher U, Nussler NC, Glanemann M, Haase R, Heise M, Bechstein WO, Neuhaus P. Venous complications after orthotopic liver transplantation. Clin. Trans- plant. 2000; 14: 235–241.

3. Gautier S.V., Voskanov M.A., Monakhov A.R., Semash K.O. The role of endovascular and endobiliary methods in the treatment of post-liver transplant complications. Russian Journal of Transplantology and Artificial Organs. 2020;22(4):140-148.

4. Katyal S, Oliver JH III, Buck DG, Federle MP. Detection of Vascular Complications After Liver Transplantation: Early Experience in Multislice CT Angiography with Volume Rendering. American Journal of Roentgenology. 2000; 175: 1735–1739. 10.2214/ajr.175.6.1751735.

5. Mullan CP, Siewert B, Kane RA, Sheiman RG. Can Doppler sonography discern between hemodynamically significant and insignificant portal vein stenosis after adult liver transplantation? Am. J. Roentgenol. 2010; 195: 1438–1443.

6. Monakhov A.R., Mironkov B.L., Dzhanbekov T.A., Semash K.O., Khizroev K.M., Gautier S.V. Correction of extrahepatic portal hypertension in pediatric patient after liver transplantation. Russian Journal of Transplantology and Artificial Organs. 2017;19(1):47-51. (In Russ.).

7. Semash K.O., Gautier S.V. Review of surgical techniques for performing laparoscopic donor hepatectomy. Russian Journal of Transplantology and Artificial Organs. 2020;22(4):149-153.

8. Granov A.M., Tarazov P.G., Granov D.A. et al. The role of interventional radiology in the pre- and postoperative period of liver transplantation // Khirurgiya. — 2010.—No. 3.—S. 31–36.

9. Darcy M.D. Management of venous outflow complications after liver transplantation // Tech. Vasc. Interv. Radiol. —2007.—Vol. 10, № 3.—P. 240–245.

10. Porrett P. M., Hsu J., Shaked A. Late surgical complications following liver transplantation // Liver Transplantation. —2009.—Vol. 15, № 11.—P. 12–18.

11. Lo C.M. Complications and longterm outcome of living liver donors: a survey of 1,508 cases in five Asian centers. Transplantation 2003;75:12–5.

12. Sanada Y., Kawano Y., Mizuta K. et al. Strategy to prevent recurrent portal vein stenosis following interventional radiology in pediatric liver transplantation. Liver Transpl 2010; accepted article.

13. Ueda M., Egawa H., Ogawa K. et al. Portal vein complications in the longterm course after pediatric living donor liver transplantation. Transplant Proc 2005; 37:1138–40.

14. Yamanaka J., Lynch S.V., Ong T.H. et al. Surgical complications and long-term outcome in pediatric liver transplantation. Hepatogastroenterology 2000; 47:1371–4.

15. Settmacher U., Nussler N.C., Glanemann M. et al. Venous complications after orthotopic liver transplantation. Clin Transplant 2000; 14:235–41

16. Kim Y.J., Ko G.Y., Yoon H.K. et al. Intraoperative stent placement in the portal vein during or after liver transplantation. Liver Transpl 2007;13(8):1145–52.

17. Ko G.Y., Sung K.B., Yoon H.K., Lee S. Early posttransplantation portal vein stenosis following living donor liver transplantation: percutaneous transhepatic primary stent placement. Liver Transpl 2007;13(4):530–6.

18. Park K.B., Choo S.W., Do Y.S. et al. Percutaneous angioplasty of portal vein stenosis that complicates liver transplantation: the mid-term therapeutic results. Korean J Radiol 2005;6(3):161–6.

19. Cheng Y.F., Chen Y.S., Huang T.L. et al. Interventional radiologic procedures in liver transplantation. Transpl Int 2001; 14:223–9.

20. Shibata T., Itoh K., Kubo T. et al. Percutaneous transhepatic balloon dilation of portal venous stenosis in patients with living donor liver transplantation. Radiology 2005; 235:1078–83.

21. Carnevale FC, Machado AT, Moreira AM et al. Midterm and longterm results of percutaneous endovascular treatment of venous outflow obstruction after pediatric liver transplantation. J. Vasc. Interv. Radiol. 2008; 19: 1439–1448.

22. Wozney P, Zajko AB, Bron KM, Point S., Starzl TE. Vascular Complications After Liver Transplantation. A 5Year Experience. Am. J. Roentgenol. 1986 October; 147 (4): 657–663.

Central Asian Journal of Medicine

LATIN AND ANCIENT GREEK MYTHOLOGY ABOUT MEDICINE AND HEALERS (Literature review)

Uktam D. Esanov[1], Abdunazar Kh. Juraev[2], Barno R Rajabova[3]

1 Associate professor of Tashkent Branch of Samarkand State University of Veterinary Medicine, Livestock and Biotechnologies, Uzbekistan

2 Associate professor of Tashkent Branch of Samarkand State University of Veterinary Medicine, Livestock and Biotechnologies, Uzbekistan

3 2nd year student of Tashkent Branch of Samarkand State University of Veterinary Medicine, Livestock and Biotechnologies, Uzbekistan

ABSTRACT

As it is well known that medical terminology is based on Latin and Greek terminology. This article describes some explanation about how mythology and God as Asclepius and religion affects to the appearance of medicine according to some literature review. While reading the article reader will understand that Asclepius was the founder of family medical school and will know the most revered children of the asclepian God were: Hygieia - goddess of Health from this name comes modern terminology –Hygiene, all - round healing Panacea - patron of medicinal healing (Greek Panacea-cure for all diseases), Machaon, became a famous military surgeon, and Podalirius is famous for treating internal diseases. As well as it is interesting to reader the appearance of the snake as a symbol of medicine for all over the world.

Key words: mythology, medicine, Greek Gods, Hygiene, Hellas, healing, Apollo, doctor, care.

INTRODUCTION

The beginning of Latin and ancient Greek mythology dates back to the thousand-year history of the peoples of the Aegean Basin. Among the gods of the Olympic pantheon, many were associated with healing, maintaining health and a healthy lifestyle.

The gods in ancient Hellas were considered anthropomorphic: they were depicted in the form of people and all human beings with both good and bad qualities and passions. Respect for the gods in ancient Hellas was expressed not with sadness, but with pleasure, not with self-deprecation and self - rejection, but

with noisy public entertainment-theatrical performances, gymnastic festivals and Olympic Games. One of these gods is Asclepius. Asclepius was originally a mortal and later became the god of medicine and healing, according to the ancient Greeks. The myth of Asclepius is connected to the origins of **medical science** and the **healing arts**.[1]

The cult of the physician God Asclepius originated in 7th century BC in Hellas. The prototype of this mythological hero was the real - life legendary healer - King of Thessaly during the Trojan War (1240-1230 BC) and the head of the family medical school-Asclepius.

Later, Asclepius, known for his medical art, was recognized as a demigod. According to legend, The God Asclepius married Epiona, daughter of Merops, ruler of the island of Kos. The island of Kos, later became one of the Centers of medical knowledge of Ancient Greece. The Asclepiad family (i.e. descendants of Asclepius) flourished here.

The island of Kos was one of the Centers of medical knowledge of ancient Greece.

The most revered children of the asclepian God were the following: Hygieia - goddess of Health (Greek Hygieia, Latin Hygia - health) from this name comes modern terminology –**Hygiene,** all - round healing Panacea - patron of medicinal healing (Greek Panacea-cure for all diseases), Machaon, became a famous military surgeon, and Podalirius is famous for treating internal diseases. According to legend, they all learned the art of healing from their father. An integral attribute of Asclepius (in ancient Rome – Esculapius i.e. physician) and his daughter Hygieia (in ancient Rome - Salus or Latin Salus – health) in ancient art was the serpent, which was revered in antiquity as a symbol of wisdom, renewal and represented the forces of nature. Asclepius is depicted as a young beautiful woman with a serpent wrapped in a serpent (i.e., a staff of a staff), while Hygieus is depicted as wearing a long cloak, holding a hand, and watered from a vessel.

According to Greek mythology, Asclepius, who first appeared next to the young Asclepius after the serpent defeated him over the Iron boar (the titan from which the gods were transformed into a serpent-creature), became the master of the Asclepius snakes, who killed Titan and learned his Serpent language. There is another legend, according to which, once Asclepius was sitting in the bed of a sick person, a snake appeared and wrapped in his wand. He killed her. Then immediately another snake appeared with grass in its mouth. He rubbed the dead

[1] https://www.greeka.com/greece-myths/asclepius/#:~:text=Asclepius%20was%20originally%20a%20mortal,science%20and%20the%20healing%20arts.

snake with grass, and the dead snake was resurrected. Asclepius found the herb and has used it with success ever since. In another, similar story, he healed a snake from encroaching death. To say thanks, the snake quietly whispered his knowledge on the healing arts into Asclepius's ear.[2]

Later, the image of a stick surrounded by a snake and a bowl with a snake became the main embodiment of Medicine in some countries, which, according to some authors, symbolizes the wisdom and power of nature's healing powers, according to the authorities, gives rise to fear of its unknown powers (snake poison was poison and medicine).

As a symbol of the Medicine, the snake has been known since ancient times, therefore, the roots of the symbol of medicine should be sought in a primitive society where people worship snakes.

Some researchers attribute this to the use of snake venom for medicinal purposes. Others believe that the snake has become a symbol of medicine, because it seems to be reborn like the patient's body after the skin is drained and treated. Some doctors and medical students misunderstand why the snake is a symbol of medicine. Statistics says that only 6% of doctors knew the real symbol of medicine, "Staff of Asclepius"[3]

The caduceus is the staff of Greek God Hermes. It is winged with two serpents coiling around it. It represents Hermes (or the Roman Mercury), the messenger of the gods, guide of the dead and protector of merchants, shepherds, gamblers, liars, and thieves, this comes in several history books of the Great Silk Road.

By extension, the caduceus is also a recognized symbol of commerce and negotiation, two realms in which balanced exchange and reciprocity are recognized as ideals that is why we can see this as a consigna symbol in Customs offices of many countries.

On the island of Kos (3rd century BC), the first shrines named after him were built-the asclepeions (asclepieion in Greek).

The most majestic was considered the shrine of Asclepius in Epidaurus. Its central building was the chapel of Asclepius (4th century BC).

Its basement is marked as connected by a mineral spring.

A mineral spring with a natural healing effect and a Cypress Garden (with healing air) were a mandatory place in the selection of places for the construction of temples in ancient Ellada.

[2] https://www.thecollector.com/why-was-greek-god-asclepius-linked-with-snakes/

[3] https://www.dailyrounds.org/blog/only-6-of-doctors-knew-the-real-symbol-of-medicine-staff-of-asclepius/

Spring water was used as one of the main medicines, and therefore it was considered sacred. On the territory of the reserve there was also a bathhouse, a library, a gymnasium and a stadium (running track), a theater. Numerous statues depicting gods were raised everywhere; they are monuments erected in honor of famous healers; stelae with texts engraved on cases of successful healing.

In the process of excavations at Epidaurus, a large number of images of healed body parts, as vows of gratitude, were found. They were made of marble, gold, silver and were given to the residence in gratitude for the services. These are marble arms and legs, silver hearts, golden eyes, ears, etc.

Only one thing was not allowed: it was impossible to die in the mask.

In both Epidaurus and other Asclepeians, all religious rites excluded from sacred sites are associated, in particular, with birth and death.

That is why, sometimes, pregnant women and incurable patients who came to give birth from the most remote places of ancient Greece were expelled behind the Holy Wall.

The servants of Asclepeion strictly controlled the cleanliness of the temple and its pilgrims. Anyone who entered would bathe in the waters of the holy spring and then offer sacrifices to the gods.

Thus, the Asclepius settlements in ancient Greece were not hospitals in our understanding. Professor V. P. According to Karpov, they had a “medico-sanatorium” appearance.

Asclepeion only accepted Asclepian followers who gave the service a sacred medical “oath", and those who joined the asclepean community.

In Asclepeion, healing is empirical and duo reading techniques are united. The main means of treatment: drug treatment, hydrotherapy, Gymnastics exercises. Asclepius was such a capable disciple that he surpassed his master in the art of healing: he learned not only to cure diseases, but also to bring the deceased back to life. He would do this with the help of the blood of the Medusa Gorgon given to him by the wise Athens. But the underworld God Hades complained to Zeus that the shadows of the dead began to disappear from his property due to the magical art of the physician Asclepius. And the supreme god Zeus, taking care of the authority of the gods, and their duties being encroached on by the doctor Asclepius, struck him with his lightning bolts. Thanks to the care of his loving father Apollo, Asclepius' body was taken to Olympus – thus, after his death, he became valued and deified. The Romans, who later adopted the pantheon of the Greek gods, named Asclepius Esculapius.

REFERENCES

1. https://www.greeka.com/greece-myths/asclepius/#:~:text=Asclepius%20was%20originally%20a%20mortal,science%20and%20the%20healing%20arts.

2. https://www.thecollector.com/why-was-greek-god-asclepius-linked-with-snakes/

3. https://www.dailyrounds.org/blog/only-6-of-doctors-knew-the-real-symbol-of-medicine-staff-of-asclepius/

4. Gigen G.YU. Mify/ Perevod s lat., kommentariy D.O. Torshilova, pod obshchey redaktsiyey A.A. Takho-Godi. — 2-ye izd., ispr. — SPb.: Aleteyya, 2000. — S. 1-128. Gigen G.Yu. Myths/ Translated from Latin, commentary by D.O. Torshilov, under the general editorship of A.A. Tahoe Godi. — 2nd ed., ispr. — St. Petersburg: Aleteya, 2000. — pp. 1-128.

5. Mify Drevney Gretsii/Per. s angl. Pod red. i s poslesl. A.A. Takho-Godi. – M., Progress, 1992. – S.134 – 137. Myths of Ancient Greece/Translated from English. Ed. and with an afterword by A.A. Tahoe-Godi. – M., Progress, 1992. – pp.134 – 137.

Central Asian Journal of Medicine

ON THE ISSUE OF ASSESSING THE TOXICITY RISK OF FORTIFICANT FOR STAPLE FOODS

Olga L. Elinskaya[1], Natalia V. Voronina[2], Jakhongir O. Khamdamov[3]

1 MD, Senior Researcher, Head of the Preventive Toxico-Hygienic Laboratory of the Department of Sanitary and Epidemiological Welfare of the Main Medical Department under the Administration of the President of the Republic of Uzbekistan

2 Doctor of Medical Sciences, Senior Researcher, Associate Professor, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan

3 Independent researcher, Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

The most promising solution to the problem of micronutrient deficiency is the enrichment of mass consumption products with missing vital micronutrients, in particular fortifiers. The aim of the research was to assess the risk of toxicity of the Vitamin & Mineral Premix fortificant (vitamin and mineral premix), manufactured by AQC Chemlab Private Limited, India, when used on experimental animals after intragastric administration. The research was carried out in accordance with the legislative and regulatory and methodological documentation. Biochemical blood tests were performed on a semi-automatic biochemical analyzer "CYANSmart" with software (Cypress Diagnostics, Belgium) according to standard methods. A detailed analysis of peripheral blood was determined in the Goryaev chamber. Experimental tests were carried out in compliance with the rules adopted by the European Convention for the Protection of Vertebrates for Experiments or Other Scientific Purposes (ETS No. 123. Strasbourg, 1986). According to the results of toxicological studies, the tested fortifier "Vitamin & Mineral Premix" (vitamin and mineral premix), manufactured by AQC Chemlab Private Limited, India, does not have a negative effect on the health of experimental animals in the intragastric route of admission, according to the parameters of acute toxicity, it refers to low-hazard substances, does not have a cumulative, irritating effect on the mucous membranes of the eyes, sensitizing effect and does not cause pathological and structural changes in the internal organs of experimental animals. This fortifier meets the safety requirements in terms of toxicological indicators.

Key words: fortificant, vitamin and mineral premix, toxicological assessment, safety.

INTRODUCTION

It is proved that the deficiency of certain vitamins and trace elements contributes to the development of alimentary-dependent diseases, and thereby causes significant damage to health, expressed in a decrease in resistance to various diseases, the effect of harmful factors of the production environment and environmentally unfavorable environmental factors, a reduction in professional longevity and life expectancy of the population [1, 2, 6,]. The most promising solution to the problem of micronutrient deficiency is the enrichment of mass consumption products with missing vital micronutrients [3,4,5]. Fortification of staple foods that are widely distributed and widely consumed will help improve the nutritional status of a significant part of the population and does not require any changes to the diet or an individual decision to comply with the regime [7,]. In accordance with the requirements of the Law of the Republic of Uzbekistan "On sanitary and epidemiological welfare of the population", all new additives, including fortifiers for staple food imported or produced in the country, are subject to mandatory toxicological assessment in order to determine their medical and biological safety for public health when used. Presented for toxicological evaluation fortificant "Vitamin & Mineral Premix" (vitamin and mineral premix), manufactured by AQC Chemlab Private Limited, India for food fortification "Vitamin & Mineral Premix" contains 200 g of: vitamin B1 – 1,4; vitamin B2 – 1,9; vitamin B3 – 10,69; vitamin B9 – 0.9; vitamin B12 – 0.002; iron – 16.3; zinc – 26.78.

The methodological approach to assessing the safety of the fortifier "Vitamin & Mineral Premix" included the following research areas:

- determination of the oral medium-lethal dose;
- determination of cumulative (subacute) action;
- study of the irritating effect on the mucous membranes;
-study of the sensitizing properties of the composition of the fortifier.

During the research, there were no extraordinary circumstances that could affect the quality and reliability of the results obtained.

The aim of the research was to assess the risk of toxicity of Vitamin & Mineral Premix fortificant when used on experimental animals after intragastric administration.

Materials and methods of research. The studies were conducted in accordance with the following regulatory and methodological documentation: GOST 32644 "Testing methods for the effects of chemical products on the human body. Acute oral toxicity - a method for determining the acute toxicity class", MR

No. 012-3/0244 "Procedure and methodology of pre-registration toxicological and hygienic examination of food additives" and GOST 32641 "Test methods for the effects of chemical products on the human body. Determination of toxicity with repeated / repeated oral administration of the substance in rodents. 28-day test". Biochemical blood tests were performed on a semi-automatic biochemical analyzer "CYANSmart" with software (Cypress Diagnostics, Belgium) according to standard methods (AST, ALT, alkaline phosphotase, total protein- kits of Cypress Diagnostics reagents, Belgium), hematocrit was determined on a hematocrit centrifuge (Cypress Diagnostics, Belgium), a detailed analysis of peripheral blood was determined in Goryaev's cell.

Experimental studies were carried out on small laboratory animals (white rats and mice) in accordance with the current regulatory and methodological framework. When extrapolating the obtained toxicological data from animals to humans, interspecific differences in the toxic effect in experimental animals, the degree of toxicity and danger of the additive, the specifics of a particular experiment (methods and methods of introducing the substance into the body, seasonal and circadian rhythms, etc.), uncertainty factors were taken into account.

When assessing the irritating effect on the skin and mucous membranes of the eyes, the sensitizing effect was used by direct transfer of experimental results to humans. Experimental tests were carried out in compliance with the rules adopted by the European Convention for the Protection of Vertebrates for Experiments or Other Scientific Purposes (ETS No. 123. Strasbourg, 1986).

For the experiment, the animals received the fortifier "Vitamin & Mineral Premix" in terms of 100 g of animal weight. The dose was administered as an aqueous solution (99%), the solvent was distilled water. A statistical method of variation series analysis was used to quantify the primary experimental data. The reliability of the difference between the data of the experimental and control groups of animals was assessed according to the Student's t –criterion, guided by a 5% ($p<0.05$) significance level, taking into account the number of animals participating in each experiment in accordance with the requirements of O'ZDST 8.072:2018 for conducting experimental studies.

Results and discussion

Under experimental conditions, the acute toxicity of the studied fortificant "Vitamin & Mineral Premix" was established on 2 types of laboratory animals (white mongrel rats and mice) with a single intragastric intake of each drug name in doses of 2000, 3500 and 5000 mg/kg of animal weight (Table 1).

Table 1

Lethal effects of the studied premix in intragastric administration to laboratory animals of both sexes

Name	Dose mg/kg	number of animals in the group/ number of dead animals	Clinical picture of intoxication	LD_{50}, mg/kg
Vitamin & Mineral Premix	2000	6/0	missing	> 5000
	3500	6/0	missing	
	5000	6/0	missing	

During the next day of observation, the animals maintained a normal reaction to external stimuli, the general condition and behavior of the animals was satisfactory. All the animals were active and willingly ate food, woolly coats and visible mucous membranes did not change. Thus, the results of observations of experimental animals in acute experience make it possible to attribute the fortifier "Vitamin & Mineral Premix" to hazard class IV (GOST 12.1.007), and according to the hygienic classification to hazard class V (low-hazard substance). To study the effect on the mucous membranes, a single inoculation of 0.05 ml of an aqueous solution (50%) of Vitamin & Mineral Premix fortifier was carried out into the conjunctival sac of the right eye of a guinea pig, the left served as a control (in group 3 individuals). Under the influence of a dietary supplement, there was no hyperemia, edema or lacrimation. The average group total score of mucosal irritation severity (Iir) after termination of contact was 0 points (Table 2).

Table 2

Evaluation of the irritating effect of the studied fortificant on the mucous membranes of the eyes

Product Name	Hyperemia conjunctiva	Edema of the eyelids	ptosis or blephorospasm	discharge from the eye	Iir, points
Vitamin & Mineral Premix	0/3	0/3	0/3	0/3	0

Consequently, the obtained research data showed that Vitamin & Mineral Premix fortifier has no irritating effect on the mucous membranes of the eyes (Iir=0). The cumulative ability of the investigated fortifier "Vitamin & Mineral Premix" was evaluated in a subacute experiment by the method of "subchronic toxicity" on white rats weighing up to 120 g.

The studied fortificant "Vitamin & Mineral Premix" was received by experimental animals for 28 days in the form of an aqueous solution. The initial dose was 1/10 of the maximum tolerated in terms of animal weight (500 mg / kg), followed by an increase of 1.5 times every 4 days. Control animals received

distilled water in an equivalent volume. The experimental animals were monitored throughout the experiment according to the following indicators: survival during the experiment, general condition, animal activity, feed intake, water consumption, body weight dynamics, morphological and biochemical composition of blood. No behavioral abnormalities were observed in the animals taken in the experiment during the entire observation period. Similarly to the control animals, they were active, neat, ate food well and responded adequately to external stimuli. There were no signs of intoxication and fatal outcomes. The determination of the body weight of the animals was made before the start of administration and at the end of the introduction of the fortifier "Vitamin & Mineral Premix" (Fig. 1).

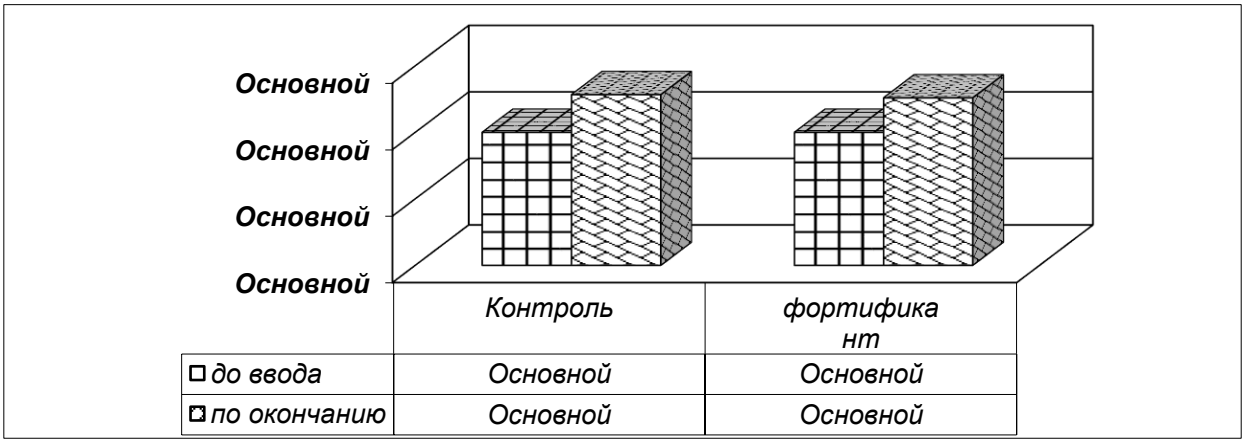

Fig. 1. Dynamics of body weight gain (%)

At the same time, there were no significant differences between the control and experimental groups.

In the study of hematological parameters of peripheral blood of experimental animals receiving the studied complex dietary supplement, no significant changes were found in any of the studied parameters (number of erythrocytes, 1012 / l; hemoglobin, g / l; leukocytes, 109 / l) (Table 3).

Table 3.

Averaged indicators of the morphological composition of rat blood under the subchronic effect of the studied fortifier

Groups	observation period	Гематологические показатели				
		hematocrit, %	hemoglobin concentration, g/l	thrombocrit, %	leukocytes, $\cdot 10^9$/л	red blood cells, $\cdot 10^{12}$/л
Control, distillation. water	before administration	35,4±1,1	132,6±4,0	0,461±0,02	14,71±2,23	6,76±1,39
	at the end	33,8±1,5	135,1±3,2	0,459±0,01	14,65±3,60	6,80±1,81
Vitamin & Mineral Premix	before administration	34,5±1,2	133,1±2,5	0,446±0,03	14,68±2,43	6,66±1,25
	at the end	35,2±1,8	135,2±4,1	0,448±0,03	14,70±2,66	6,72±1,21

The total number of erythrocytes, leukocytes, hemoglobin content, hematocrit and thrombocrit in all experimental animals did not differ statistically significantly from the control. As the results of studying the biochemical parameters of the blood serum of experimental and control animals showed, the activity of transaminase enzymes (AsT, AlT) and alkaline phosphatase (ALP) of experimental animals did not significantly differ from those of the control group. The indicators of total protein (TP) content of the control and experimental groups were also significantly the same (Table 4).

Table 4.

Biochemical blood parameters of white rats under subchronic exposure to fortificant (Mch±m)

Groups	Observation period	Biochemical parameters			
		AlT, E/l	AsT, E/l	AlT, E/l	TP,g/l
Контроль, дистил. вода	before administration	55,3±2,8	115,2±6,1	350,9±21,8	66,2±2,7
	at the end	57,2±3,5	114,9±6,2	340,9±22,3	66,1±2,3
Vitamin & Mineral Premix	before administration	54,3±3,2	113,8±6,2	330,8±21,8	64,8±2,6
	at the end	55,7±2,8	114,2±5,6	340,5±23,4	66,3±2,7

At the end of the experiment, control group rats and animals treated with Vitamin & Mineral Premix fortificant were euthanized by administering ether to anesthesia and the condition of internal organs was assessed visually during autopsy. According to the results of microscopic examination of organs, there were no differences between the experimental and control groups. The determination of the relative mass coefficients of the internal organs showed that the fortificant did not cause degenerative changes in the lymphoid and most important internal organs. Studies have shown that daily intragastric administration to rats in an increasing dose of Vitamin & Mineral Premix fortificant for 28 days does not cause lethal effects, does not lead to changes in physiological parameters, does not cause dystrophic or destructive changes in parenchymal organs and is not accompanied by irritation of mucous membranes. Thus, the conducted subchronic experiment showed that Vitamin & Mineral Premix fortifier does not have cumulative properties. When studying the sensitizing effect in experimental animals, 5 days after the subchronic experiment, sensitization was detected by setting a skin scarification test with a drop of minimal dilution of the fortifier

"Vitamin & Mineral Premix" (test - antigen), which does not cause a visible reaction in animals of the control group (50% dilution), to animals of the control

group, the permissive dose was administered in the same way as to experimental animals: a drop of the additive was applied to a section of the lateral surface of the trunk, then an incision was made with a scarifier through a drop 1-1.5 cm long. Detection of sensitization is carried out 4-24-48 hours after scarification of the studied complex additive. The skin reaction at the scarification site is taken into account according to the appropriate scale (Table 5).

Table 5.

The results of the evaluation of the sensitizing effect of the studied fortifier

Tested concentration	Hyperemia	Hyperemia and seal Blister	Blister up to 5 mm, hyperemia around	Blister up to 10 mm, lichenification	Is, ponts
Control, distil. water	0/6	0/6	0/6	0/6	0
Vitamin & Mineral Premix	0/6	0/6	0/6	0/6	0

Testing carried out after the scarification test did not reveal sensitizing properties in the Vitamin & Mineral Premix fortifier, as a result of which there was no need for a detailed allergy study (Is =0).

Conclusion. Based on the results of toxicological studies, it was found that the tested fortificant "Vitamin & Mineral Premix" in the intragastric route of admission does not have a negative effect on the health of experimental animals, according to the parameters of acute toxicity refers to low-hazard substances, does not have a cumulative, irritating effect on the mucous membranes of the eyes and sensitizing effect. Dystrophic, necrotic and inflammatory changes in animals observed in the experiment, as well as differences in the structure of their internal organs were not found. Consequently, the results obtained allow us to conclude that with repeated oral intake into the body, the fortificant "Vitamin & Mineral Premix", manufactured by AQC Chemlab Private Limited, India, meets the safety requirements according to toxicological indicators.

REFERENCES

1. Voronina N.V. Upravleniye sistemoy vyyavleniya, korrektsii vitaminnoy nedostatochnosti v organizovannykh kollektivakh, nakhodyashchikhsya na reglamentirovannom pitanii // Voyennaya meditsina. - 2017.- №4. – S.55-58. Voronina N.V. Management of the system for detecting, correcting vitamin

deficiency in organized groups on a regulated diet // Military Medicine. - 2017.- №4. - P.55-58.

2. Gerasimenko N.F. Zdorovoye pitaniye i yego rol' v obespechenii kachestva zhizni / N. F. Gerasimenko, V. M. Poznyakovskiy, N. G. Chelnakova // Tekhnologii pishchevoy i pererabatyvayushchey promyshlennosti APK – produkty zdorovogo pitaniya. – 2016. – № 4. – S. 52–57. Gerasimenko, N. F. Healthy nutrition and its role in ensuring the quality of life / N. F. Gerasimenko, V. M. Poznyakovsky, N. G. Chelnakova // Technologies of the food and processing industry of the agro-industrial complex - healthy food products. – 2016. – No. 4. – P. 52–57

3. Loktev D. B., Zonova L. N. Produkty funktsional'nogo naznacheniya i ikh rol' v pitanii cheloveka // Vyatskiy meditsinskiy vestnik. 2010. №2. S. 48-53; 3. Loktev D. B., Zonova L. N. Functional products and their role in human nutrition. Vyatskiy Medical Bulletin. 2010. №2. pp. 48-53;

4. Spirichev V. B., Trikhina V. V., Poznyakovskiy V. M. Obogashcheniye pishchevykh produktov mikronutriyentami – nadezhnyy put' optimizatsii ikh potrebleniya // Polzunovskiy vestnik. - 2012. - №2/2. - S. 9-15. Spirichev V. B., Trikhina V. V., Poznyakovsky V. M. Fortification of food products with micronutrients is a reliable way to optimize their consumption // Polzunovskiy Vestnik. - 2012. - No. 2/2. - S. 9-15.

5. Spirichev V. B., Shatnyuk L. N., Poznyakovskiy V. M. Obogashcheniye pishchevykh produktov vitaminami i mineral'nymi veshchestvami. Nauka i tekhnologiya. 2-ye izd. Novosibirsk: Sib. univ. izd-vo, 2005. - 548 s. Spirichev V. B., Shatnyuk L. N., Poznyakovsky V. M. Enrichment of food products with vitamins and minerals. Science and technology. 2nd ed. Novosibirsk: Sib. univ. publishing house, 2005. - 548 p.

6. Tvorogova T.M., Korniyenko Ye.A. Mikronutritivnyy defitsit i kishechnaya mikrobiota kak faktory, vliyayushchiye na immunnyy otvet, rol' mikrobioty i yeye metabolitov // Effektivnaya farmakoterapiya. - 2020. - T. 16. - № 10. - S. 6–11. Tvorogova T.M., Kornienko E.A. Micronutrient deficiency and intestinal microbiota as factors influencing the immune response, the role of microbiota and its metabolites // Effective Pharmacotherapy. - 2020. - T. 16. - No. 10. - S. 6–11.

7. Allen L et al., eds. Guidelines on food fortification with micronutrients. Geneva, World Health Organization and Food and Agricultural Organization of the United Nations, 2006.

Central Asian Journal of Medicine

RESULTS OF TOXICITY STUDY OF BIOLOGICAL FERTILIZER "YER MALHAMI" FOR INHALATION CHRONIC EFFECTS

Guzal F. Sherkuzieva[1], Feruza I. Salomova[2], Nargiz R. Samigova[3], Feruza U. Yuldasheva[4]

1 Ph.D., Associate Professor of the Department of Environmental Hygiene, the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: guzal.sherquzieva@gmail.com

2 M.D., Professor, Head of the Department of Environmental Hygiene, the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: fsalomova@mail.ru

3 Ph.D., Associate Professor of Communal and Occupational Hygiene, the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: nargizsam@rambler.ru

4 Assistant of the Department of Environmental Hygiene, the Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

Population growth is forcing followers to seek ways to increase food production. One such way is to increase the productivity of crops by providing them with additional sources of nitrogen bound. In recent years, Uzbekistan has made extensive use of bio-preparations in agricultural production, and new branches of the biological industry - bio-factories and bio-laboratories - have been established. Consequently, the number of workers in contact with biological pollutants that are not safe for human health is increasing. **Methods of research:** The subject of our research was biological fertilizer "Yer malhami". The study of the toxicity and nature of biofertilizer biological activity was carried out in accordance with the requirements of the guidelines "Towards the formulation of studies to substantiate the MAC of bioinsecticides of the environment", and "Guidelines for the Integrated Hygienic Assessment of New Pesticides", Guidelines for the Definition of Plant Biological Protection Agent "Yer Malhami" in the Ambient Air and Air Working Area. A chronic four-month inhalation experiment. **Conclusion:** Generalizing the results of the 4-month biofertilizer exposure of white rats, 483.3 mg/m3 toxic, 48.6 mg/m3 threshold and 9.76 mg/m3 - inactive.

Key words: nitrogen, nitrozoamines, sulfhydril groups, Student criterion, Biofertilizer, Lactic acid.

INTRODUCTION

Research Relevance: Population growth is forcing followers to seek ways to increase food production. One such way is to increase the productivity of crops by providing them with additional sources of nitrogen bound. Therefore, in the leading countries of the world large-scale mineral nitrogen production has been created (50 million. tons per year). Its application has increased world plant production by about one third. But it turned out that the global application of mineral nitrogen has many negative sides. One of the main ones is the accumulation of nitrites and nitrates in the environment, the decline in food quality and their negative impact on human health. Another method known for nitrogen input into soil is biological nitrogen fixation by various soil microorganisms. The latter is the cheapest and most environmentally friendly source of nitrogen for agriculture. There are innumerable environmental problems, but biological pollution plays a significant role among them.

In recent years, Uzbekistan has made extensive use of bio-preparations in agricultural production, and new branches of the biological industry - bio-factories and bio-laboratories - have been established. Consequently, the number of workers in contact with biological pollutants that are not safe for human health is increasing.

The increase in crop yields due primarily to the use of fertilizers is undeniable. Nitrogen fertilizers play a crucial role in this process, as they are used to introduce nitrogen into the soil, which is transformed into protein compounds by plants. Nitrogen fertilizers have a beneficial effect on plants: they improve their chemical composition, protein content, carotene. At the same time, the use of mineral fertilizers in excessively large quantities can have an adverse impact on the quality of plant food, which is expressed primarily in the accumulation of nitrates, nitrites and nitrozoamines, changes in macro- and microelement composition.

When high doses of nitrogen fertilizers are applied to the soil, especially nitrate (over 200-300), a significant amount of nitrate is cumulated in plants under adverse weather conditions. The greatest accumulation occurs in the stalks of maize, roots and bottoms of beet, green mass and hay oats, green plants of wheat, rye and in many weeds, and more in the root part. The nitrate content in the stalks is significantly higher than in the leaves. This implies that nitrate accumulation is more pronounced in those plants and parts of them that feed livestock. However, they are later converted into food of animal origin, which poses a risk to humans. The critical norm of fertilizer nitrogen for grasses, for example, is 100-120 kg/ha. At higher doses, the yield increase is negligible and the biological value of the feed is drastically reduced due to the exceedance of the critical nitrate level in dry

matter and an increase in the non-white fraction of raw protein. There are known crops that accumulate large quantities of nitrates and crops that are less prone to their accumulation. The first are, first of all, radishes, beet red, spinach, lettuce, celery, and the second - tomatoes, cucumbers, carrots, peas. The bio-products used in agricultural production are either protective against pests and diseases or fertilizers. The main positive property of biopreparations compared to chemicals is their specificity and low toxicity for humans and warm-blooded animals.

Methods of research: The subject of our research was biological fertilizer "Yer malhami". The study of the toxicity and nature of biofertilizer biological activity was carried out in accordance with the requirements of the guidelines "Towards the formulation of studies to substantiate the MAC of bioinsecticides of the environment", and "Guidelines for the Integrated Hygienic Assessment of New Pesticides", Guidelines for the Definition of Plant Biological Protection Agent "Yer Malhami" in the Ambient Air and Air Working Area. A chronic four-month inhalation experiment. Integral indicators were used as tests reflecting the general state of organs and systems in the toxicological experiment: general state, behavior of animals, dynamics of body mass. To assess the action of "Yerr malhami" on the morphological composition of peripheral blood, the content of hemoglobin, the number of erythrocytes, white cells, eosinophils was determined by conventional methods. The determination of the content of sulfhydril groups in the blood was carried out by spectrophotometric method. The results of the studies were processed according to the generally accepted method of variation statistics with the estimation of the validity of differences in empirical samples according to the Student criterion. The differences were considered valid under $P<0.05$.

Research findings: Biofertilizer is intended for pre-seedbed treatment of seeds and seedlings of vegetable, industrial crops, potatoes, roots of young fruit tree seedlings, forest crops to accelerate the growth of plants, increase the yield, improve its quality, suppress phytopathological microflora. The "Yer Malhami" has been shown to be effective in agricultural production tests. Cotton yields increased by more than 8 to 10 per cent.In order to develop the MPC "Yer malhami" in the air of the work area, studies have been conducted to substantiate the threshold of the chronic inhalation effect of the drug. Based on the results of the toxicometry of the drug for the 4-month chronic experiment, we had previously worked out the following concentrations in the treatment chambers: 483.3 3 3.07; 48.65 0.6; 9.76 0.2 mg/m3. Animals were sucked daily for 4 hours a day in 200 liters of sealed chambers. At 4-hour-a-month inhalation in experimental animals, there was no fatality or visible clinical effects of intoxication throughout the experience. Toxicity was judged on the basis of a number of integral and

biochemical indicators: body weight dynamics, the content of lactic and pyrogravic acids in the blood, LDG activity and alkaline phosphatase. The long-term inhalation of biofertilizer caused statistically visible changes by the end of the experiment in all "Yer malham" animals with a concentration of 483.35 3.07 mg/m3 in the first group. For example, the increase in animal body mass began to decline after 2 weeks of the experiment, remaining at low values until its end with a high degree of confidence (P<0.01, P<0.001). In animals of the second and third groups the increase in body mass was at the level of control values and did not go beyond physiological oscillations (Table 1).

Table 1

White rats with 4-month inhalation "Yer malhami"

Groups and concentrations in mg/m^3	statistical indicators	Terms of study in months						
		background	0,5	1	2	3	4	recovery period
I - 483,3	M±m P	134,35±1,22 >0,05	149,75±1,22 <0,01	165,65±1,35 <0,001	183,4±1,59 <0,001	201,2±1,72 <0,001	219,2±2,15 <0,001	241,6±2,94 <0,05
II - 48,6	M±m P	138,35±1,04 >0,05	156,6±1,29 >0,05	176,7±1,84 >0,05	194,75±2,15 >0,05	213,8±1,96 >0,05	230,65±2,15 >0,05	252,85±2,21 >0,05
III - 9,8	M±m P	134,5±1,10 >0,05	153,5±1,04 >0,05	172,75±1,10 >0,05	190,95±1,35 >0,05	212,25±1,53 >0,05	234,2±1,84 >0,05	258,75±6,70 >0,05
Control	M±m	137,1±1,10	156,4±1,35	176,15±1,41	196,05±1,84	217,26±1,96	238,75±2,15	251,85±2,21

Long-term inhalation of "Yer malhami" at a concentration of 483.3 mg/m^3 resulted in a persistent breakdown of carbohydrate exchange in experimental animals. The levels of lactic and pyro-vitic acids were 44.1 and 2.33 mg (P<0.001) as shown in Figure 1 and Table 2.

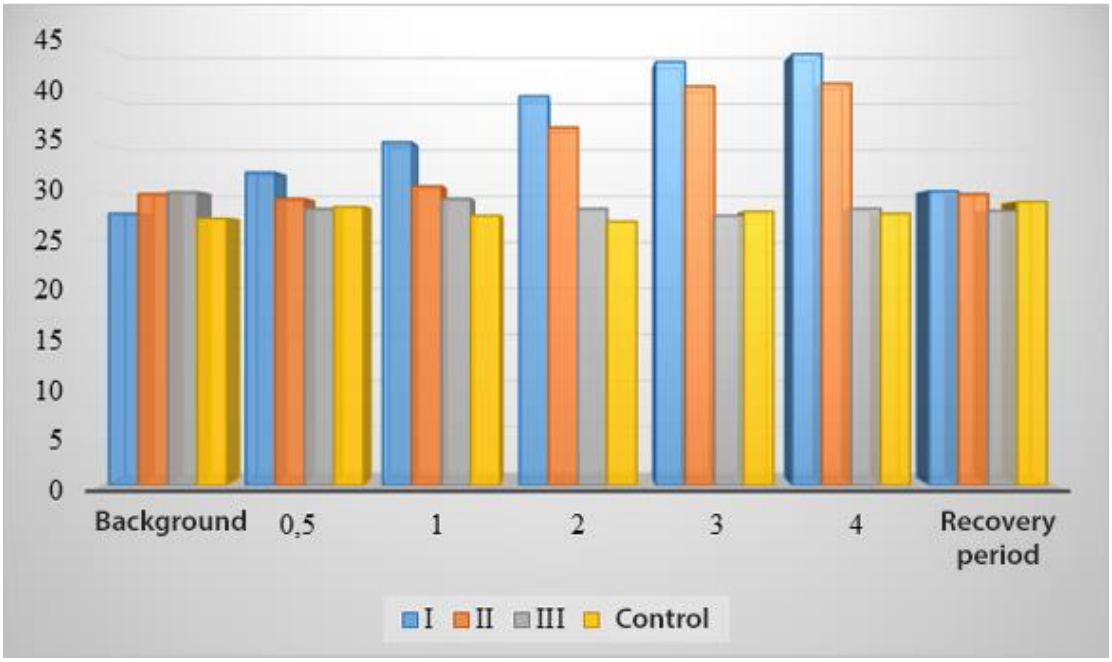

Figure 1. Lactic acid content in experimental animals at inhalation "Yer malhami"

Table 2

Pyro acid content in experimental animals Inhalation of "Yer Malhami" (mg/%)

Groups and concentrations in mg/m^3	statistical indicators	Terms of study in months						
		Background	0,5	1	2	3	4	recovery period
I - 483,3	M±m P	2,28±0,088 >0,05	2,45±0,14 >0,05	2,64±0,17 >0,05	2,82±0,21 <0,05	3,15±0,26 <0,01	4,05±0,28 <0,001	2,5±0,088 >0,05
II - 48,6	M±m P	2,2±0,10 >0,05	2,36±0,10 >0,05	2,55±0,12 >0,05	2,99±0,14 <0,01	3,11±0,21 <0,01	3,5±0,24 <0,001	2,29±0,11 >0,05
III - 9,8	M±m P	2,3±0,11 >0,05	2,19±0,13 >0,05	2,2±0,12 >0,05	2,35±0,12 >0,05	2,3± 0,11 >0,05	2,33± 0,15 >0,05	2,31± 0,12 >0,05
Control	M±m	2,33±0,12	2,25±0,14	2,33±0,12	2,26±0,12	2,21±0,12	2,33±0,12	2,31±0,10

In animals receiving "Yer malhami" at a concentration of 48.6 mg/m3, carbohydrate metabolites of pyruvate and lactate also accumulated in the blood, but since the third month of the experiment and the level of indicators was lower. The drug concentration of 9.8 mg/m3 did not affect the above tests. The enzyme activity of lactate dehydrogenase in the first group of white rats increased towards the end of the second month and remained high until the end of the experiment. In animals of the second group, the activity of lactate dehydrogenase was increased, but the values of the indicator were lower (fig. 2).

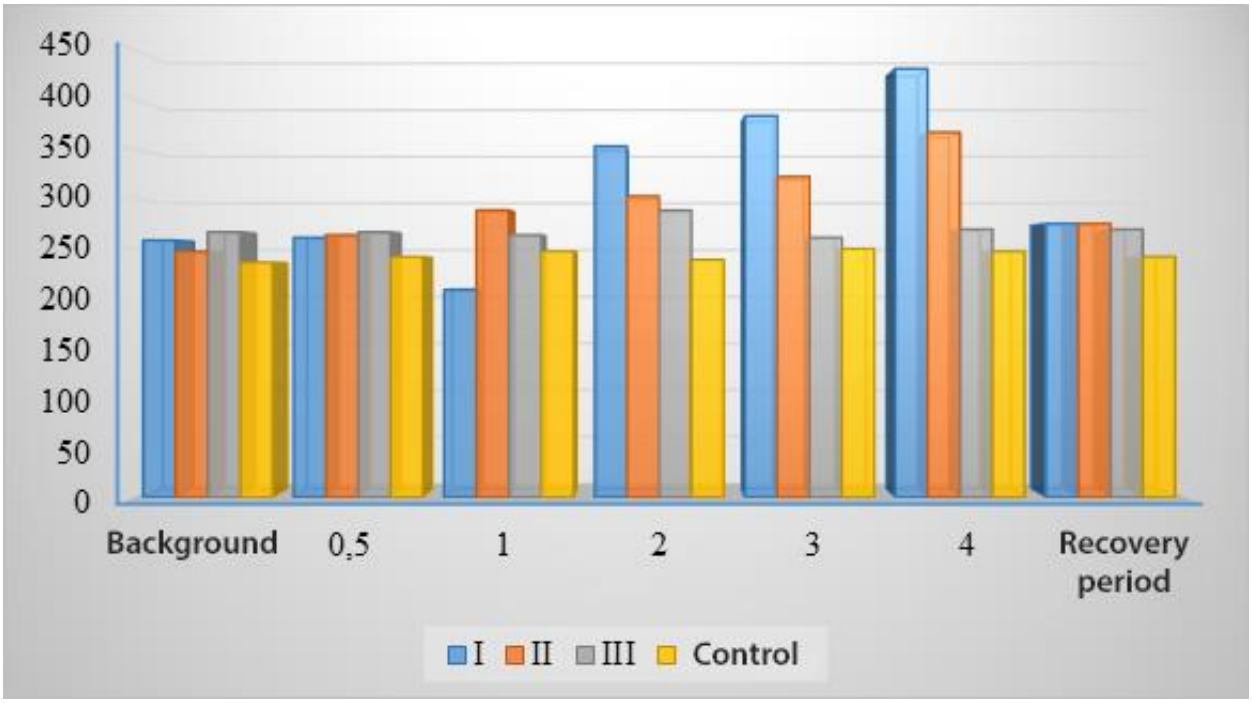

Figure 2. Activity of lactate dehydrogenase in experimental animals at inhalation "Yer malhami"

The functional state of the liver was assessed by the state of alkaline phosphatase enzyme activity. Activation of alkaline phosphatase enzyme activity in animals of the second group that received the drug in concentration. 48.6 mg/m^3, alkaline phosphatase activity was 2.74 mmol/l to the 4th month of the experience, with a target value of 0.9 mmol/l. In the third group of white rats, the level of alkaline phosphatase did not differ from the control values. Changes in the internal organs were detected by histomorphological studies in animals of the 1st and 2nd groups, noted: in the lungs, in the course of small vessels and bronchial oedema dystelectase, interstitial pneumonia. In the liver, grainy dystrophy of hepatocytes, cyclonic infiltrates along the triads and in the center of the lobes. In the brain, perivascular edema. In the kidneys - edema capsules Shumlyansky, granular dystrophy of the epithelium of twisted canals, venous full blood. In the spleen, follicle atrophy, macrophage reaction is expressed. In the heart, intercostal edema, intertrabecular thrombi, cardiocyte fragmentation.

Conclusion: Generalizing the results of the 4-month biofertilizer exposure of white rats, 483.3 mg/m^3 toxic, 48.6 mg/m^3 threshold and 9.76 mg/m3 - inactive.

REFERENCES

1. MUC 4263-87. Methodical instructions for hygienic evaluation of new pesticides: utv. USSR Ministry of Health 13.03.87 g. - Kiev, 1988. - p. 5.

2. Guidelines for the definition of plant biological protection agent "Yer malhami" in the ambient air and the air of the work area. - Tashkent, 1995. - 10 p.

3. Guidelines for conducting studies to support MAC of bioinsecticides in the environment.

4. Sherkuzieva G.F., Hegay L.N., Samigova N.R. Toxicity and danger of the food mixture "MELLA CROISSANT" // XIX International Scientific and Practical Conference: Modern World: Nature and Man: to the 175th anniversary of I.I.I. Mechnikov. Kemerovo, 2020. - C. 275-281.

5. Sherkuzieva G.F., Salomova F.I., Samigova N.R., Hegay L.N. Results of studies of acute and chronic toxicity of food additive " Fass hungel " // Collection of materials of the republican scientific and practical conference with international participation. - Minsk, 2022. - P. 442-447.

Central Asian Journal of Medicine

VENOUS THROMBOSIS

Akmal A. Irnazarov[1], Vali R. Khasanov [2], Ilhom R. Beknazarov[3], Rustambek A. Karimov[4], Dinara Kh. Irnazarova[5]

1 Doctor of Medicine, professor of the Faculty and Hospital Surgery Department No.1, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: akmal.irnazarov1980@gmail.com

2 PhD, Specialist of the Endovascular Surgical Department, Multidisciplinary Clinic of Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: vali180978@gmail.com

3 Assistant lecturer of the Faculty and Hospital Surgery Department No.1, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: beknazarov.ilhomjon@gmail.com

4 Assistant lecturer of the Faculty and Hospital Surgery Department No.1, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: doc.karim0ff@gmail.com

5 Assistant lecturer of the Department of Obstetrics and Gynecology in Family Medicine, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: akmal.irnazarov1980@gmail.com

ABSTRACT

This paper describes the distribution and complications of venous thrombosis of deep veins of the lower extremities. It is emphasized that the main method of treatment for this pathology is surgical, namely endovascular. Endovascular treatment methods significantly reduce the risk of pulmonary embolism and the development of post-thrombophlebitic syndrome.

Key words: Deep vein thrombosis of lower extremities, pulmonary embolism, thrombolysis, thrombectomy.

INTRODUCTION

Epidemiology of deep vein thrombosis of the lower extremities.

Today, deep vein thrombosis (DVT) of the lower extremities is an urgent problem of modern medicine. The clinical picture, due to the fact that it is common

for DVT and pulmonary embolism (PE), is often “silent” and, therefore, is not diagnosed in time or is detected only at autopsy. Therefore, the incidence and prevalence of this disease are often underestimated.

The annual incidence of venous thromboembolism (VTE) is 0.1-0.27%, affecting up to 5% of the population during their lifetime. The risk of recurrent thromboembolism is higher in men than in women. It is believed that the annual incidence of DVT of the lower extremities is 80 cases per 100,000. About 900,000 cases of DVT are registered annually in the United States. Between 5% and 15% of patients with untreated DVT die from a pulmonary embolism. Venous thromboembolism occurs in almost every 2 cases per 1000 pregnancies and is the leading cause of maternal and morbidity mortality [23,25,30].

In Europe, the incidence of DVT of the lower extremities is detected in 4.8-9.6 people per 10,000 populations every year [24,28].

According to epidemiological data, VTE is characterized by a high recurrence rate: even in patients on anticoagulant therapy, the frequency of early recurrent episodes reaches 2% after 2 weeks from the manifestation of the first event, 6.4% - by 3 months, 8% - by 6 months and up to 25% - within 5 years. At the same time, the frequency of VTE relapses does not depend on the picture of the clinical manifestation of the first episode [29,37].

A third of patients with venous thrombosis develop PE. In the first month, mortality reaches up to 6% for DVT and 10% for PE, although autopsy studies show that the already high mortality rates are probably underestimated. Autopsy results have shown a mortality rate as high as 30% based on the observation that many PEs are not diagnosed at the time of death [9,11].

According to the results of the multicenter study ICOPER (Cooperative Pulmonary Embolism Registry) [26], the mortality of patients three months after the treatment was 17.4% [32].

S.A. Sushkov [20] in his study revealed the likelihood of PE in patients with floating thrombosis. In this case, the thrombus has one attachment point in the distal part, and in the proximal part - the area of the thrombus, the so-called embolus, sways freely in the bloodstream. To date, despite numerous developments in the search for a pathogenetic method for treating these complications, the issue of finding unified algorithms for the perioperative management of patients with embolism -prone DVT is also acute and is under active search by scientists [3,8].

Causes of acute venous thrombosis

The development of DVT of the lower limb depends on many factors, these include:

1) Age over 40 years.

2) Obesity.

3) Hospitalization in a hospital for the purpose of an operation or in case of a sudden exacerbation of a chronic disease.

4) Trauma and fractures of the lower extremities.

5) Pregnancy and postpartum period.

6) Bed rest (more than 3 days).

7) Air travel.

8) The use of oral contraceptives and hormone therapy.

9) Varicose veins of the lower extremities.

10) Oncological diseases.

11) Chronic heart failure.

12) Severe lung disease.

13) Postponed ischemic stroke.

14) Acute and chronic infections, sepsis.

15) Venous thrombosis in history or in close relatives in the direct line of kinship [1,13].

The development of deep vein thrombosis in relatively young people in the absence of obvious prerequisites may be the result of genetically determined disorders of hemostasis [18]. The combination of several risk factors leads to a significant increase in the risk of thrombosis.

Back in 1865, R. Virchow described a combination of pathological factors that are the main trigger for intravascular thrombus formation and are known as the triad Virchow. It includes changes in the properties of blood, injury to the vessel wall and slowing down the blood flow.

Thrombophilia. An important point in the development of DVT belongs to the phenomenon of thrombophilia [10,16]. At the XV International Congress on Thrombosis and Hemostasis (Jerusalem, 1995) and at the XIII meeting of the European and African Sections of the International Society of Hematology (Istanbul, 1996), the terms “thromboembolic syndrome” and “hypercoagulemia” were combined into a single concept of “thrombophilia”. This term currently means disorders of hemostasis and hemorheology, characterized by an increased tendency to develop thrombosis of blood vessels, which are based on acquired and genetically determined disorders in various parts of hemostasis and hemorheology [5,39]. The role of hereditary thrombophilia in the genesis of DVT has been actively investigated since 1993, when the Dutch scientist B. Dahlback discovered resistance of factor V of the blood coagulation system to the inactivating effect of active protein C in members of a Swedish family [36].

Clinical diagnosis of deep thrombosis veins of the lower extremities.

In the scientific literature, when DVT is suspected, an external examination with a detailed history of the disease, taking into account intrafamilial morbidity and assessing risk factors is recommended. Attention should be paid to complaints of patients, such as: swelling in the lower leg or the entire lower limb; pain in static and in the calf muscle in motion; a combination of pain with asymmetric edema, which serve as predictors of the development of DVT.

May-Thurner syndrome is characterized by compression of the left common iliac vein, overlying the right common iliac artery. Vibratory pulsation is believed to cause hyperplasia in response, in a compressed segment of the vein, followed by progressive stenosis. Due to the slow and chronic nature of this process, the stenosis becomes hemodynamically significant, the collateral veins to the contralateral iliac veins and the inferior vena cava enlarge over time. When blood flow in a vein slows down, spontaneous thrombosis can occur, especially if the patient has a risk factor for developing DVT such as increased blood clotting.

The literature emphasizes that each symptom alone provides an 11-22% chance of DVT [2,23]. However, cases of DVT without pronounced signs of the disease, that is, without characteristic symptoms, are not uncommon, especially in bedridden patients. Considering that PE is a possible sign of the development of DVT, experts recommend an analysis of the level of D-dimer in the blood as a diagnosis and/or exclusion of DVT [38]. The sensitivity index of a specific blood test for D-dimer is 96-100% [22,33].

Ultrasound imaging of the veins is the most important diagnostic test for lower extremity DVT. Duplex ultrasound imaging has a mean sensitivity and specificity of 97% and 94%, respectively, with mean positive and negative predictive values of 97% and 98% for symptomatic proximal DVT [12,15].

Contrast-enhanced venography also does not show pelvic veins due to contrast dilution in deep pelvic veins. Pelvic vein thrombosis has been reported in the literature, diagnosed in 1-4% of studies using venography or ultrasound imaging. The authors convincingly show that the use of these diagnostic methods underestimates the true prevalence of isolated pelvic vein thrombosis.

Unlike ultrasound imaging or enhanced venography, ***CT venography*** (CTV) and magnetic resonance venography better reflect the picture of blood flow in the inferior vena cava and pelvic veins, which has been proven by various large studies [34,42]. CT can be performed by direct injection of contrast into the femoral or cubital vein. CT can be recommended as a standard for diagnosing PE [34].

Treatment of venous thrombosis

The treatment of patients in this category is aimed at solving the problems formulated back in 1998 by S. Haas from the Institute of Experimental Surgery. The essence of the solution is:

1) prevent the development of PE;

2) limit thrombotic damage and prevent its transition to venous lines of a larger caliber;

3) restore venous blood flow;

4) to carry out the prevention of retrombosis.

An important component of the therapy of patients with venous thrombosis of the lower extremities is the complexity, and the standards of treatment should be optimal for a particular patient, since DVT of the lower extremities in the absence of optimal therapy in 10-20% has a threat in the development of clinically manifesting PE. The basis of therapy is the use of indirect and direct anticoagulants. The effectiveness of anticoagulants reaches 70-80% [27].

The mechanism of action of unfractionated heparin (UFH) and low molecular weight heparin (LMWH) drugs on blood coagulation factors is similar, but there are differences in the pharmacodynamic properties, bioavailability and pharmacokinetics of the drugs. LMWHs have predominantly anti-Xa activity and inhibit thrombin directly to a lesser extent. LMWHs have a long half-life, in connection with which the frequency of their appointment is reduced to once a day [6,31].

In modern practice, clinicians tend to use direct oral anticoagulants. Warfarin is the most commonly prescribed oral anticoagulant for the treatment and secondary prevention of venous thromboembolism, is a vitamin K antagonist. The anticoagulant effect develops due to the ability of drugs to reduce the formation of vitamin K-dependent coagulation factors. But the range of their therapeutic effects is narrow, when used, increased monitoring of the degree of coagulation is required, and there is a negative interdrug effect [21].

Rivaroxaban is another oral reversible direct acting factor X inhibitor with a rapid onset of action and dose - proportional pharmacokinetics and pharmacodynamics. The drug is fast-acting with high oral absorption [7]. The course of treatment with Rivaroxaban for PE and DVT is carried out according to the standard scheme: 15 mg 2 times a day for 3 weeks, then 20 mg 1 time per day for a period set individually. This treatment protocol eliminates the need for continuous monitoring of laboratory parameters, as well as the selection and adjustment of the dose of the drug depending on the age and weight categories of the patient.

Thrombolytic therapy (TLT) is a type of pharmacological therapy aimed at restoring blood flow in a vessel due to the lysis of a thrombus within the vascular bed. In 1938, the isolation of the enzyme streptokinase by β-hemolytic streptococcus group A was proven. In 1940, the mechanism of action of the enzyme was described, based on its binding to plasminogen in the blood, leading to its conversion into its active form - plasmin.

Thrombolytics with the conversion of the inactive protein plasminogen into the active proteolytic enzyme plasmin. Plasmin, in turn, provides fibrin lysis. Thrombolytics (fibrinolytics) are drugs whose action is aimed at the destruction of blood clots. Unlike antiplatelet agents and anticoagulants, which lower blood viscosity and prevent blood clots, thrombolytics are able to dissolve already formed blood clots. Therefore, antiplatelet agents and anticoagulants are the prevention of blood clots, and thrombolytics are their treatment.

Currently, there are five generations of thrombolytic drugs:

The first generation is the enzymes that are found in nature. They change blood plasmin and favor the acceleration of the synthesis of plasminogen into plasmin. The fibrinogen activators of the first generation are fibrinolysin, streptokinase, urokinase, which paved the way for the use of these enzymes as thrombolytic agents to destroy the fibrin network with the problem of systemic bleeding. Fibrinolysin is the most abundant plasma protein. Its effectiveness is characterized by early application. Streptokinase is a single-chain polypeptide that exhibits an indirect fibrinolytic effect by activating the circulating zymogen plasminogen, is a microbial plasminogen activator secreted by several strains of β-hemolytic Streptococci, can cause anaphylactic reactions, so repeated administration is often impossible [14].

Fibrin -specific agents are ***second-generation drugs*** that have been artificially produced using selective and genetic engineering. Acting directly on blood clots. The almost absence of shortcomings makes these funds the most popular at the present time. Second-generation plasminogen activators have a targeted thrombolysis, as first generation plasminogen activators showed non-specific degradation of fibrin and caused systemic fibrinolysis with concomitant destruction of hemostatic proteins resulting in bleeding. Alteplase has such advantages as increased stability in plasma, increased half-life (90-105 minutes), improved fibrin binding and reduced administration time from 60 to 2 minutes, affects thrombus formation without affecting hemostasis, does not cause bleeding. Prourokinase - designed as a fibrinolytic agent, can mediate specific clot lysis in the presence of fibrin, leading to better patency without any significant increase in bleeding.

Improved recombinant activators - ***third generation*** thrombolytic drugs. The advantage of these drugs: a relatively long-term effect, as well as an improvement in the ability to find a blood clot. Third generation plasminogen activators have been developed to improve structural and functional properties such as longer half-life, resistance to inhibitors, safety and increased efficacy, and increased fibrin specificity. Their long clearance makes it easy to administer one or two doses of the drug up to 3 hours after the formation of a blood clot. Later administration of the drug is fraught with a violation of the degree of vascular patency with the impossibility of their restoration and preservation of the valvular apparatus. Reteplase - is characterized by complete, rapid and stable thrombolysis and long-term effect, it is mostly used in hemorrhagic stroke. Tenecteplase - used as a method of thrombolysis in myocardial infarction, it has increased pharmacological properties and a stable effect without significant bleeding.

The fourth generation of drugs has not been studied enough. Compared to previous generations, these means of combined action. The difference is a quick and intense effect on the thrombus.

The fifth generation is a combination of natural and recombinant active substances.

The most popular and widely used as thrombolytic therapy are drugs of the 2nd generation. The decisive arguments in their use are numerous studies, minimal side effects, and most importantly, the release by the pharmaceutical industry on an industrial scale.

In many clinical guidelines for the treatment of DVT, the active tactics of surgical and catheter methods of treatment in selected patients with the level of evidence are classified as class 2.

Regional catheter thrombolytic therapy allows to achieve a high concentration of the drug in the thrombus, use the introduction of small doses of fibrinolytics, which contributes to a significant reduction in hemorrhagic complications, treatment time. Any proposed regimen for the treatment of DVT aims for the fastest and most complete thrombolytic effect in the venous system, but in practice, as a rule, partial recanalization is detected rather than complete restoration of vein patency.

Surgical methods are aimed at restoring vein patency and thrombo -reduction, they can be performed both by traditional and rapidly developing endovascular methods. catheter technologies [38].

Currently, the main surgical methods include: application of NVC; thrombectomy; ligation of the femoral vein, which is due to many reasons [19].

Promising is the widespread introduction of the so-called hybrid technology, the essence of which is thrombectomy from the iliac-femoral segment, with stenting of the iliac vein with the imposition of a temporary arteriovenous fistula [4].

Meanwhile, surgical (direct) thrombectomy can be performed only through a wide laparotomic approach; it is technically complex, accompanied by significant surgical trauma, blood loss, and the risk of intraoperative thromboembolism. Prospects for effective treatment of this category of patients were opened by endovascular catheter thrombectomy after the installation of temporary cava filters [17,35].

Indications for endovascular treatment are: <14 days old lower extremity DVT, without severe comorbidities and phlegmasia.

Endovascular thrombectomy can be divided into two groups, depending on how the thrombus is removed - in its entirety or by aspiration of thrombotic masses after their disobstruction. And the use of modern devices for thrombectomy, rheolytic systems thrombectomy Angiojet, systems with ultrasound support, rotary aspiration devices show encouraging results and significantly reduce the time of the procedure [15].

There is a controversy in clinician circles about the search for an effective thrombolytic, the duration of its administration. There is also no consensus on the use of a temporary cavafilter during catheter-guided thrombolysis (Haig Y. et al., 2016). Some authors, when using it, show low invasiveness and safety of the installation, achieving positive results in terms of reducing complications (Gurman P. et al., 2015). In contrast, the data of other authors indicate that its use is ineffective; moreover, the risk of thromboembolic complications does not decrease with this method [42].

In the work of K. Ksirajan et al. in 17 patients on the Angiojet device thrombus lysis was achieved (>50%) in 59% of cases. R.L. Bush et al. (2018), presented complete and partial thrombus resolution in 65% and 35% of cases. Martinez Trabal. et al. achieved a positive result in 92% of the veins of the lower extremities. When comparing the results of fibrinolytic therapy in the hospital period of complex treatment according to the randomized clinical trial “ATTRACT” (2017), the picture is as follows: significant bleeding was in 1.7%. According to some authors, such as: N. Meneveau (1998), the maximum applied dose of streptokinase was 1.45 ml units. in 25 patients - 12%, S. Patra (2014) in 105 patients, the maximum dose of streptokinase was 2.65-5.05 ml units, bleeding was observed in 1.9% [40].

Thus, DVT and PE are the leading causes of morbidity and mortality worldwide, which are in the field of view of modern clinical medicine. The relevance and significance of this problem is expressed in the constant growth, the presence of thrombotic complications, in the "silent" course, which makes early diagnosis difficult. The available treatment and prevention protocols do not always lead to effective results, which requires further scientific research in this direction.

REFERENCES

1. Belova A.D. Evaluation of the effectiveness of outpatient and inpatient treatment of patients with thrombosis of the veins of the lower extremities. Ambulatory surgery: hospital -replacing technologies. - 2011. - No. 3/4. - S. 17-18.
2. Bokeria L.A., Zatevakhin I.I., Kirienko A.I. Russian clinical guidelines for the diagnosis, treatment and prevention of venous thromboembolic complications // Phlebology. - 2015. -T. 9, No. 4. - 42 p.
3. Borovsky S.P. Venous thromboembolic complications in patients with oncological pathology. View of the X-ray surgeon // Slavic venous forum: Mater. Intern. Congress (Vitebsk, May 28-29, 2015). - Vitebsk: VSMU, 2015. - P.94-95.
4. Ignatiev I.M., Akchurin F.R., Zanochkin A.V., Volodyukhin M.Yu., Bredikhin R.A., Khairullin R.N. Experience in the treatment of floating thrombosis in the system of the inferior vena cava // Journal named after Academician Petrovsky B.V. - 2015. - No. 3. - P.36-44.
5. Kirienko A.I., Panchenko E.P., Andriyashkin V.V. Venous thrombosis in the practice of a therapist and surgeon. - M.: Planida, 2012. -336 p.
6. Krivoshchekov E.P. Rivaroxaban in the treatment of acute vein thrombosis of the lower extremities // Slavic Venous Forum: Mater. Intern. Congress (Vitebsk, May 28-29, 2015). - Vitebsk: VSMU, 2015. - P.117-118.
7. Kurginyan Kh.M. Clinical cases of the effective use of rivaroxaban as a treatment for thrombotic complications in patients with oncological and systemic diseases.
8. Lobastov K.V., Barinov V.E., Schastlivtsev I.V., Laberko L.A. The Caprini scale as a tool for individual risk stratification of postoperative venous thromboembolism in a high-risk group. Khirurgiya. Journal them. N.I. Pirogov. - 2014. - No. 12. - P. 16-23.
9. Medvedev A.P., Nemirova S.V., Pichugin V.V., Shirokova O.R., Sobolev Yu.A. Open embolectomy in the treatment of massive pulmonary thromboembolism // Medical Almanac. - 2013. - No. 4 (28) - P. 35-37.

10. Momot A.P., Grigoryeva E.V., Panov M.Yu. et al. Predictors of venous thrombosis in medical thromboprophylaxis in orthopedics // Medicine and education in Siberia. - 2012. - No. 2. - From 45-50.

11. Muminov Sh.M., Akhmedov R.A., Kim D.L., Abdullaev Sh.M., Dadamyants N.G. Modern approaches in the diagnosis and treatment of thrombosis of the inferior vena cava system // Slavic Venous Forum. Mater. Intern. Congress. - Vitebsk, 2015. - S. 129.

12. Muminov Sh.M., Dadamyants N.G., Kim D.L. Database of color duplex scanning of patients with thrombosis of the veins of the lower extremities and pelvis // Certificate No. DG U 00322 on the official registration of the computer program dated 01/05/2016.

13. Muminov Sh.M., Khamidov B.P. et al. Immediate and long-term results of the treatment of thrombosis of the veins of the lower extremities and pelvis // Bulletin of Emergency Medicine. - 2018. - V.11, No. 2. - P.12-18.

14. Onuchin P.G., Nagovitsyn S.V., Motovilov M.A. thrombolysis urokinase and new oral anticoagulants in the treatment of patients with acute venous thrombosis. // Angiology and vascular surgery - 2015.- V.21, No. 2.- P.452-453.

15. Osiev A.G., Vishnyakova M.V., Gegenava B.B. Endovascular methods of treatment of pathology of the venous system // Almanac of Clinical Medicine. - 2015. - No. 43. - From 82-89.

16. Petrikov A.S., Shoikhet Ya.N., Belykh V.I., Kostyuchenko G.I. and others. Hyperhomocysteinemia and venous thromboembolic complications // Phlebology. - 2012. - No. 1. -S. 14–18.

17. Prozorov S.A. Complications observed during the implantation of cava filters and at different times after it. Indications for removal of kava filters. (literature review) // X-ray surgical methods of diagnosis and treatment. - 2016. - No. 45. – C.38-44.

18. Sadikova Sh.E., Muminov Sh.M., Abdullaev Sh.M., Shamsutdinova D.B. Molecular analysis of polymorphisms of the M T HFR, FV and FII genes in patients with deep vein thrombosis of the lower extremity // Bulletin of Hematology. - St. Petersburg, 2013. - V.9, No. 2. – From 45-51

19. Soroka V.V., Andreichuk K.A. Clinical recommendations (protocol) for the provision of emergency medical care for acute venous thrombosis. - M., 2014. - C. 10-11.

20. Sushkov S.A. et al. A differentiated approach to the treatment of patients with floating deep vein thrombosis of the lower extremities // Kharkov School of Surgery. - 2016. - No. 1 (76). - P.7-14.

21. Khruslov M.V. Efficiency of the system of centralized monitoring of INR in patients taking warfarin for venous thrombosis // Phlebology. - 2013. - No. 4. - P. 52-56.

22. Shulgina L.E. etc. Ultrasonic angioscanning and the level of D - dimer in the diagnosis of deep vein thrombosis in patients with central paresis and paralysis // Phlebology.- 2014. - V.8, No. 2.- P.104.

23. Beckman MG, Hooper WC, Critchley SE et al. Venous thromboembolism. A public health concern // Am. J. Prevent. Med. - 2010. - Vol. 38, Suppl. 4. – P.495–501.

24. Cuker A., Arepally GM, Chong BH, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: heparin-induced thrombocytopenia // Blood Adv. - 2018. - Vol.2, No. 22. - R.3360 - 3392.

25. Fowkes FGR Epidemiology of venous disorders. Venous and lymphatic diseases. - Elsevier, 2007. - P. 15-25.

26. Goldhaber S. Z., Visani L ., De Rosa M . Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER) // Lancet. - 1999. - Vol. 353, No. 9162. - R. _ 1386-1389.

27. Haas S. Management of venous thromboembolism // Hamostaseologie. - 1998. - Vol. 18. - P. 18-26.

28. Heit JA Predicting the risk of venous thromboembolism recurrence // Am. J. Hematol. - 2012. - Vol.87, Suppl 1. - R.63–67.

29. ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to global disease burden // Thromb. Res. - 2014. - Vol. 134. - P. 931-938.

30. John A., Heit1 Frederick A., Spencer Richard H. The epidemiology of venous thromboembolism // J. Thromb. Thrombolysis. - 2016. - No. 41. - R.3-14.

31. Junqueira DR, Zorzela LM, Perini E. Unfractionated heparin versus low molecular weight heparins for avoiding heparin-induced thrombocytopenia in postoperative patients // Cochrane Database Syst Rev. - 2017. - N4. – CD 007557.

32. Kasper W., Konstantinides S., Geibel A., Olschewski M. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry // J. Am. Coll. Cardiol. - 997. - Vol. 30, no. 5. - R.1165-71.

33. Kelly J., Hunt BJ Role of D-dimers in diagnosis of venous thromboembolism // Lancet. - 2002. - N 359. - P.456-8.

34. Montgomery KD, Potter HG, Helfet D L. Magnetic resonance venography to evaluate the deep venous system of the pelvis in patients who have an acetabular fracture // J. Bone Joint Surg. Am. - 1995. - N77. –P.1639-49.

35. Othieno R., Okpo E., Forster R. Home versus in-patient treatment for deep vein thrombosis // Cochrane Database Syst Rev. - 2018. - No. 1. - CD003076.

36. Price DT, Ridker PM Factor V Leiden mutation increases risk for thromboembolism // Ann. Intern. Med. - 1997. - Vol. 127. - P. 895-903.

37. Schulman S., Lindmarker P., Holmstroom M. et al. Post-thrombotic syndrome, recurrence, and death 10 years after the fist episode of venous thromboembolism treated with warfarin for 6 weeks or 6 months // J. Thromb. haemost. - 2006. - Vol.3. – P.734-742.

38. Schutgens RE, Ackermark P., Haas FJ, Nieuwenhuis HK, Peltenburg HG, Pijlman AH et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis // Circulation. - 2010. - Vol.107. – P.593-7.

39. Shaheen K., Ageno W., Bozzato S. et al. Role of factor V Leiden or G20210Aprothrombinmutation in patients with symptomatic pulmonary embolism and deep vein thrombosis: a meta-analysis of the literature // J. Thromb.Haemost. - 2012. - Vol. 10(4). - P. 732-737.

40. Sharifi M., Freeman W., Bay C. et al. Low incidence of post-thrombotic syndrome in patients treated with new oral anticoagulants and percutaneous endovenous intervention for lower extremity deep venous thrombosis // Vasc. Med. - 2015. - Vol. 20, No. 2. - P. 112–116.

41. Vedantham S., Goldhaber SZ, Julian JA, Kahn SR, Jaff MR, Cohen DJ at al. Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis // The new england journal of medicine. - 2018. -N27. – P.2240-2252.

42. Witt DM, Nieuwlaat R., Clark NP et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: optimal management of anticoagulation therapy // Blood Adv. - 2018. - Vol.2, No.22. - P.3257 - 3291.

Central Asian Journal of Medicine

SPECIFIC ASPECTS OF DISEASES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND HUMAN IMMUNODEFICIENCY VIRUS CONCOMITANT

Barno Kh. Shagazatova[1], Feruza S. Mirkhaydarova[2]

1 DSc, Professor of the Department of №2 Internal medicine and Endocrinology, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: bshagazatova@gmail.com

2 Assistant of the Department of №2 Internal medicine and Endocrinology. Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: mirkhaydarova.f@gmail.com

ABSTRACT

In recent years, Type 2 diabetes has been growing rapidly in pictures and spreading rapidly among the younger class of the population. This is manifested by an increase in the number of cases of infection with HIV (human immunodeficiency virus), among other diseases. One of the characteristic features in the concomitant meeting of HIV infection and diabetes mellitus is associated with a sharp decompensation of glycemic indicators in patients and a strong influence on this by the Roxy-emotional state.

Key words: diabetes mellitus, HIV infection, glycemia.

INTRODUCTION

In this article we will tell you how to do it. Due to the fact that there are currently a number of measures related to environmental protection, including in the field of health and social protection of the population, as well as in the field of health, as well as in the field of health, including in the field of health, in the field of health, health, health, health care, health care and social protection of the population, as well as in the field of health care, as well as in the field of health care, health care, health care and social protection of the population, as well as in another way. In this article we will tell you how to do it. Due to the fact that there are currently a number of measures related to environmental protection, including in the field of health and social protection of the population, as well as in the field

of health, as well as in the field of health, including in the field of health, in the field of health, health, health, health care, health care and social protection of the population, as well as in the field of health care, as well as in the field of health care, health care, health care and social protection of the population, as well as in another way.

The diabetes is one of the most common diseases in the world. In many countries around the world, diabetes of sugar is an urgent medical and social problem. The urgency of diabetes is characterized by rapid growth and high divoral between all endocrinous diseases [11.23-14b]. According to IDF diabetes satin, 424.9 million diabetes in the world have been registered and by 2045, this figure is expected to reach 628.6 million.

Additional ARTOs, including the main risk factors, are more cholesterol and high blood pressure, which is 15% of diabetes in patients with HIV, including excess cholesterol and high blood pressure. The use of antioges and proteaza inhibitors further enhances the risk of low levels of lipodi history, stable inflammatory suitable for HIV (Liliya Ten, Plos One, 2021). Professor Lorens Slama and colleagues in Paris were studied by HIV in a period of 1094 patients with HIV, 156 of which were diabetes. 75% of diabetes were men. The participants' average ART duration was 12 years. 38% of patients with examinations were not developed, and 116 of those diagnosed also did not receive the optimal necessary treatment (http // Life4ME.Plus). We, too, we have studied the specifics of the interaction and clinical diseases in patients with diseases in the medical and suitable diabetes in our research.

Objective: HIV infection, in diabetics and patients with HIV, assessment of carbohydrate and lipid metabolism indicators.

Materials and methods of research: HIV infection and patients with suitable type of diabetes were divided into groups of 2 during the primary development of the diabetes. The 1st group is a group of patients with HIV, and the average age of 42.3 ± 1.35, which is 42.3 ± 1.35. Of these, 26 are women and 12 are men. Of these, 28 patients receive the Art, and 10 patients do not accept Art. There are 13 groups of 2 groups of patients, 9 are women and 4 are men. Their average age is 45.6 ± 1.86 years. All patients receive an Art (ART duration 6.5 ± 0.61); Duration of QD 8.4 ± 0.72; HIV duration is 6.7 ± 0.53.

Results. Below are the results of HIV infection sites in groups of 2 in the group:

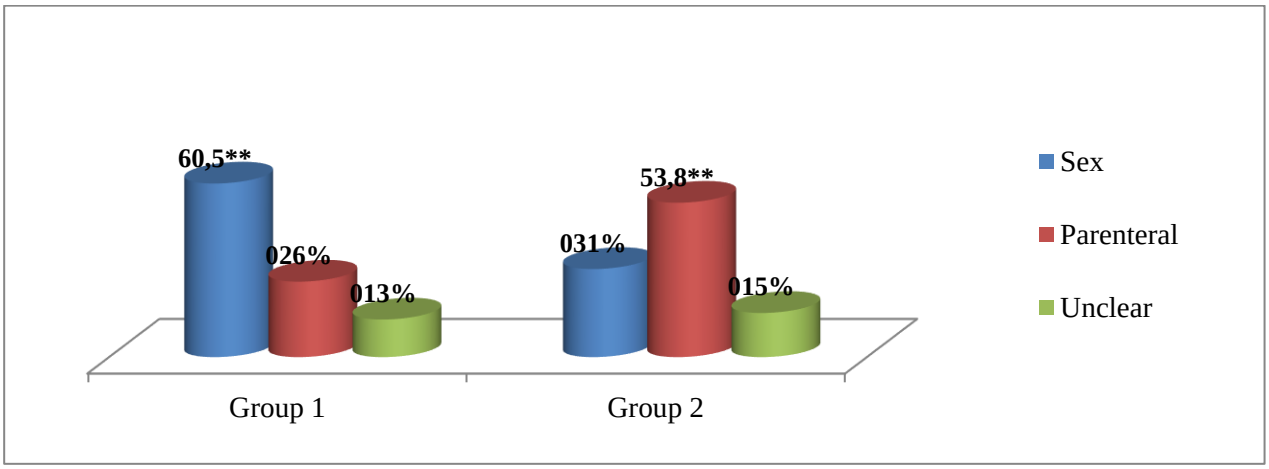

Figure 1. Mechanisms of infection of human immunization virus in groups

Sexual transmission of HIV in group 1 was 60.5%, in group 2 it was 30.7% (r<0.01). Damage by parenteral mechanism was 26.3% in group 1 and 53.8% in group 2 (r<0.01). Most parenteral procedures (24%), blood transfusions (1%), dentist (19.5%) and gynecologist (27%), podiatrist visits (31%), narcotics (0.5%) and operative interventions (6%). He organized the transmission of HIV infection through the parenteral mechanism.

During the study of the coexistence of HIV infection and QD type 2, patients were characterized by general clinical indicators in these groups (Table 1).

Table 1

Infection of human immutuality virus and the clinical characteristics of patients with the 2nd Type of diabetes together

Indicators	Group 1 n=38	Group 2 n=13	P
Gender: Female	26 / 68,4±7,6	9 / 69,2±13,3	>0,05
Male	12 / 31,6±7,6	4 / 30,8±13,3	>0,05
Age	42,3±1,5	45,6±3,6	>0,05
Duration of acquired immunodeficiency virus infection	8,4±0,56	6,5±1,2	>0,05
Duration of antiretroviral therapy	4,7±0,36	5,0±1,0	>0,05
Duration of type 2 diabetes	4,9±0,43	8,4±1,4	< 0,05
Body mass index	25,0±0,87	26,6±1,2	>0,05
Waist circumference	93,4±2,2	93,0±2,8	>0,05
Thigh circumference	97,4±2,0	101,4±2,4	>0,05
Abdominal index	0,96±0,012	0,92±0,017	< 0,05
CD4 lymphocyte count	419,2±45,1	396,7±64,0	>0,05
Viral download	258195,2±195375,8	31372,8±23154,2	<0,05

According to the results in this table, the age of patients in group 2 was greater than in group 1. The difference between body mass index and waist and hip circumference was not reliable. However, the abdominal index was found to be significantly higher in group 1 than in group 2 (r<0.05). Although the CD4 lymphocyte count was higher in group 1, the results showed that the results were not reliable. Viral load was also higher in group 1. In addition, compensation of glycemic indicators was evaluated in these groups (Table 2).

Table 2

Evaluation of the compensation of glycemic indicators in groups

Indicators	Group 1 n=38	Group 2 n=13	P
Glycemia level, mmol/l	7,4±0,29	9,1±0,63	<0,05
Glycated hemoglobin,%	7,6±0,23	8,5±0,38	<0,05
Insulin, μTB/ml	18,4±1,0	19,6±1,6	>0,05
HOMA index	6,1±0,44	8,0±0,46	<0,05

As shown in Table 2, postprandial glycemia and glycated hemoglobin values were reliably higher in group 2. The amount of dietary insulin was not significantly different between the groups. It can be seen that the HOMA index scores were also reliably higher in group 2 patients. All these indicators mean that carbohydrate metabolism compensation has not been achieved in patients with primary diabetes type 2. In addition, the correlation of body mass index with indicators of excess body weight in patients has motivated the study of lipid metabolism disorders. For this reason, the state of lipid metabolism (Table 3) was evaluated in this category of patients.

Table 3

Evaluation of lipid metabolism disorders in groups

Indicators	Group 1 n=38	Group 2 n=13	P
Total cholesterol	5,9±0,15	5,8±0,29	>0,05
Triglycerides	3,3±0,14	2,52±0,25	< 0,05
High density lipoproteins	1,01±0,08	1,23±0,10	>0,05
Low density lipoproteins	3,38±0,20	3,41±0,35	>0,05
Very low density lipoproteins	1,49±0,06	1,14±0,11	< 0,05
Atherogenic index	4,9±0,15	4,8±0,29	>0,05

Table 3 can clearly see changes in lipid metabolism indicators in 2 groups. In this case, the difference between the above 2 groups was not reliable. However, when the amount of TGs and zzhlps is determined, the difference between them is reliable and in patients 1 indicators showed higher results. In patients with HIV, the tracing of lipid metabolism is sharply.

When analyzing patients in the study taking hypoglycemic drugs due to glycemic decompensation, it was found that 8 of these patients were taking hypoglycemic drugs. 5 of them received sulfonylurea, and 3 received intermediate-acting insulin in monotherapy. They did not regularly check the glycemic index of the meal in dynamics. Therefore, we were unable to stratify by treatment group due to insufficient evidence. Non-adherence to medication, indifference to self-control, HIV infection and type 2 QD were assessed as having no cure, and a low will to live was manifested by poor glycemic performance in patients. Therefore, the SF-36 questionnaire was administered to determine the extent to which quality of life indicators were impaired in patients. In filling out this questionnaire, based on patient consent, all patients filled in the indicators that they considered necessary without the influence of others.

All indicators were summarized and mental and physical health indicators were calculated. All parameters were compared with the results of 25 patients with type 2 diabetes in the control group without HIV infection (Table 4).

Table 4

Evaluation of the results of the groups on the basis of SF-36 surveys

Indicators	Main group	Control group	P
Physical fitness	49,0±0,69	60,8±0,61	P<0,05
Daily activities based on physical condition	50,0±0,01	77,0±0,01	P<0,01
General state of health	16,0±0,69	66,0±0,41	P<0,001
Life activity	15,0±0,01	55,0±0,01	P<0,001
Social activity	35,0±1,15	64,0±2,32	P<0,05
Daily activities based on physical condition	40,0±4,59	66,67±0,03	P<0,001
Mental health	31,20±0,37	58,48±1,31	P<0,05
Physical component of health	**36,5±0,05**	**64,7±0,48**	**P<0,001**
The mental component of health	**30,3±1,53**	**63,3±0,61**	**P<0,001**

Based on the data presented in this table, it can be said that the values of all points were significantly different between the main group and the control group (P<0.001). The unsatisfactory result of the physical component of health in the 2nd group is explained by the presence of various macro and micro vascular complications typical of diabetes in patients, while the unsatisfactory result of the mental component of health in the main group is explained by the low confidence in living and the negative outlook of the disease. This, in turn, was reflected in a severe deterioration of quality of life indicators.

It is not without possibility that mental disorders pass under the guise of depression and serve to develop such characteristics as severe depression and lack of faith in life. In this regard, another questionnaire was administered to the patients to determine to what extent these changes in health reflect the state of depression. Gamelton's depression questionnaire was given to each of the patients and the following result was obtained by summing up the collected values in them (Figure 2).

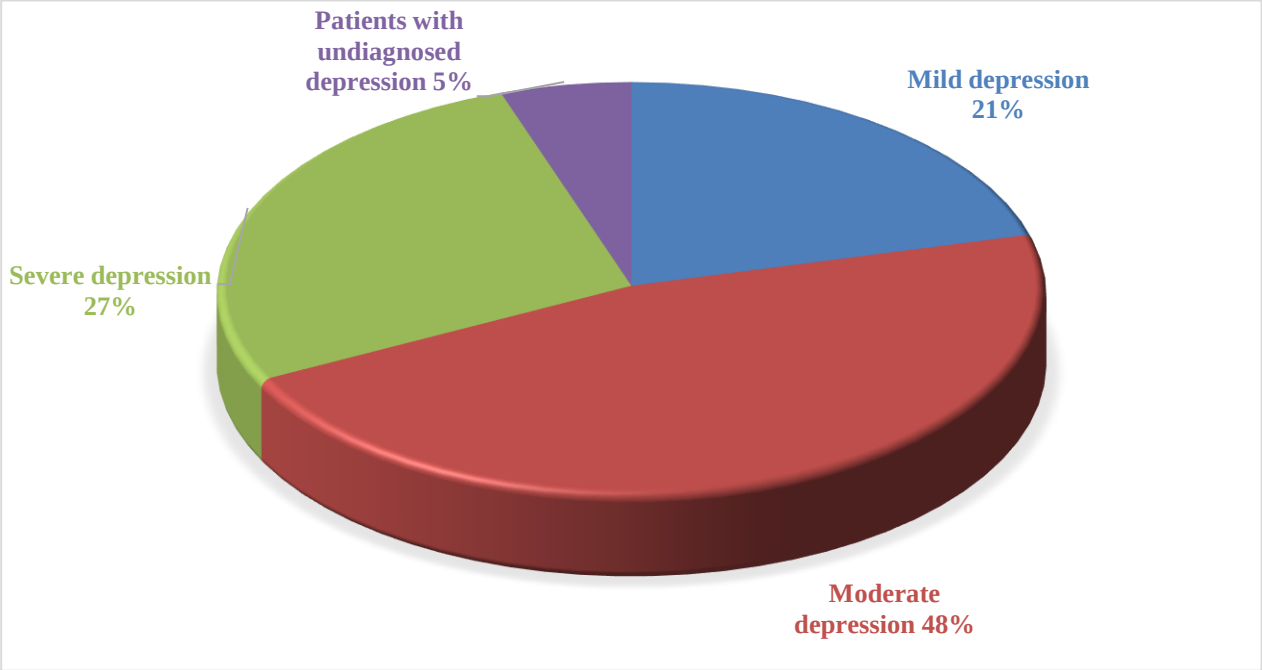

Figure 2. Prevalence of depression in study patients.

According to the results of the Gamelton questionnaire, 21% of patients had mild depression, 46.5% of moderate depression, 27.3% of severe depression, and 5.2% of patients had no depression. This, in turn, proves that the mental disorders identified in the SF-36 questionnaire in patients are under the guise of depression. In order to increase the effectiveness of treatment in this category of patients, it is necessary to remove them from depression. In this way, it is possible to establish self-monitoring of patients, through which it is possible to achieve early detection and prevention of diseases and complications that may develop in them.

CONCLUSION:

1. When studying patients who were observed together with HIV type 2 QD, the rate of sexual transmission was 60.5% in those with primary HIV type 2 QD followed by parenteral transmission in patients with HIV infection after primary QD type 2 (53, 8%) was dominated by HIV infection.

2. When type 2 diabetes and HIV infection come together, it was found that the decompensation of glycemic indicators occurs in 58%. The highest violation of glycemic indicators was observed in patients with HIV infection after primary diabetes ($r<0.05$). 9.8% of these patients received sulfonylurea products and 5.8% received intermediate-acting insulin.

3. According to the SF-36 questionnaire, the physical component of health in patients is 36.5±0.01 (in the control group, this indicator is 64.7±0.48; $r<0,001$), the mental component of health is 30.3±1.53 (in the control group, this indicator is 63.3±0.61; $r<0,001$) was equal to According to the results of the Gamelton questionnaire, mild depression was observed in 21%, moderate depression in 46.5%, and severe depression in 27.3% of patients.

REFERENCES

1. Aliev A.V., Rakhimova G.N., Ismailov S.I. Epidemiologiya saharnogo diabeta i prediabeta v Uzbekistane: rezultati skrininga / / Journal klinicheskoy i teoriticheskoy medisini. - 2017.- №2.- The C.58-61.

2. Gulinskaya O, V., Tsirkunov V.M. Insulinorezistentnost u pasientov VICH infektiey // Sovremennie problemi infeksionnoy pathologii cheloveka. - Minsk, - 2016. - 75-78.

3. Christina X.R., Jurgen K.R. VICH 2014/2015. - Berlin, 2015.- 917.

4. Levi D.E. Vich I SPIDa pathogenesis. -Perevod 3-go izdaniya. M.: Nauchniy Mir, 2016. – 736.

5. Sovet ekspertov. Klinicheskie rekomendasii po lecheniyu saharnogo diabeta 2 tipa.- Tashkent.-2019.- 4-10.

6. Alter G., HeckermanD., SchneidewindA. etal. HIV-1 adaptation to NK-cell-mediated immunepressure //Nature.- 2014.-R.76-79.

7. American Diabetes Association. “Standards of medical care in diabetes – 2018 abridges for primary care providers”/ Clinical Diabetes 36.1 (2018):14-37.

8. Davies, Melanie J. et al. “Management of hyperglycaemia in type 2 diabetes,2018. A consensus report by the American Diabetes Association (ADA) and the EASD”. Diabetologia (2018):1-38.

9. UNAIDS. Global HIV & AIDS statistics. - 2020

10. Ledwaba L, Tavel AJ, Paul Khabo P et al. Pre-ART Levels of Inflammation and Coagulation Marfers Are Strong Predictors of Death in a South African Cohort with Advanced HIV Disease.//PLoS One. – 2012

11. Incidence and Risk Factors for Prediabetes and Diabetes Mellitus Among HIV-infected Adults on Antiretroviral Therapy: A Systematic Review and Meta-analysis. Nansseu JR, Bigna JJ, Kaze AD, NoubiapJJ.Epidemiology. 2018 May;29(3):431-441. doi: 10.1097/EDE.0000000000000815.

Central Asian Journal of Medicine

THE SIGNIFICANCE OF SIMULATION TRAINING FOR FAMILY PHYSICIANS AS A TOOL FOR OBJECTIVE SELF-ASSESSMENT

Rano K. Dadabaeva [1], Oybek F. Eshmamatov [2], Zebo I. Ruzieva [3], Ozoda A. Mirzabekova[4]

1 Candidate of Medical Sciences, Associate Professor, Head of the Department of advanced training of doctors of the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: rdadabaeva@mail.ru

2 Assistant of the Department of advanced training of doctors of the Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: oybekeshmamatov@gmail.com

3 Assistant of the Department of advanced training of doctors of the Tashkent Medical Academy, Tashkent, Uzbekistan

4 Assistant of the Department of advanced training of doctors of the Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

The article presents data on the study of the importance of simulation training for family doctors in the system of postgraduate continuing medical education. Along with the study of the professional and organizational structure of medical cadets studying at the Department of Advanced Training of Doctors of the Tashkent Medical Academy, a survey was conducted on the knowledge of using various simulators. As a result of the work carried out, it was found that the use of simulation teaching methods in the system of postgraduate education contributes to an objective self-assessment of their professional competence, which serves as a motivation for them to improve their knowledge and improve the quality of medical services in primary health care.

Key words: family medicine, public health, primary health care, advanced training of doctors, simulation teaching methods.

INTRODUCTION

Today, higher medical education is undergoing a deep modernization to train specialists of a new quality. One of the main directions is to improve the quality of

practical skills of graduates. But how to do that? The data published in the journal Healthcare based on the results of a survey of 1,000 young doctors show that only 23% of graduates rated their training at the university as good, 55% as satisfactory, and 22% as unsatisfactory. An even more serious situation manifested itself when young doctors assessed their practical skills and abilities formed at the university - only 12% considered their quality to be good [1,2].

In the system of postgraduate continuous medical education, at present, simulation training is one of the most popular modern methods, the main purpose of which is to develop the knowledge and practical skills of medical workers [4,5]. This will help the student of advanced training courses to independently assess their professional knowledge, skills and competencies, as well as confidently use them in full-fledged practical activities.

In the 2020-2021 academic year, 476 family doctors from 6 regions of the Republic of Uzbekistan were trained in 10 general advanced training courses (144 credits) and 9 thematic advanced training courses (72 credits) at the Department of Advanced Training of Doctors of the Tashkent Medical Academy. Practical classes on the use of simulators in the amount of 18 credits for each type of advanced training were held at the Department of Clinical Modeling of the Tashkent Medical Academy.

Purpose of the study: to study the importance of simulation training in advanced training courses for family doctors in the system of postgraduate continuing medical education.

Materials and methods. We have studied the organizational structure of medical students studying at the Department of Advanced Training of Physicians and obtained the following results.

Out of 300 students, 94 people. (31.3%) work in urban family polyclinics (SP), 206 people. (68.7%) - in rural family polyclinics and the so-called points of family doctors (formerly - rural medical center). When divided into groups according to age categories, doctors aged 25-30 years amounted to 2 people. (0.67%), 31-40 years old - 40 people. (13.3%), 41-50 years old - 107 people. (35.7%), 51-60 years old - 113 people. (37.7%) and 61-70 years old - 38 people. (12.6%). The work experience of the studied students in primary health care was as follows: up to 5 years - 7 people (2.3%), 6-10 years - 69 people. (23%), 11-20 years old - 102 people. (34%) and more than 20 years - 122 people (40.7%).

We also conducted a survey of all students of advanced training courses, using a questionnaire specially designed for primary care physicians and consisting of the following questions:

1. Are you familiar with the tasks of the simulation training system?

2. What methods of simulation training do you know?

3. What do you think is the advantage of simulation training for you personally?

4. What is the importance of simulation training in acquiring practical skills in the field of family medicine?

5. What skills do robot simulators require to master?

6. What skills can be strengthened through the Virtual Patient Program?

7. In what specialty do you think simulation training contributes to the acquisition of a wider range of skills?

8. Are simulation training hours sufficient in postgraduate continuing medical education? If not enough, what is your suggestion?

9. What other simulations do you think are needed to acquire the skills used in primary health care?

10. Problems that you have while working on simulators?

Results and analysis. When studying the results obtained, the following was established: the largest part (37.7%) of doctors trained at the Department of Advanced Training of Doctors of the Tashkent Medical Academy were of pre-retirement age (51-60 years old - 113 people), followed by students 41-50 years old - 107 people (35.7%), young professionals under the age of 35 accounted for 0.67%. These figures indicate that the majority of physicians currently working in primary health care are near retirement age or are already retired. In addition, family physicians aged 61-70 years make up 12.6% of the total number of trainees who have completed advanced training, and are the most numerous category with a work experience of 20 years or more (40.7%).

Analysis of the survey conducted among the students showed the following. To the question 1 “Do you know the tasks of the simulation training system?” received the answer "No" in 100%. To the second question of the questionnaire 2 “What methods of simulation training do you know?” all listeners of listeners indicated ECG and cardiopulmonary resuscitation, and 85% - ophthalmootoscopy. To question 3 “What do you think is the advantage of simulation training for you personally?” the absolute number of listeners answered almost the same “In improving their knowledge and practical skills. To the next question 4 “What is the importance of simulation training in acquiring practical skills in the specialty of a family doctor?” - 80% of doctors indicated very high.

Next, to question 5, “What skills do you need to use robot simulators to master?” the studied audience unanimously indicated the specialty "family doctor". At the same time, the majority of respondents noted that the current teaching hours of simulation classes (12 credits) are not enough in continuing medical education,

and the volume of these classes should be increased to at least 18 hours, which was the answer to the question “Are teaching hours of simulation training sufficient in postgraduate continuing medical education? If not enough, what is your suggestion? To the question “In your opinion, in which specialty does simulation training contribute to the acquisition of a wider range of skills?” All doctors (100%) noted that it was for family medicine specialists. “What skills can be strengthened through the Virtual Patient Program?” – family doctors noted the high efficiency of working with this simulator, as it contributes to the development of most of the practical skills necessary for family doctors. “Problems you have while working on simulators?” - the final question, to which the answer was received from all the surveyed listeners about the problems that arise when working with simulators, mainly there is a lack of skills in using computer technology and gadgets.

In the process of conducting the study, in accordance with international data, it was revealed that a properly organized methodological approach of teachers is the use of algorithms of practical skills that make the assimilation of skills clearer faster, automatism and the correctness of the performance of the skill are laid. And also the use of simulation technologies leads to mastering professional practical skills at a higher level than their theoretical description [3].

As a result of the above results and their analysis, it was found that the introduction of the simulation method of training in postgraduate continuing medical education / advanced training of doctors provides a continuous / systematic increase in the professional knowledge, competence, qualifications and skills of family doctors. The inclusion of simulation teaching methods in the components of their professional development creates an opportunity for doctors to evaluate their own knowledge, acquire additional knowledge and skills on an individual basis, and improve their personal competence. This, in turn, contributes to improving the quality of medical services provided by family doctors to the population.

Conclusions:

1. Simulation methods for teaching family doctors in the system of postgraduate continuing medical education are introduced into the curriculum for advanced training of doctors at the Tashkent Medical Academy;

2. The use of simulation teaching methods in the advanced training cycles of family doctors will help them objectively assess their personal competence;

3. The inclusion of simulation teaching methods in the process of professional development of practitioners increases the attractiveness of educational programs

and serves as a motivation to improve their knowledge in this educational institution;

4. The introduction of a simulation method of training in the advanced training of family doctors is of great importance in protecting public health by improving the quality of medical services provided at the primary health care level.

REFERENCES

1. Avdeeva V.G. «Innovative technologies in the system of continuous medical education. Experience in training specialists of the disaster medicine service and emergency medical care. // Medical education and professional development, No. 1, 2010, 23-26 b.

2. Bulatov S.A. "Teaching Practical Skills: Russian and International Experience". Medical Education and Professional Development, No. 1, 2010. 31-35 b.

3. Frank J.R., Shell L. Competency-Based medical education theory of practice. Medical Thecher. 2010; 32(8): 638–46.

4. Gadaev A.G., Abdurahimova L.A., Dadabaeva R.K. “Wissenschaftlicher ansatz in der medizinischen ausbildung: entwicklung einer prognostischen karte der krankenentwicklung”// Berlin Studies Transnational Journal of Science and Humanities. – 2021. Vol.1 Issue 1.5 Pedagogical sciences. P. 85-93.

5. Turchina Zh.E., Sharova O.Ya., Nor O.V., Cheremisina A.V., Bitkovskaya V.G. “Simulation training as a modern educational technology in the practical training of students of a medical university//Modern problems of science and education. - 2016. - No. 3. - 22-24 b.

6. Kobayashi L., Patterson M.D., Overly F.L., Shapiro M.J., Williams K.A., Jay G.D. Educational and research implications of portable human patient simulation in acute care medicine. Academic Emergency Medicine 2008 Nov;15(ll):l 166-74. Epub 2008 Jul 14.

7. Murin S., Stollenwerk N.S. Simulation in procedural training: at the tipping point. Chest. 2010; 137: 1009–11.

8. Novikova O.V., Chernikov I.G., Davydova N.S. Technology of simulation training at the Ural State Medical University at the present stage and development prospects. In: II Congress of the Russian Society for Simulation Education in Medicine ROSOMED-2013. Moscow, 2013. Available at: http://www.laparoscopy.ru/doktoru/view_thesis.php?theme_id=43&event_id=16.

9. Rodgers D.L., Securro S.J., Pauley R.D. The effect of highfidelity simulation on educational outcomes in an advanced cardiovascular life support course. Simulat Hlth. 2009; 4: 200–6

10. Svistunova A.A., red. Simulation training in medicine. Compiled by Gorshkov M.D. Moscow: Publishing House of the First Moscow State Medical University named after V.I. THEM. Sechenov; 2013

Central Asian Journal of Medicine

THE ROLE OF GENETIC FACTORS IN THE TREATMENT TACTICS OF DUODENAL ULCERS COMPLICATED BY BLEEDING

Oktyabr R. Teshaev [1], Olim R. Mavlyanov [2], Suxrob U. Alimov [3]

1 Doctor of Medicine, professor of the department of surgical diseases in family medicine of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: oktyabrteshayev@gmail.com

2 Doctor of Medicine, professor of the department of surgical diseases in family medicine of the Tashkent medical academy, Tashkent, Uzbekistan.
E-mail: olimboy.mavlyanov@gmail.com

3 Doctor of Philosophy, assistant of the department of surgical diseases in family medicine of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: dr.sukhrob@mail.ru

ABSTRACT

In the etiology of peptic ulcer, hereditary burden plays a certain role. Therefore, when studying the nature of hereditary predisposition to gastric ulcer (GU) and duodenal ulcer (DU), an important direction is the identification of genetic markers. In order to fulfill the tasks set in accordance with the purpose of the research, 725 patients with duodenal ulcer disease complicated with bleeding.

In our research, the relationship between body composition and clinical and laboratory indicators of bleeding was determined in the examination of patients with a complicated course of duodenal ulcer disease according to the most important clinical signs. Thus, in patients with duodenal ulcer disease complicated by bleeding, it was possible to choose treatment methods, size and type of surgery, taking into account the peculiarities of the constitutional body structure.

Key words: helecobaktery pylori, gastric ulcer, duodenal ulcer, bleeding, hereditary, reduction.

INTRODUCTION

In the etiology of peptic ulcer, hereditary burden plays a certain role. Therefore, when studying the nature of hereditary predisposition to gastric ulcer (GU) and duodenal ulcer (DU), an important direction is the identification of

genetic markers. In this regard, it is fundamentally important to study the N-acetyltransferase involved in the implementation of genetic information, and to elucidate the relationship of hereditary characteristics with the pathology of the ulcer. 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 the literature data, there is a relationship between the acetylation process and the etiology and pathogenesis of a number of diseases: peptic ulcer of the stomach and duodenum, ulcerative colitis, heart failure, infertility and peritoneal 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.

It should be noted that, in addition to genetic factors, environmental factors have claimed an etiological role in peptic ulcer: HP, non-steroidal anti-inflammatory drugs, cigarette smoking, stress and dietary factors.

Until the 19th century, ulcerative ulceration was uncommon, whether in the East or West. The rate of infection varies widely between Asians. This is low in Malays and Indonesians, in whom stomach ulcers and stomach cancer are uncommon. This is very high in India, where duodenal ulcers are common, but stomach ulcers and cancer are not. In the Chinese and Japanese, cancer is common, high, but the Chinese have a higher incidence of duodenal ulcer than the Japanese. HPi is believed to be the main cause of PU, and other environmental and genetic factors contribute to the formation of ulcers, supporting the concept of etiological heterogeneity. The description of the first stomach ulcer in human history probably belongs to a Chinese man who died 2,000 years ago in the Western Han Dynasty.

According to Abuzarov E.R. the nature of pathological changes in the ultrastructure of the gastric mucosa differs in patients with PU depending on the H. pylori genotypes, polymorphic loci of cytokine genes (IL-1 and IL-10), as well as the presence of combined (HP+M.heorhinis) infection. Molecular genetic markers of predisposition to PU and duodenal ulcer have been identified. It was found that the IL-1B-511C allele and the IL-1B-511C/C genotype increase the risk of developing GU and duodenal ulcer associated with HP, while the IL-1B-511T allele, the IL-1B-511C/T genotype reduce the likelihood of developing the disease. At the same time, the authors believe that genetic influences are of moderate importance for liability to peptic ulcer. Genetic influences for peptic ulcer disease are independent of genetic factors important for HP infection.

MATERIAL AND METHODS

In order to fulfill the tasks set in accordance with the purpose of the research, 725 patients with duodenal ulcer disease complicated with bleeding were treated in inpatient conditions between 2013 and 2021 in the surgical departments of the Urgench branch of the CCP 1 and the Republican Scientific Center for Emergency Medical Care. Patients were examined. Complaints of all patients were asked, EGDFS, UQT, USI, blood groups, hemostasis indicators, examinations were conducted.

Out of 725 patients, 525 were men and 200 were women. The ratio of men to women was 2.6:1. The majority of patients were able-bodied men. Age of patients: (according to 2017 BJSST classification) 344 (47.45%) 18-44-year-olds, 206 (28.45%) 45-59-year-olds, 133 (18.3%) 60-74-year-olds , 42 (5.8%) were patients aged 75-90 years.

First, 126 (17.4%) patients had gastric ulcer disease and duodenal ulcer disease in their anamnesis, 284 (39.2%) patients had ulcer disease up to 1 year, 76 (10.5%) patients had 1 - 3-year-old ulcer, 57(7.8%) patients had 3-5-year ulcer, 81(11.2%) had 5-10-year ulcer, 101(13.9%) had more than 10-year ulcer. many were ill within a year of ulcer disease.

RESULTS AND DISCUSSION

All patients had a specific course of the disease: 2-3 hours before the onset of bleeding, pain in the epigastric area increased, mainly at night, the pain was constant (in 341 patients), and decreased after the onset of bleeding. They (352 patients) felt general weakness, (178 patients) dizziness, (183 patients) nausea, "coffee grounds" type (627 patients), and (39 patients) vomiting of black blood was observed. After 8-12 hours after the reduction of pain in the abdomen, tarry stools were observed (in 511 patients).

When 511 patients were examined in the reception, the stool color was observed as coffee grounds, which indicates bleeding from the upper part of the gastrointestinal tract.

Primary wound disease complicated bleeding in 397 patients, bleeding recurred in 285 patients, and bleeding was observed multiple times in 43 patients. The time from the onset of bleeding to hospitalization varied from 2 hours to 1 week. Esophagogastroduodenofibroscopy was performed in all patients with gastroduodenal ulcer. We found a significant difference in the localization of the ulcer in the duodenal bulb. Ulcers complicated by bleeding were located in the posterior wall of the root of the duodenum in 473 patients, bleeding ulcers were located in the anterior wall in 97 patients, in the lesser curvature in 92 patients, and in the greater curvature in 58 patients.

I A – patent rapid bleeding in 12 (1.65%) patients;

IV – continuous capillary bleeding in 40 (5.5%) patients;

II A – bleeding in a large thrombosed vessel seen in 163 (22.5%) patients (thrombus diameter < 2 mm);

II V – 451 (62.2%) patients were covered with a large thrombus (thrombus size > 2 mm in diameter);

II S – 59 (8.15%) patients had no symptoms of bleeding (black spot, black spot).

Bleeding rate analysis of 725 patients was performed, and 227 (31.3%) patients had grade I bleeding, 347 (47.9%) had grade II bleeding, and 151 (20.8%) had grade III bleeding. shows.

The wound size was 0.5 cm in 167 patients, 1.0 cm in 463 patients, 1-2.0 cm in 60 patients, and more than 2.0 cm in 35 patients.

Among those examined, 462 (63.7%) patients were smokers. 263 (36.8%) examined patients had stress in their anamnesis.

173 (28.9%) patients had gastroduodenal ulcer with hypertension, 97 (13.37%) with cardiovascular disease, 128 (17.65%) patients with ulcer disease with joint disease, 269 (37.1% of cases were accompanied by anemia, 72 (9.9%) cases were accompanied by chronic cholecystitis without stones, pancreatitis and hepatitis.

In 697 (96.2%) patients, an emergency endoscopic examination was performed in the first hours after hospitalization, the nature and source of bleeding was determined, and important morphological criteria were obtained to determine the risk of recurrence of bleeding.

The following tasks were also assigned to the diagnosis of bleeding from a wound:

1. To study the source of bleeding, to determine the nature of the wound, to know whether the bleeding has stopped or resumed;

2. Determining the level of blood loss and the ability of the body to cover it;

3. Assessment of pathological disorders in the patient's organs and systems, disorders of the hemostasis system associated with blood loss.

A mild level of bleeding intensity was found in 27 (22.7%) patients, a moderate level in 67 (56.3%) patients, and a severe level in 25 (21%) patients, that is, 2/3 of 119 patients (77, More than 3%) were admitted to the department with moderate and severe intensity of bleeding. The condition of blood hemostasis system was studied in 119 patients. When the bleeding stopped, the patients, as well as the blood hemostasis system, underwent a clinical examination.

In 725 patients with a bleeding duodenal ulcer, the level and condition of blood loss were compared, which is given in Table1

Degree of blood loss	**1 degree 227 (31,3%)**	**2 degree 347 (47,9%)**	**3 degree 151 (20,8%)**
The severity of the patient's condition, which is fully determined by general clinical signs	Satisfactory 218 (30,3%).	Moderate severity 357 (49,2%)	Severity level 150 (20,7%)

Table 6 shows that the nature of the change of these indicators is related to the level of blood loss, from which it can be seen that blood loss is observed with a decrease in the amount of total protein. Bilirubin, AST, ALT did not show changes related to bleeding 1. Thus, the diagnosis of a bleeding duodenal ulcer, the degree of blood loss and the intensity of bleeding are based on clinical, endoscopic and laboratory data.

The most common symptoms are tarry stools and weakness. Often, bleeding from a wound occurs against the background of white syndrome.

Correlations between bleeding and body composition were found in all examined patients.

Correlation between body structure and indicators of hemostasis in female and male patients with asthenic body structure.

Complicated bleeding of gastric and duodenal ulcer diseases, asthenic body structure, female patients with body structure and indicators of hemostasis system (platelet aggregation, QIV, thrombin generation time, QFTV, PTI) a strong inverse correlation (r= - 0.47) was found between A correct correlation was found between platelet aggregation and fibrinogen, as well as between body composition and thrombin generation time (r=0.56), ($p<0.05$). in male patients with asthenic body structure, a strong inverse correlation (r= - 0.38) was found between body structure and indicators of the hemostasis system (platelet aggregation, thrombin generation time). A correct correlation was found between platelet aggregation and fibrinogen, as well as between platelet aggregation and QFTV (r= 0.61). ($p<0.05$).

A strong inverse correlation between body composition and indicators of hemostasis system (QIV, thrombin generation time, PTI) was observed in female patients with normosthenic body composition, with bleeding complications of gastric and duodenal ulcers. correlation (r= - 0.79) was determined. A correct

correlation was found between platelet aggregation and thrombin generation time, body structure and platelet aggregation, QIV and QFTV, as well as between body structure and fibrinogen amount (r= 0.62). (p<0.05). In male patients, a strong inverse correlation (r= - 0.76) was found between normosthenic body structure and indicators of hemostasis system (QIV, Platelet aggregation, QFTV). and between the amount of fibrinogen, a correct correlation was found (r= 0.53) (p<0.05).

Strong inverse correlation between body composition and indicators of hemostasis system (QIV, thrombin generation time, QFTV) in female patients with hypersthenic body structure, complicated bleeding of gastric and duodenal ulcers correlation (r=-0.90) was found.

Correlation between body structure and indicators of hemostasis in female and male patients with normosthenic body structure.

A correct correlation was found between platelet aggregation and fibrinogen amount, platelet aggregation and thrombin generation time, and between QIV and QFTV (r= 0.87). (p<0.05).

In male patients, a strong inverse correlation (r=-0.83) was found between hypersthenic body structure and hemostasis system indicators: platelet aggregation and thrombin formation time, as well as QFTV and fibrinogen.

A correct correlation was found between platelet aggregation and fibrinogen, as well as between PTI and thrombin generation time (r= 0.80), (p<0.05).

Correlation between body structure and indicators of hemostasis in female and male patients with hypersthenic body structure.

It is appropriate to use the obtained results as a criterion for assessing the condition of patients with gastric and duodenal ulcers complicated by bleeding, which indicated the need for very early surgical intervention when changes in the indicators of the hemostasis system were observed.

A correct correlation was found between thrombin generation time and QFTV (r=0.71). (p<0.05).

CONCLUSIONS

1.Thus, in patients with duodenal ulcer disease complicated by bleeding, it was possible to choose treatment methods, size and type of surgery, taking into account the peculiarities of the constitutional body structure.

2.It is necessary to assess the patient's condition and implement treatment tactics, taking into account the body structure (asthenic, normosthenic, hypersthenic) of patients with duodenal ulcer disease complicated by bleeding.

REFERENCES

1. Bondarenko V. M., Matsulevich T. V. Intestinal dysbiosis, as a clinical and laboratory syndrome. M .; 2007.

2. Gabbasova L.V. Clinical and genetic study of duodenal ulcer: Abstract. dis. for a job. student Art. Candidate of Medical Science - Izhevsk., 2013. – 20 P.

3. Gabidullova D.A. et al. Influence of the acetylation phenotype on the clinic, prognosis, course and treatment of acute coronary syndrome // Bulletin of the Samara Scientific Center of the Russian Academy of Sciences - 2010. - V. 12. - No. 1 (6). P. 1592-1594.

4. Dubinskaya E.D. et al. Importance of N-acetyltransferase-2 gene polymorphism in patients with infertility and peritoneal form of endometriosis // Reproduction Problems - 2014 - No. 1- P.41-46.

5. Dugina V.V. The effect of immunomodulators ribomunyl and lycopia on immunity indicators in gastric and duodenal ulcers. Modern technologies in medicine. - 2012. - 1. - P. 75-79.

6. Isakov V. A., Domaradsky I. V. Helicobacteriosis. M .; 2003.

7. Karkishchenko N.N. et al. Highly specific species primers for the Nat1 and Nat2 genes for comparative studies in humans and laboratory animals // Biomedicine - 2014- No. 2- P. 4–24.

8. Mavlyanov A.R. Prediction and choice of surgical intervention for complicated gastroduodenal ulcers Diss. for job registration Doctor of Medical Science 2000. - Tashkent.

9. Minushkin O.N. Antacids in the practice of a gastroenterologist. Russian medical journal. Digestive apparatus diseases. - 2004. - T.6. - No. 1.

10. Satyrova T.V. et al. Variability of the phenotype of N-acetyltransferase in patients with ulcerative colitis // VESTNIK VSMU - 2010 - Volume 9. - No. 1 - P. 1-8.)

11. Rudyk Yu.S., Brewer S.N. Applied value of pharmacogenetics in the treatment of patients with heart failure // Ukrainian therapeutic journal 2013. - No. 1. - P.84-92)

12. Zimmerman Ya.S. Peptic ulcer: actual problems of etiology, pathogenesis, differentiated treatment // Clinical medicine. – 2012. – No. 8. – P.11-18.

13. Shcherbatov I.A., Protolinsky I.O. Mathematical modeling of complex multicomponent systems // Vestnik TSTU. – 2014. – Volume 20. – No. 1. – P.17-26.

14. Furuta T., Shirai N., Xiao F. et all. Polymorphism of interleukin-1beta affektsthe eradication rates of HP by triple therapy //Clin. Gastroenterol. Hepatol – 2004.-Vol. 2. N1. – P.22-30.

15. Laine L., Schoenfeld P., Fennerty M. B. Therapy for Helicobacter pylori in patients with non-ulcer dyspepsia: A meta-analysis of randomized, controlled trial. Arm. Intern. Med. 2001; 134: 361—369.

16. Malaty H.M., Graham D.Y., Isakson I., Engstrand L., Pederson N.L. "Are genetic influences on peptic ulcer dependent or independent of genetic influences for Helicobacter pylori infection?", Arch. Intern. Med., vol. 160, no. 1, 2000

17. Meucci G., di Battista R., Abbiati C. et al. Prevalence and risk factor of Helicobacter pylori-negative peptic ulcer: A multicenter study. J. Clin. Gastroenterol. 2000; 31: 42—47.

18. Rotter J.I., Grossman M. Genetic aspects of ulcer disease. Advances in ulcer disease. – Amsterdam, Experta Med., 1980. –p. 7-26.

19. Sugimoto M. Furuta T., Shirai N. Influences of proinflammatory and anti-inflammatory cytokine polymorphisms on eradication rates of clarithromycin-sensitivestrains of HP by triple therapy //Clin. Pharmacol. Ther. – 2006.-Vol. 80. -P.41-50.

20. Amrit K. Kamboj, Patrick Hoversten, Cadman L. Leggett, Upper Gastrointestinal Bleeding: Etiologies and Management, Mayo Clinic Proceedings, Volume 94, Issue 4, 2019, Pages 697-703, https://doi.org/10.1016/j.mayocp.2019.01.022.

21. Kathryn Oakland, Changing epidemiology and etiology of upper and lower gastrointestinal bleeding, Best Practice & Research Clinical Gastroenterology, Volumes 42–43, 2019. https://doi.org/10.1016/j.bpg.2019.04.003.

22. Omar Kherad, Sophie Restellini, Myriam Martel, Alan Barkun, Proton pump inhibitors for upper gastrointestinal bleeding, Best Practice & Research Clinical Gastroenterology, Volumes 42–43, 2019,

23. Robert T. Kavitt, Anna M. Lipowska, Adjoa Anyane-Yeboa, Ian M. Gralnek, Diagnosis and Treatment of Peptic Ulcer Disease,The American Journal of Medicine, Volume 132, Issue 4, 2019, Pages 447-456, https://doi.org/10.1016/j.amjmed.2018.12.009.

Central Asian Journal of Medicine

SOCIO-HYGIENIC ANALYSIS OF RISK FACTORS IN PATIENTS WITH DISEASES OF THE ENDOCRINE SYSTEM

Nizom J. Ermatov[1], Nodir K. Khaydarov[2], Ikhtiyor U. Abdulkhakov[3], Anvar N. Shukurov[4], Bobomurod B. Ortikov[5]

1 DSc, Professor, Head of the department of Hygiene of children, adolescents and hygiene of nutrition, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: n.ermatov@tma.uz

2 DSc, professor, rector of the Tashkent Dentistry Institute, Tashkent, Uzbekistan
E-mail: n.ermatov@tma.uz

3 Independent researcher of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: mironsho@rambler.ru

4 Independent researcher of the Tashkent medical academy, Tashkent, Uzbekistan
E-mail: anvar.shukurov@ssv.uz

5 PhD, Senior teacher at the Department of the Hygiene of children, adolescents and hygiene of nutrition, Tashkent Medical Academy, Tashkent, Uzbekistan
E-mail: bobomurodortiqov89@gmail.com

ABSTRACT

The study was conducted among 1375 (726 men and 649 women) patients aged 18-69 living in rural and urban areas of the Bukhara region, registered in the Bukhara Endocrinological Dispensary. Questionnaire data collected from patients evaluated using the “case-control” method. The risk factor with the greatest impact on health status is malnutrition (OR-15.6; 95% CI 12.9-18.8). As risk factors, not only low fruit consumption, but also the consumption of citrus fruits with allergenic properties the odds ratio was 12.6. In cases of high consumption of sweets, the odds ratio was 10.5 (from 8.7 to 12, 5), in addition, in cases of insomnia and heavy physical work, the odds ratio was 2.0. The results shows that the main part of the risk factors for the disease is associated with nutrition.

Key words: diabetes mellitus, case-control method, risk factors.

INTRODUCTION

Based on the WHO report, more than 537 million people aged 20-79 are living with diabetes mellitus today. This figure is expected to reach 643 million by

2030 and 783 million by 2045. More than 3 out of 4 adults live in low- and middle-income countries.

According to the World Health Organization (WHO), one of the leading causes of major non-communicable diseases, including the cardiovascular system, diabetes mellitus and some forms of malignant diseases, is an unhealthy lifestyle, malnutrition, non-compliance with the daily routine, overweight, irregularity is associated with nutrition [1,11,12,15,16].

Diabetes mellitus caused 6.7 million deaths in 2021, 1 death every 5 seconds. Due to the severity of this problem, WHO has declared diabetes as the epidemic of the 21st century.

The diet of the majority of the adult population does not meet the principles of a healthy diet due to the consumption of foods containing simple carbohydrates and a large amount of animal fats, and the diet is not enough fresh fruits and vegetables, fish and seafood, which leads to weight gain and obesity, its prevalence increased from 19% to 23% over the past 8-9 years, which leads to an increase in the risk of developing diabetes mellitus, diseases of the cardiovascular system, etc. [6, 9, 11, 12, 13,16,17]

According to the World Health Organization, non-compliance with the rules and norms of physical activity and nutrition, excessive consumption of foods and sweets with a high content of salt, sugar and fat, as well as insufficient intake of vitamins and minerals can lead to growth and mental retardation in young people, and in adults is the cause of the development of cardiovascular diseases, diseases of the endocrine system, dangerous tumors and a number of other diseases leading to premature death of people [10,11, 12,14,16].

A number of studies have shown that the development of type 2 diabetes mellitus is primarily influenced by harmful environmental factors, as well as a violation of the daily regimen, a violation of the diet, a decrease in the amount of proteins, fats, and vitamins. and minerals in the daily diet, as well as an increase in the amount of carbohydrates [3, 4, 7, 8, 9, 10, 11, 16, 17].

Environmental risk factors in the development of type 2 diabetes are shown in the works of a number of authors. Of more than 200 reported cases of type 2 DM assessed in 60 studies, 82 showed a significant association with the following characteristics: air pollution, dietary and physical activity, environment and proximity to streets are the most studied environmental determinants of prevalence [1, 4,13, 15,16,17]. Taking into account the analysis of the conducted studies, the socio-hygienic analysis of risk factors for the occurrence of diseases of the endocrine system in patients is one of the urgent tasks facing industry workers today.

Objective. Analysis of risk factors of patients with diseases of the endocrine system.

Materials and methods. 1375 patients (649 men and 726 women) living in villages and cities of the Bukhara region were registered in the regional endocrinological dispensary, their age ranged from 18 to 69 years. The data collected by patients on the basis of questionnaires were evaluated using the case-control method.

Statistical processing of the obtained data was carried out using the SPSS 16.0 and Statistica 6.0 programs for Windows.

Results and discussion

One of the main goals of our study is to identify risk factors that determine the development of the disease in patients with diabetes mellitus and substantiate the dependence of these factors on the development of the disease.

To achieve the goal, risk factors for developing type 2 diabetes mellitus were analyzed on the basis of the case-control group in a ratio of 1:1 (1375:1375), and healthy patients were taken as the control group. For the purpose of socio-hygienic analysis of the results obtained, the main ones were identified and a socio-hygienic analysis was carried out according to gradations of risk factors.

The main socio-hygienic factors affecting the health status of patients with diabetes mellitus and their results are presented in Table. 1.

Table 1

Lifestyle factors affecting people with diabetes (1:1 ratio)

Risk factors	Gradation of risk factors	Case group (P1)	Control group (P2)	P=P1/P2	M	95% II (DI)
Indiscriminate eating	yes	1007	205	4,9	15,6	12,9-18,8
	no	368	1170	0,3		
Fruit consumption	less	1243	586	2,1	12,7	10,2-15,6
	enough	132	789	0,2		
Sweets consumption	more	1119	405	2,8	10,5	8,7-12,5
	normal	256	970	0,3		
Consumption ща epy flour products	more	998	295	3,4	9,7	8,1-11,5
	less	377	1080	0,3		
Level of alcohol consumption	more	485	88	5,5	8,0	6,2-10,2
	less	890	1287	0,7		
Ratio of vegetable consumption	less	994	365	2,7	7,2	6,7-8,2
	enough	381	1010	0,4		
Consuming spicy food	more	901	304	3,0	6,7	5,6-7,9
	less	474	1071	0,4		
Use of vegetable oil	more	983	381	2,6	6,5	5,5-7,7
	less	392	994	0,4		

Late meal	After 20.00	978	376	2,6	6,5	5,5-7,7
	Until 18.00	397	999	0,4		
Eating too much salt	more	855	306	2,8	5,7	4,8-6,8
	normal	520	1069	0,5		
Hypodynamic state	less activity	966	406	2,4	5,6	4,7-6,6
	more activity	409	969	0,4		
Sleepiness	yes	701	239	2,9	4,9	4,1-5,8
	no	674	1136	0,6		
Obesity	exists	623	230	2,7	4,1	3,4-4,9
	no	752	1145	0,7		
Fatigue	exists	445	145	3,1	4,1	3,3-4,9
	no existance	930	1230	0,8		
Stress	excess	487	232	2,1	2,7	2,2-3,2
	less	888	1143	0,8		
Overweight	exists	437	230	1,9	2,3	1,9-3,3
	no	938	1145	0,8		
Insomnia	less	509	307	1,7	2,0	1,7-2,4
	good	866	1068	0,8		
Doing heavy physical work	yes	411	245	1,7	2,0	2,7-4,1
	no	964	1130	0,9		

As can be seen from Table 1, the concept of healthy eating behavior and culture, which is considered one of the main factors of a healthy lifestyle, and the state of non-compliance with it, showing the main indicator and the highest ratio, the most important factor in the development of the disease and the risk factor that has the greatest impact on the health status of patients (SHN-15.6; 95%-II 12.9-18.8).

It can be seen that a patient in the group (risk factor) (type 2 diabetes mellitus) is 15.6 times more likely to develop the disease compared to the control group.

The next major risk factor was the state of fruit consumption, most of our patients consumed less fruit and consumed citrus fruits with allergenic properties, NR-12.6 (ranging from 10.2 to 15.6).

The odds ratio was 10.5 (from 8.7 to 12.5) in the case of high consumption of sweets (mainly sugar, various sugar-rich cookies, waffles, confectionery products).

In the Bukhara region, which is one of the main regions of our country, a traditional dish of dough, called kayish in the national and local languages, is eaten mainly in the evening. It consists of 80% dough, beans, onions, vegetable oil and meat. The meat in this dish mainly consists of horse meat, lamb and beef. Salt is used in excess in this dish to prevent the dough from being crushed or sticking together.

It was found that most of our patients ate this dish. The consumption level of the rest of the dough products was relatively low, and the ratio of total dough products to consumption level was 9.6. The confidence interval was from 8.1 to 11.5.

The main role and importance of vegetables is to provide vitamins and minerals to the daily diet.

Vegetables are not restricted in people with diabetes, overweight, and obese and obese people.

The use of pumpkin, turnip, cucumbers, cabbage is more recommended. Insufficient vegetable intake was found and the odds ratio was 7.2.

The next risk factors are hypodynamic status, followed by overweight, obesity, fatigue, excessive sleep and strenuous exercise.

Based on the information presented above, a prognostic table was created to grade all risk factors (see Table 2).

Table 2

Prediction table for grading risk factors affecting adults with diabetes

Risk factors	Gradation of risk factors	SHN indicator	Prognostic indicators
Indiscriminate eating	yes	15,6	15,6
	yes	**1**	
Fruit consumption	less	12,7	12,7
	enough	**1**	
Sweets consumption	more	10,5	10,5
	normal	**1**	
Consumption ща epy flour products	more	9,7	9,7
	less	**1**	
Level of alcohol consumption	more	8,0	8,0
	less	**1**	
Ratio of vegetable consumption	less	7,2	7,2
	enough	**1**	
Consuming spicy food	more	6,7	6,7
	less	**1**	
Use of vegetable oil	more	6,5	6,5
	less	**1**	
Late meal	After 20.00	6,5	6,5
	Until 18.00	**1**	
Eating too much salt	more	5,7	5,7
	normal	**1**	
Hypodynamic state	less activity	5,6	5,6
	more activity	**1**	

Sleepiness	yes	4,9	4,9
	yes	**1**	
Obesity	exists	4,1	4,1
	yes	**1**	
Fatigue	exists	4,1	4,1
	no existance	**1**	
Stress	excess	2,7	2,7
	less	**1**	
Overweight	exists	2,3	2,3
	yes	**1**	
Insomnia	less	2,0	2,0
	good	**1**	
Doing heavy physical work	yes	2,0	2,0
	yes	**1**	
Minimum ∑ P P=19 **Maximum ∑ P P=115,7**			

This table shows all 19 risk factors and calculated their lowest and highest prognostic values.

According to the socio-hygienic analysis of risk factors for patients with diabetes, it can be seen that the population does not adhere to a healthy lifestyle during the day, the collapse of lifestyle, the radical collapse of healthy eating habits and culture, the growth of hypodynamic conditions and the rapid development of this type of disease in diabetes are the main risk factors. Given the above, it is necessary to carry out rehabilitation work among patients.

Conclusion

1. The most important risk factors for the disease were violation of the daily regimen of controlled patients, their irrational diet during the day, excessive consumption of confectionery during the day, consumption of pastries in the evening, excess salt.

2. Low consumption of fruits and vegetables in the daily diet should be considered as one of the risk factors for the development of the disease, and the prevention and treatment of the disease should be created by including these products in the diet.

3. It is necessary to control the body mass index in patients with the use of dinners, fried and flour dishes. This, in turn, reduces the motor activity of patients, causes them to be overweight, obese, and causes insomnia. This will disrupt the healing process.

4. Alcohol, smoking, and a sedentary lifestyle are some of the following risk factors for developing diabetes in patients.

REFERENCES

1. Adylova Z.U., Adylov Sh.K. Distribution of non-communicable diseases and the structure of the main types of non-communicable diseases // European studies. 2016. No. 5 (16). URL: https://cyberleninka. ru/article/ n/ rasprostrannost-neinfektsionnyh-zabolevany-i-struktura-osnovnyh-tipov-neinfektsionnyh-zabolevany (Date of access: 03/07/2023).

2. Andreeva E.E., Onishchenko G.G., Klein S.V. Hygienic assessment of priority risk factors of the environment and the state of health of the population of Moscow // Health risk analysis. – 2016. – no. 3 (15). - S. 23-34.

3. Sagdullaeva M.A., Ermatov N.Zh., Bobomurodov T.A. Hygienic analysis of the incidence of premature babies // New day in medicine. - Tashkent. -2022. - No. 10 (48). -B. 251-256.

4. Ermatov N.Zh., Abdulhakov I.U. Effect of nutrition and other risk factors for the development of various pathological conditions, including diseases of the endocrine system // Collection Scientific and Practical Confensation of the Burned 130th anniversary of the Bukhara Regional Multidisciplinary Medical Center. - Buhara.-October 30, 2021.-p.406-408

5. Ermatov N.Zh., Abdulkhakov I.Yu. The role of vitamins in the daily diet in the nutrition of patients with diabetes mellitus // New Day in Medicine 3 (35), 2021. P. 246-256.

6. Dendup T. et al. Environmental risk factors for developing type 2 diabetes mellitus: a systematic review //International journal of environmental research and public health. – 2018. – Т. 15. – №. 1. – С. 78.

7. Ermatov N.J., Bobomurodov T.A., Sagdullaeva M.A. Hygiene analysis of risk factors affecting the growth and development of pre-term children //Art of Medicine. International Medical Scientific Journal. 2022. – Т. 2. – №. 3. –P. 270-277

8. Ermatov N.J., Abdulxakov I.U. Analysis of vitamins in the daily diet of patients with diabetes //Фундаментальные и прикладные научные исследования XLVIII международная научно-практическая конференция. 15 сентября, 2021-С.188-189.

9. Ermatov N.J., Abdulxakov I.U. Hygienic Analysis of the Nutrient Composition of the Daily Diet of Patients with Diabetes Mellitus //American Journal of Medicine and Medical Sciences 2021, 11(9): 649-657

10. Ermatov N.J., Abdulxakov I.U. Influence of diet and other risk factors on endocrine system diseases // ACADEMICIA: An International Multidisciplinary Research Journal, P. 182-189

11. Ermatov N.J., Abdulxakov I.U. Socio-hygienic assessment of the incidence rate among various strata of the population-based on the materials of appeals and in-depth medical examinations //International Journal of Health & Medical Sciences, 2021 4(3), 309-314.

12. Giles-Corti B. et al. City planning and population health: a global challenge //The lancet. – 2016. – Т. 388. – №. 10062. – С. 2912-2924.

13. Kerner W, Brückel J; German Diabetes Association. Definition, classification and diagnosis of diabetes mellitus. Exp Clin Endocrinol Diabetes. 2014 Jul;122(7):384-6. doi: 10.1055/s-0034-1366278. Epub 2014 Jul 11. PMID: 25014088

14. Mahajan A, Donovan LE, Vallee R, Yamamoto JM. Evidenced-Based Nutrition for Gestational Diabetes Mellitus. Curr Diab Rep. 2019 Aug 31;19(10):94. doi: 10.1007/s11892-019-1208-4. PMID: 31473839.

15. Ojo O. Dietary Intake and Type 2 Diabetes. Nutrients. 2019 Sep 11;11(9):2177. doi: 10.3390/nu11092177. PMID: 31514301; PMCID: PMC6769664.

16. Rajagopalan S., Brook R. D. Air pollution and type 2 diabetes: mechanistic insights //Diabetes. – 2012. – Т. 61. – №. 12. – С. 3037-3045.

17. Rayanagoudar G, Hashi AA, Zamora J, et al. Quantification of the type 2 diabetes risk in women with gestational diabetes: a systematic review and meta-analysis of 95,750 women. //Diabetologia. 2016;59:1403–1411.

Contents

MUHARRIRIYAT VA NASHRIYOT BO'LIMI

Volume – 13,62 usl. printer. Circulation – 100. Format 60x84. 1/8.
Listening means «Times New Roman». Printed in TMA editorial and publisher department.
100109. St. Farabi 2, Tel.: (998 71)214-90-64, e-mail: rio-tma@mail.ru