

ISSN 2310-5577



European Science Review

2018
7-8



| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| <i>Kurbanova Zumrad Chutbaevna, Babajanova Shoiri Agzamovna,</i> VIOLATIONS OF COAGULATIVE HEMOSTASIS IN PATIENTS WITH LIVER CIRRHOSIS OF THE VIRAL ETIOLOGY | 122 |
| <i>Mirzayeva Rafiq Sahib, Kaziev Abuzer Yusif, Jafarova Gulnara Alisa</i> EVALUATION OF HEPATOPANKREATOBILIARY SYSTEM FUNCTIONAL ACTIVITIES IN POSTOPERATIV PERIOD IN GASTRIC CANCER PATIENTS | 125 |
| <i>Muminov K. P.</i> ALTERATIONS IN THE RIGHT CHAMBERS OF HEART IN COPD | 130 |
| <i>Navruzova Shakar Istamovna, Sa'dulloeva Iroda Kurbonovna, Suleymanova Gulrukh Suleyman qizi</i> CORRELATION INTERRELATION OF IMMUNOLOGICAL AND HORMONAL INDICES IN CHILDREN WITH CONGENITAL HEART DISEASES | 133 |
| <i>Nazyrov Feruz Gafurovich, Kurbaniyazov Zafar Babajanovich, Davlatov Salim</i> MODIFIED METHOD OF PLASMAPHERESIS IN THE TREATMENT OF PATIENTS WITH PURULENT CHOLANGITIS..... | 136 |
| <i>Nazyrov Feruz Gafurovich, Kurbaniyazov Zafar Babajanovich, Akbarov Mirshavkat Mirolimovich, Askarov Pulat Azadovich</i> RESULTS OF SURGICAL TREATMENT OF "FRESH" INJURIES OF MAGISTRAL BILE DUCTS..... | 142 |
| <i>Nechytailo Yuriy, Pidmurniak Olesya</i> AMBULATORY BLOOD PRESSURE MONITORING IN ADOLESCENTS WITH ENDOCRINE PATHOLOGY..... | 147 |
| <i>Rasulova Khurshidakhon Abduboriyevna, Nishonov Shokhidbek Yusufjonovich</i> STROKE BURDEN IN ASIA: TO THE EPIDEMIOLOGY IN UZBEKISTAN | 150 |
| <i>Rasulova Mukhsina Razikovna</i> FORENSIC EXAMINATION OF FRACTURES OF THE BONES OF THE NOSE | 156 |
| <i>Raximov Ilxom Raximovich</i> AN INVESTIGATION OF INDICATORS OF SOME CYTOKINES IN PATIENTS WITH CUTANEOUS LEISHMANIASIS IN THE PROCESS OF TREATMENT | 159 |
| <i>Tilliashaykhov Mirzogolib Nigmatovich, Zakhirova Nargiza Nematovna</i> FRONT IMPRESSIONS OF SMALL PANCRE WITH RECONSTRUCTION OF MUSCULAR SLOT IN PATIENTS WITH LOCALLY EXTENDED UTERINE CERVICAL CANCER ... | 163 |
| <i>Tursunova Nodira Isroilovna, Atakhanova Nigora Ergashevna</i> THE SIGNIFICANCE OF PREOPERATIVE RADIATION THERAPY IN THE TREATMENT OF UTERINE BODY CANCER, DEPENDING ON P53 AND BCL-2..... | 165 |
| <i>Ubaydullaeva Nilufar Bahromhodjaevna</i> DYNAMICS OF THE QUALITY OF LIFE OF WOMEN WITH GRAVES' DISEASE, DEPENDING ON THE DURATION OF THE DISEASE..... | 169 |
| <i>Usmanova Shakhnoza Erkinovna, Yakubov Abdujalol Vahabovich</i> INFLUENCE OF SOME I-APF ON CYTOPROTECTION MECHANISMS IN INDOMETHASIN-INDUCED GASTROPATHYARTHRITIS..... | 174 |
| <i>Khamroev Farhod Sharafovich</i> APPLICATION MAGNIT LAZER THERAPY WITH LAZER ACUPUNCTURE PATIENTS WITH INFANT CEREBRAL PALSY | 177 |

*Kurbanova Zumrad Chutbaevna,
assistant of the Department of Hematology,
E-mail: zum7.7@mail.ru*

*Babajanova Shoirra Agzamovna,
MD, professor of the Department of Hematology,
Tashkent Medical Academy*

VIOLATIONS OF COAGULATIVE HEMOSTASIS IN PATIENTS WITH LIVER CIRRHOSIS OF THE VIRAL ETIOLOGY

Abstract:

The objective of the research is to carry out comparative clinical and laboratory characteristics of coagulopathy in patients with liver cirrhosis of viral etiology.

Materials and methods: clinical studies were carried out in the hepatobiliary department of the Tashkent medical academy. The study included 80 patients with liver cirrhosis of the viral etiology, in the stage of decompensation of class B according to Child-Pugh and 20 patients with liver cirrhosis of non-viral etiology.

Results: the decrease of blood coagulation system activity is more pronounced in the group of hepatitis B (55.5%) and C (33.3%) positive patients with liver cirrhosis, in contrast to non-viral liver cirrhosis.

Keywords: hemostasis, coagulopathy, hypocoagulation, liver cirrhosis, hemorrhage syndrome.

Introduction. Over the past decades, the incidence of liver cirrhosis has remained consistently high, accounting for 30% of the total number of patients with chronic diffuse liver diseases treated in specialized hospitals. In 50–85% of patients with liver cirrhosis is complicated by portal hypertension, the manifestation of which is the extension of varicose veins in the esophagus and in the cardiac part of the stomach. Bleeding from the extension of varicose veins occurs in every fourth patient, reaching 50–70% of mortality already at the first episode [3]. The share of viral etiology of liver cirrhosis (in the outcome of chronic hepatitis B, C, B+D) is from 10 to 23,5% of all cirrhosis [2; 6]. In recent years, the number of cirrhosis has increased about 30,3% as a result of viral hepatitis C [1, 5]. The liver plays an important role in hemostasis, so diffuse lesions of its parenchyma lead to complex blood clotting disorders [8]. At present, it is believed that changes in hemostasis in liver cirrhosis affect pro- and anticoagulation systems, while maintaining a balance between them, however due to the reduced reserve of each of these systems, it easily shifts towards hypo- or hypercoagulation [7; 9]. In liver cirrhosis, changes in the hemostatic system are complex and multidirectional. Complex and ambiguous changes in the hemostatic system in patients with impaired liver function can lead to various complications. Such as bleeding is the most common clinical manifestation due to thrombocytopenia and thrombocytopathy, and a violation of the synthesis of coagulation factors, as well as the activation of fibrinolysis [4].

Development of a comprehensive assessment of hemostatic homeostasis in chronic liver diseases is in the research to solve this problem. Many pathogenetic aspects of hemorrhagic syndrome and the role of hemostatic changes are not explored

in chronic liver diseases. Analyzing hemostatic disorders in patients with liver cirrhosis of viral etiology, and appropriate hemostatic therapy on time will reduce the risk of hemorrhagic complications. In this regard, we have undertaken this study.

The objective of the research is to carry out comparative clinical and laboratory characteristics of coagulopathy in patients with liver cirrhosis of viral etiology.

Materials and methods. Clinical studies were carried out in the Hepatobiliary Department of the Tashkent medical academy. The study included 80 patients with liver cirrhosis of the viral etiology, in the stage of decompensation of class B according to Child-Pugh and 20 patients with liver cirrhosis of non-viral etiology. Group I consisted of 30 patients with positive virus of hepatitis B, group II of 20 patients with positive virus of hepatitis B and D, group III of 30 patients with positive virus of hepatitis C and group IV consisted of 20 patients with liver cirrhosis of non-viral etiology. From men – 56 (56%) and women-44 (44%). The age of patients ranged from 21 to 69 years, the average age of the examined patients was 49.2 ± 12.9 years. All patients were with a long term chronic liver disease, the duration of liver cirrhosis amounted to an average of 4.15 ± 1.74 years. Among the sick patients of reproductive age were 43.97%. The control group consisted of 20 patients who did not suffer from liver and biliary tract diseases, with negative results on hepatitis B and C markers. Hematological, hemostasiological and methods of variation statistics were used. Hematological studies were carried out on the hematological analyzer "Mindrey 3000" (China) microscopic studies of platelets were carried out on a light microscope "Micromed" (Russia), the coagulogram was studied on the coagulometer "Clot" (China) using a

set of reagents "Human", the biochemical analysis was carried out on the biochemical analyzer "Mindrey" (China) using a set of reagents "Human".

Results and discussion. Coagulation hemostasis is a cascade of reactions involving plasma coagulation factors. The process of blood clot formation is divided into 3 phases. To assess the first phase of blood clotting, the time of blood clotting by Moravitz and activated partial thromboplastin time (APTT) were investigated (table 1).

APTT-test that reveals only plasma defects of the internal system of activation of X factor in the first phase of blood

clotting. The lengthening of the APTT reflects the deficiency of plasma factors XII, XI, IX, VIII and is observed with their significant decrease (below 10–25%) and indicates the predominance of hypocoagulation, which was reliably shown in groups I and II. In group III and IV, the APTT was slightly increased.

Pronounced lengthening of blood clotting time (BCT) is observed with a deep deficiency of blood clotting factors. Blood clotting time was also significantly extended in groups I, II and III. In IV group BCT has been slightly extended.

Table 1. – Evaluation of the first phase of blood clotting in liver cirrhosis

| Groups | Start of BCT, sec | End of BCT, sec | APTT, sec |
|-----------------------|-------------------|-----------------|---------------|
| Control group, n = 20 | 125 ± 12.5* | 248 ± 13.2* | 29.1 ± 2.24* |
| I group, n = 30 | 352 ± 23.2* | 482 ± 32.5* | 39.4 ± 3.01* |
| Group II, n = 30 | 372 ± 26.5* | 488 ± 29.8* | 41.0 ± 6.80* |
| Group III, n = 20 | 212 ± 13.4* | 306 ± 19.7* | 36.57 ± 2.55* |
| Group IV, n = 20 | 139 ± 9.4* | 248 ± 11.9* | 36.5 ± 1.25* |

Note: * – $p < 0.05$ was reliable with respect to the control group

As can be seen from the table, expressed violations of the first phase of plasma hemostasis have increased in patients with cirrhosis of the liver viral etiology, while in patients with liver cirrhosis non-viral etiology were slightly shifted towards hypocoagulation. For the study of the second phase of plasma hemostasis were determined prothrombin time, prothrombin index.

Prothrombin time characterizes the first and second phases of plasma hemostasis and reflects the activity of prothrombin complex – factors VII, V, X and prothrombin factor II. The increase in prothrombin time indicates a tendency to hypocoagulation. Studies have shown a significant mixing of hemostatic system in the direction of hypocoagulation in pa-

tients of groups I and II, while patients of groups III and IV had a tendency to hypocoagulation.

The prothrombin index calculated from the prothrombin time (PT) reflects both the first phase of blood clotting (prothrombin formation) and the second phase (thrombin formation), and they were within the range of $68.47 \pm 13.2\%$ and $62.35 \pm 2.78\%$ in the first and second groups respectively. This indicated no pronounced hypocoagulation. In the III and IV groups, this was $70.39 \pm 15.29\%$ and $69.5 \pm 13.36\%$ respectively, indicating moderate hypocoagulation. Data of prothrombin time (PT) and prothrombin index (PTI) are given in (table 2).

Table 2. – Evaluation of the second phase of blood clotting in liver

| Groups | PT, sec | PTI, % |
|-----------------------|---------------|----------------|
| Control group, n = 20 | 15.57 ± 1.03* | 95.6 ± 11.79* |
| I group, n = 30 | 19.68 ± 3.01* | 65.47 ± 13.2* |
| II group, n = 30 | 20.93 ± 0.75* | 62.35 ± 2.78* |
| III group, n = 20 | 19.89 ± 2.84* | 66.39 ± 15.29* |
| IV group, n = 20 | 19.61 ± 2.29* | 69.5 ± 13.36* |

Note: * – $p < 0.05$ was reliable with respect to the control group

To characterize the third phase of blood clotting, the number of fibrinogen, plasma tolerance to heparin, thrombotest and thrombin time were determined. Fibrinogen – I factor of blood coagulation and stable protein – globulin are synthesized mainly in the liver. So the study of fibrinogen indicates a pronounced hypocoagulation. This showed a significant decrease in the concentration of plasma fibrinogen in all groups with liver cirrhosis of viral etiology. And this was more decreased in groups

I, II, and III, while in groups IV these changes were unaffected. Thrombin time is the time required for the formation of a fibrin clot in plasma when thrombin is added to it. It depends on the fibrinogen concentration and activity of thrombin inhibitors (antithrombin III, heparin); it is used to evaluate both the third phase of blood clotting and the state of natural and pathological anticoagulants. The study of the third phase of plasma-coagulation hemostatic link showed that patients of I, II, III and IV

groups had a distinct elongation of thrombin time compared to the control group. Plasma tolerance to heparin (PTH) characterizes the state of the blood coagulation system as a whole, at the same time is an indirect indicator of the state of thrombin. The lowering of TPG depends on factors V, VIII, IX, XII. Similar changes were found in the previous analysis: in patients of I, II, III and IV groups, compared with the control group, there is a clear decrease in plasma tolerance to heparin. Thrombotest

(TT) is determined by the intensity of the formation of a fibrin clot. Grade III is characterized by the inferiority of loose clot fourth degree the clot decorated and glued to the wall of the tube, V the extent of the clot fills the entire volume of the tube. The main part of the indicators of thrombotest were III degree in patients with liver cirrhosis.

Indicators of thrombin time, plasma tolerance to heparin (PTH) and thrombotest (TT) are shown in (table 3).

Table 3. – Indicators of the third phase of plasm hemostasis in liver cirrhosis

| Performance | Control group | I group | IIgroup | IIIgroup | IVgroup |
|-------------------|---------------|---------------|---------------|---------------|---------------|
| Trombin time, sec | 26.75 ± 1.67* | 37.03 ± 4.52* | 37.6 ± 4.84* | 37.73 ± 3.28* | 36.31 ± 1.56* |
| PTH, sec | 310.5 ± 35.3* | 544.7 ± 40.9* | 550.3 ± 36.2* | 537.9 ± 23.9* | 533.5 ± 36.9* |
| TT | 4.8 ± 0.10* | 3.07 ± 0.28* | 3.05 ± 0.50* | 3.13 ± 0.83* | 3.56 ± 0.43* |

Note: * – $p < 0.05$ was reliable with respect to the control group

Thus, our study of the plasma-coagulation level of hemostatic system in patients with liver cirrhosis of viral etiology showed the presence of significant deviations in the direction of hypocoagulation shift. This was manifested by the lengthening of the blood clotting time, activated partial thromboplastin time, prothrombin time, prothrombin index, plasma tolerance to heparin and thrombin time, a decrease in the amount of fibrinogen, the degree of thrombotest. Given that APTT lengthens with a deficit of factors XII, XI, IX and VIII, we can assume that the formation of these factors in patients with cirrhosis of the liver is disturbed. It should be noted that the decrease in the activity of the blood coagulation system is more pronounced mainly in I, II and III groups of patients, while hypocoagulation was insignificant in IV groups.

Conclusions:

1. The plasma coagulation hemostasis significantly deflected in the direction of hypocoagulation in the liver cirrhosis of viral etiology. This is manifested by a decrease of the blood clotting time, activated partial thromboplastin time, prothrombin time, prothrombin index, plasma tolerance to heparin and thrombin time, a decrease in the amount of fibrinogen, the degree of thrombotest.

2. It should be mentioned that the decrease in the activity of the blood coagulation system is more pronounced in patients with liver cirrhosis viral etiology in comparison with liver cirrhosis non-viral etiology.

References:

1. Бобров А. Н., Белякин С. А., Плюснин С. В. Смертельные осложнения у больных циррозом печени по данным 15-летнего наблюдения (1996–2010 гг.) в многопрофильном госпитале // Рос. журн. гастроэнтерол., гепатол., колопроктол. 2011. – т. 21. – № 1. – С. 148–153.
2. Губергриц Н. Б., Голуб Е. Ю. Хроническая абдоминальная ишемия // Сучасн. медичн.технологі. 2010. – № 2. – С. 81–90.
3. Заривчакский М. Ф., Мугатаров И. Н. и др. Профилактика пищеводно-желудочных кровотечений у больных циррозом печени // Актуальные вопросы трансфузиологии и клинической медицины. 2015. – № 1. – С. 405–411.
4. Куркина И. А., Волкова М. В., Маевская М. В., Ивашкин В. Т. Геморрагический синдром при циррозе печени // Рос. журн. гастроэнтерол., гепатол., колопроктол. 2012. – т. 22. – № 6. – С. 14–21.
5. Никифорова О. Е., Бессонова Е. Н., Строганова О. А. Особенности гемостаза для проведения альбуминового диализа у больных с терминальной стадией хронических заболеваний печени // Вестник Уральской медицинской академии науки. – 2011. – № 1 (33). – С. 44–47.
6. Ющук Н. Д. Эпидемиология инфекционных болезней: учебное пособие. – 3-е изд., перераб. и доп. – М.: ГЭОТАР – Медиа, 2014. – 496 с.
7. Clevenger B., Susan V. Mallett. Transfusion and coagulation management in liver transplantation // World Journal of Gastroenterology. 2014. – vol. 20. – P. 6146–6158.
8. Hartmann M., Cynthia Szalai, Fuat H. Saner. Hemostasis in liver transplantation: Pathophysiology, monitoring, and treatment // World Journal of Gastroenterology. 2016. – vol. 22. – No. 4. – P. 1541–1550.
9. Lisman T., Porte R. J. Rebalanced hemostasis in patients with liver disease: evidence and clinical consequences // Blood. – 2010. – vol. 116. – No. 6. – P. 878–885.