American Journal of Interdisciplinary Research and Development
ISSN Online: 2771-8948
Website: www.ajird.journalspark.org
Volume 14, March, 2023

STATE OF VASCULAR-THROMBOCYTARY HEMOSTASIS IN CHRONIC LIVER DISEASES OF VIRUS ETIOLOGY

Nuriddinova Nodira Faxriddinovna.,
Kurbonova Zumrad Chutbaevna
Tashkent Medical Academy, Tashkent
e-mail: abdurahimnadi@gmail.com

Annotation
The review of the literature provides information on changes in vascular-platelet hemostasis, platelet count, disorders of adhesion and aggregation properties, hemorrhagic complications in chronic liver disease. The results of the study of vascular-platelet hemostasis in patients with chronic liver diffuse disease were analyzed.

Keywords: Hepatotropic viruses, hepatitis, liver cirrhosis, platelets, adhesions, aggregation.

The physiology of the hemostasis system is closely related to the function of the liver, because liver cells produce most of the factors of the coagulation and fibrinolytic system. As a result, chronic or acute diseases of this organ have a profound effect on the hemostasis system. Symptoms such as bleeding from varicose veins of the esophagus, hematoma, hemorrhagic purpura, nasal bleeding, odontorrhea, menorrhagia are among the actual clinical problems for patients with liver cirrhosis [9].

Among the pathogenetic changes of hemostasis, the pathology of vascular-platelet hemostasis associated with angiotrophic, adhesion, aggregation activities of platelets, microcirculatory disorders leads to the exacerbation of this disease, the emergence of severe complications, the formation of chronic forms of liver diseases [1]. Histological activity and development of fibrosis increase endothelial damage, decrease the number and function of platelets [6].

Platelets, which are a component of the vascular-platelet stage of hemostasis, are damaged quantitatively and qualitatively in chronic diffuse liver diseases (CDLD). In CDLD, thrombocytopenia, which is a characteristic pathology of cellular hemostasis, develops thrombocytopathy, manifested by impaired adhesion and aggregation functions [19].

Thrombocytopenia is a decrease in the number of platelets from 150 x109/l, which can occur in chronic and acute liver failure. The main cause of thrombocytopenia in patients with liver cirrhosis is hypersplenism, in which increased sequestration of platelets in the spleen is observed. In addition, intoxication of the body, impaired synthesis of platelets

due to folic acid deficiency, decreased production of thrombopoietin in the liver, disseminated intravascular coagulation syndrome in CDLD, production of autoantibodies can be the main causes of thrombocytopenia. In patients with decompensated liver cirrhosis, 90% of platelets are sequestered in the spleen [8].

In a study by Fusegawa H. and co-authors (2002), patients with chronic hepatitis C and liver cirrhosis found a significant decrease in the number of platelets. Also, the study of various forms of liver disease associated with chronic hepatitis B virus (chronic hepatitis 8.4%, cirrhosis 27.5% and hepatocellular carcinoma - 34.5%) showed a decrease in the number of platelets. In conclusion, thrombocytopenia in CDLD is one of the main problems leading to the development of major bleeding [19].

Platelets are not only involved in blood clotting, but also produce many growth factors necessary for the development of organs and tissue regeneration. At the same time, it suppresses the activity of hepatic stellate cells, which produce collagen and reduce liver fibrosis. The regenerative effect of platelets is directly on hepatocytes, liver sinusoidal endothelial cells and Kupffer cells. It plays an important role in platelet repair of liver damage and is used as an antifibrotic therapy [21]. Another study found that platelet transfusion improved liver function in patients with liver cirrhosis [18]. But in recent years, the treatment of hemostasis pathology reduces the transfusion of blood components, which in many cases helps to prevent the complications of hemocomponent therapy and the risk of hemotransmissible infections [10].

The main disturbance of hemostasis in liver diseases is associated with adhesion and aggregation dysfunction of platelets [17]. According to M.N. Ustinova, the increase in the aggregation function of platelets is observed with an increase in the activity of organospecific enzymes and transaminases. An increase in the activity of transaminases is a sign of cytolytic syndrome, in which a decrease in platelet aggregation is observed [7].

In patients with severe cytolysis and mesenchymal inflammatory syndrome, a decrease in the activity of cyclic adenosine monophosphate, cyclic guanosine monophosphate, P-thromboglobulin, platelet factor 4 and cyclic adenosine monophosphate leads to a decrease in platelet aggregation ability. In the decompensation phase of liver cirrhosis, profound changes in platelet function are observed [6]. The amount of alpha granules, beta-thromboglobulin and platelet factor 4 in the blood serum is up to 7 times higher than in healthy people. In chronic liver diseases, the megaplatelet fraction increases in the morphological parameters of platelets. In the studies of Sayed D., it was found that active platelets, active monocytes, aggregation of monocytes and platelets are high in liver cirrhosis [21].

At the same time, the effect of antioxidant protective enzymes on platelets, the role of lipid peroxidation products in the destabilization of erythrocyte and platelet membranes is known. Disturbances of platelet aggregation function in patients with CDLD determine the degree of impairment of the antioxidant defense system [10].

Hemostasis disorders in end-stage liver disease have a major impact on the prognosis of liver transplantation. Liver transplantation can cause profound changes in the hemostasis system. Depletion of clotting factors and platelets can cause massive bleeding during surgery, and ischemia and tissue injury can aggravate coagulopathy [13].

Disruption of intrahepatic hemodynamics, which is of great importance in the development of liver cirrhosis, leads to endothelial dysfunction and is the basis of the pathogenesis of chronic hepatitis [1]. Endothelial cells of the liver sinusoids not only act as a barrier between the sinusoids and the liver parenchyma, but also actively participate in the inflammatory reaction, enhance adhesion and antigen production, destroy anti-inflammatory substances or, on the contrary, produce inflammatory mediators emits [3]. At the same time, the effect of the endothelium on aggregation is related to the production of prostacyclin, nitric oxide. The mechanism of action of prostacyclin and nitric oxide is the release of calcium ions from platelets, which reduces the aggregation function of platelets. The anticoagulant effect of the endothelium is associated with the production of endogenous heparins, tissue thromboplastin inhibitor, tissue plasminogen activator, thrombomodulin, antithrombin III. Endothelial dysfunction predicts the pathogenesis of a number of diseases. Today, the pathogenetic role of endothelial dysfunction is recognized and is an important link in the development of cardiovascular diseases, diabetes, bronchial asthma, oncological diseases, intoxication infections. The activity of single-layer vascular endothelium is important in treatment and prevention practices, which is the reason for the emergence of a new strategic concept of vascular medicine [4].

Endothelial cells are damaged under the influence of immune complexes, inflammatory mediators, and viruses [9]. Coagulation factors of the hemostasis system are produced by endothelial cells and hepatocytes, which ensure the interdependence of liver function and vascular endothelium. Endothelial dysfunction develops in liver diseases, which is considered the cause of many pathological processes. Endothelial damage leads to the production of biologically active substances, which disrupts the balance between the synthesis of coagulation and anticoagulant factors. In endothelial dysfunction, the balance between vasodilation, production of angioprotective, prothrombotic and proliferative factors is disturbed [18].

Violation of the functional state of the endothelium leads to an increase in the cytolytic process in the liver. Von Willebrand factor, which is an indicator of the hemostasis system, increases in liver cirrhosis [14]. In the study of M.J. Hollestelle, it was shown that the amount of von Willebrand factor in the plasma increases more than 10 times during the decompensation stage of liver cirrhosis. This number of platelets helps to compensate for their reduced adhesion function [15]. In patients with liver cirrhosis, binding of platelets to Willebrand factor decreases by 50%, which increases the risk of hemorrhagic complications [12]. Regardless of the etiology, the activity of the Willebrand factor is much higher in CDLD [13].

Many factors of blood coagulation are synthesized by endothelial cells and hepatocytes, so the liver and endothelium have an effect on hemostasis. In CDLD, the spectrum of biologically active substances produced by the endothelium changes, which leads to an imbalance between the synthesis of prothrombogenic and antithrombotic, dilatant and spastic factors. As a result, the synthesis of vasoconstrictors and procoagulants increases, which leads to vessel spasm. As a result of long-term exposure to a harmful factor, the endothelium begins to cause a number of systemic pathological processes (inflammation, thrombosis, etc.) [9]. Prostacyclin, increased synthesis of nitric oxide releases calcium ions from smooth muscles and platelets, which prevents spasm of blood vessels and aggregation of platelets, helps to activate defective platelets under natural conditions [11].

Thrombomodulin, which acts as a thrombin receptor, is also synthesized in vascular endothelium. It determines the direction and speed of the hemostasis process. This protein, which binds thrombin and removes it from the blood clotting system, activates protein C up to a thousand times and forms antithrombotic complexes together with anticoagulant proteins VIIIa, C and S to prevent clotting. Thus, thrombin, the most active factor of coagulation, is synthesized by the liver and blocked by the endothelium through thrombomodulin receptors [22].

Death and fibrosis of the liver parenchyma in patients with liver cirrhosis with repeated thrombosis or hypercoagulation thrombotic complications (in the portal vein system, mesenteric veins, liver veins, veins of limbs, pulmonary embolism); causes the development of portopulmonary syndrome (lung endothelial dysfunction, microvascular thrombosis in the lungs). Portal vein thrombosis occurs in 0.6–26% of patients with liver cirrhosis. The prevalence of portal vein thrombosis increases with advancing liver disease [16].

Hypercoagulation associated with chronic liver disease can lead to liver parenchymal damage and death [5]. In the last ten years, laboratory diagnostics of hemostasis and fibrinolysis system in CDLD have undergone significant changes. Standard complex tests for the detection of hemostasis disorders lose their diagnostic value in this group of patients [4]. The problem of predicting hemorrhagic syndrome in liver cirrhosis with the help of modern laboratory tests remains open. There is no standard strategy for the treatment and prevention of hemorrhages in CDLD. Randomized controlled trials are needed to evaluate laboratory tests in predicting bleeding or thrombosis in patients with cirrhosis.

REFERENCES

1. Бабаджанова Ш.А., Курбонова З.Ч., Тожибоева Д.А. Характеристика адгезивной и агрегационной функции тромбоцитов у больных с циррозом печени вирусной этиологии // Ўзбекистон гематологлари ва трансфузиологларининг IV халқаро илмий-амалий конгресси. - Тошкент, 2018, - Б. 19-21.

2. Булатова И.А. Функциональное состояние эндотелия и его диагностическая значимость при оценке тяжести хронических диффузных заболеваний печени: автореф. дис. канд. мед.наук. – Екатеринбург, 2009. – 17с
3. Иноятова Ф.Х., Бабаджанова Ш.А., Курбанова Н.Н., Курбанова З.Ч. Гемостаз: основные принципы функционирования, методы оценки, патофизиологические аспекты: методическое пособие. – Ташкент, 2014. – 46 с.
4. Курбонова З.Ч. Вирус этиологияли сурункали гепатит ва жигар циррозида гемостаз тизими бузилиши хусусиятлари: автореф. дис. кан. мед. наук. – Тошкент, 2019. -45 с.
5. Курбонова З.Ч. Нарушение сосудисто–тромбоцитарного звена гемостаза у больных с хроническими гепатитами и циррозом печени вирусной этиологии // Журнал проблемы биологии и медицины. – 2018. - № 3 (102). – С. 40-43.
6. Курбонова З.Ч., Бабаджанова Ш.А. Функциональная характеристика тромбоцитов у больных циррозами печени вирусной этиологии // Российская наука в современном мире. – Москва, 2019. – С. 47-48.
7. Курбонова З.Ч., Бабаджанова Ш.А. Нарушение системы гемостаза при хронических диффузных заболеваниях печени: монография. Тошкент, "Ҳилол нашр" босмахонаси, 2021. С. 106-108.
8. Курбонова З.Ч., Бабаджанова Ш.А. Изучение агрегационной функции тромбоцитов у больных с циррозами печени вирусной этиологии // Сборник материалов III международного молодежного научно-практического форума «Медицина будущего от разработки до внедрения», Оренбург, 2019. -С. 482.
9. Куркина И.А., Волкова О.С., Маевская М.В., Ивашкин В.Т. Геморрагический синдром при циррозе печени // Рос. Журн. гастроэнтерол., гепатол., колопроктол. – 2012. – № 22 (6). – С.14–21.
10. Павлов Ч.С., Шульпекова Ю.О., Золотаревский В.Б., Коган Е.А., Ивашкин В.Т. Современные методы ранней диагностики фиброза печени // Клиническая медицина. – 2005. – № 12. – С. 58–60.
11. Саидов А.Б., Сайфутдинова З.А., Каримов Х.Я. Лекарственно-индуцированный токсический гепатит: современные воззрения // Назарий ва клиник тиббиёт, 2021. -№3. – Б. 52-58
12. Сайфутдинова З.А., Каримов Х.Я., Саидов А.Б. Механизмы нарушений при токсическом повреждении печени и пути их коррекции с помощью нового аминокислотного раствора на основе сукцината натрия и маннитола // Журнал теоретической и клинической медицины-2021. - №3. –Б. 7-11.
13. Серов В.В., Бушуева Н.В., Игнатова Т.М., Апросина З.Г. Факторы вируса и хозяина в развитии и прогрессировании хронических вирусных гепатитов С и В // Российский журнал гастроэнтерологии, гепатологии и колопроктологии. – 2006. – № 4. – С. 12–23.

14. Устинова М.Н. Агрегация тромбоцитов у больных хроническими диффузными заболеваниями печени и ее коррекция внутривенной озонотерапией: автореф. дис. кан. мед.наук. – Москва, 2005. –25 с.
15. Al Ghumlas A.K., Abdel Gader A.G., Al Faleh F.Z. Haemostatic abnormalities in liver disease: could some haemostatic tests be useful as liver function tests? //Blood Coagul Fibrinolysis. – 2005. – Vol. 16(5), –P. 329–335.
16. Batirova A.S., Bakanov M.I., Surkov A.N. The modern concepts of hemostasis system under Chronicdiseases of liver: the publication review // Klin. Lab. Diagn. – 2015. – Vol. 60(8), P. 40–44.
17. Bienholz A., Canbay A., Saner F.H. Coagulation management in patients with liver disease // Med. Klin. Intensivmed Notfmed. – 2016. –Vol. 111(3), – P. 224–234.
18. Caldwell S.H., Hoffman M., Lisman T. et al. Coagulation disorders and hemostasis in liver disease: pathophysiology and critical assessment of current management // Hepatology. – 2006. – Vol. 44, – P. 44.
19. Francoz C., Belghiti J., Vilgrain V. et al. Splanchnic vein thrombosis in candidates for liver transplantation: usefulness of screening and anticoagulation // Gut. – 2005. Vol. 54 (5), – P. 691–697.
20. Hartmann M., Cynthia S., Fuat H. Hemostasis in liver transplantation: Pathophysiology, monitoring, and treatment // World Journal of Gastroenterology. – 2016. – Vol. 22 (4), – P. 1541–1550.
21. Hollestelle M.J., GeertzenH. G.M., Straatsburg I.H., van Gulik T. M., van Mourik J. A. Factor VIII expression in liver disease // Thromb Haemost. – 2004. – Vol. 91, – P. 267–275.
22. Hollestelle M.J., Poyck P.P., Hollestelle J.M., Marsman H.A., Mourik J.A., Gulik T. M. Extrahepatic factor VIII expression in porcine fulminant hepatic failure // J. Thromb Haemost. – 2005. – Vol. 3, – P. 2274–2280.
23. Huard G., Bilodeau M. Management of anticoagulation for portal vein thrombosis in individuals with cirrhosis: A systematic review // Int. J. Hepatol. –2012. – Vol. 2012, – P. 6–7.
24. Iancu R.I., Iancu D., Murărescu D., Nechifor M., Costuleanu M. Platelet functions in acute and chronic experimentally induced hepatopathia // Rev. Med. Chir. Soc. Med. Nat. Iasi. – 2010. – Vol. 114(4), – P. 1101–1106.
25. Kurokawa T., Ohkohchi N.. Platelets in liver disease, cancer and regeneration // World J. Gastroenterol. – 2017. – Vol. 23(18), – P. 3228–3239.
26. Kurbonova Z.Ch., Babadjanova Sh.A. Violations of coagulative hemostasis in patients with liver cirrhosis of the viral etiology. European science review. 2018, 7-8:122-125.
27. Northup P.G., Fallon M.B., Sundaram V. Hypercoagulation and thrombophilia in liver disease //J. Thromb. Haemost. – 2008. –Vol. 6, – P. 2–9.

28. Sayed D., Amin N.F., Galal G.M. Monocyte–platelet aggregates and platelet micro–particles in patients with post–hepatitic liver cirrhosis // Thromb Res. – 2010. – Vol. 125(5), – P. 228–233.
29. Tripodi A. Hemostasis abnormalities in cirrhosis // CurrOpinHematol. – 2015. – Vol. 22, – P. 406.