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Modern Aspects of the Study and Treatment of Hemophilia B in the Republic of Uzbekistan

Juraeva Nodira Tukhtapulatovna [1]
Mahmudova Aziza Dzhumanovna [2]
Ismatova Gulira Nazimovna [3]
Mamatkulova Dilrux Fayzullaevna [4]

[1] *Doctoral student, Republican Specialized Scientific and Practical Medical Center of Hematology, Tashkent, Uzbekistan*
[2] *Doctor of Medical Sciences, Republican Specialized Scientific and Practical Medical Center of Hematology, Tashkent, Uzbekistan*
[3] *Republican Specialized Scientific and Practical Medical Center of Hematology, Tashkent, Uzbekistan*
[4] *Candidate of Medical Sciences, Republican Specialized Scientific and Practical Medical Center of Hematology, Tashkent, Uzbekistan*

Annotation. Hemophilia B is the hereditary disease of the blood coagulant system linked to X-chromosome, which is characterized by decreasing or molecular anomalies of the IX factor of coagulation. The coagulation factor IX gene is localized on the X chromosome (Xq27.1-q27.2), it is characterized by X-linked recessive inheritance. The relevance of studying this subject is that at untimely diagnostics and late begun treatment hemophilia can lead to serious consequences. In the treatment of patients with hemophilia, the main component is timely adequate lifelong replacement therapy, which makes it possible to replenish the level of the deficient factor in the plasma. The main goal of such hemostatic therapy is to increase the content of the deficient factor in the patient's blood to an effective level. The aim of this work is to study the level of factor IX in patients with hemophilia during replacement therapy with plasma drugs of blood coagulation factors.

Key words: hemarthrosis, coagulopathy, hemorrhage, blood coagulation.

INTRODUCTION

Hemophilia is a rare hereditary disease associated with impaired coagulation (the process of blood clotting). With this disease, hemorrhages occur in the joints, muscles and internal organs, both spontaneously and as a result of trauma or surgery. With hemophilia, the risk of death of a patient from a hemorrhage in the brain and other vital organs increases sharply, even with a minor injury. Patients with severe hemophilia are subject to disability due to frequent hemorrhages in the joints (hemarthrosis) and muscle tissue (hematomas). Hemophilia refers to hemorrhagic diathesis caused by a violation of the plasma link of hemostasis (coagulopathy).

Hemophilia B is caused by a deficiency of plasma coagulation factor IX and is characterized by hematoma-type bleeding. Factor IX is a component of plasma thromboplastin. The cause of bleeding is a violation of the first phase of blood coagulation - the formation of thromboplastin due to a hereditary deficiency of the

antihemophilic factor. Clinically, as mentioned earlier, it manifests itself in the hematoma type of bleeding, which is characterized by hemarthroses, hematomas, late bleeding, etc. As a result of Factor IX deficiency, the blood may not clot for several hours, as a result of which anemia may develop. The leading symptoms of hemophilia B are increased bleeding from the first months of life; subcutaneous, intermuscular, subfascial, retroperitoneal hematomas caused by bruises, cuts, various surgical interventions; hematuria; profuse post-traumatic bleeding; hemarthrosis of large joints with secondary inflammatory changes that lead to the formation of contractures and ankylosis.

Usually men suffer from the disease (sex-linked inheritance), while women usually act as carriers of hemophilia and can give birth to sick sons or carrier daughters.

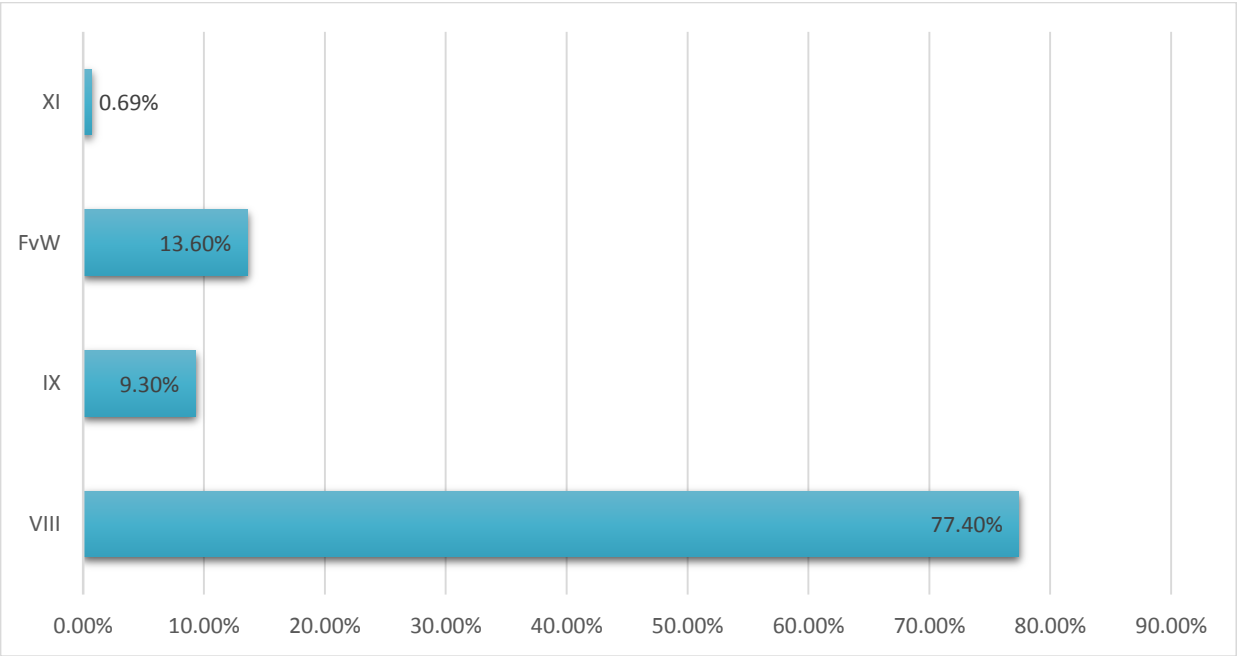
Types of hemophilia are distinguished on the basis of a deficiency of a certain blood clotting factor in the patient's body. Basic information about the types of the disease is presented in the **table.1.**

Table.1.

Type	Description
Hemophilia A	It is diagnosed in 84-86% of people suffering from the pathology in question. Caused by a deficiency of coagulation factor VIII (antihemophilic globulin).
Hemophilia B	Occupies a share of 12-13% of clinically diagnosed cases of hemophilia. It develops against the background of a deficiency of coagulation factor IX (thromboplastin)
Hemophilia C	It occurs no more than 1-2%. It becomes the result of insufficient production of factor XI of blood coagulation.

Coagulation factor deficiency % of patients in the group of hereditary coagulopathy in the Republic of Uzbekistan. The total number of patients was: 2040. Of these, Hemophilia A-1580 (77.4%), Von Willebrand's disease-257 (13.6%), Hemophilia B-189 (9.3%), Hemophilia C-14 (0, 69%), (**Fig. 1**)

Figure 1. Frequency of hereditary (Hemophilia A, B, C and von Willebrand disease) coagulopathy in the Republic of Uzbekistan (%): **VIII**-1580(77.4%), **FvW**-257(13.6%),**IX**-189(9.3%),**XI**-14(0.69%).



Coagulation factor deficiency; % of patients in the group of hereditary coagulopathy in Republic of Uzbekistan.

Scientific novelty

Early detection and improvement of diagnosis and treatment of patients with Hemophilia B in the Republic of Uzbekistan, as well as reduction of disability and mortality among them.

Materials and research methods.

Diagnosis is based on anamnesis data: signs of increased bleeding in other family members, clinical signs of the disease and laboratory data.

Coagulological examination is carried out in stages:

First stage. Coagulation screening for suspected hemorrhagic conditions: activated partial (partial) thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), fibrinogen amount (according to Claus), bleeding time by a standardized method (for example, according to Ivy) or instrumental evaluation of platelet function.

Second stage. It is performed with isolated APTT prolongation, or in the absence of a change in screening and the presence of clinical signs of a mild form of hemophilia.

Correction test (APTT correction by mixing the patient's plasma with normal plasma): activity of factors VIII, IX, XI and XII, ristocetin cofactor activity (Villebrand factor activity).

Third stage. It is carried out at the revealed decrease in activity f. IX.

Determination of a specific inhibitor to reduced factor IX.

Determination of a non-specific inhibitor (lupus anticoagulant) is performed with a decrease in the activity of several blood coagulation factors, prolongation of lipid-dependent tests (APTT with sensitive reagents)

The diagnosis and severity of hemophilia is established after a decrease in factor IX activity is detected, and in the absence of evidence for an acquired hemorrhagic condition associated with the appearance of an inhibitor.

APTT is the time it takes for a clot to form after the addition of special reagents to the blood plasma. This indicator is of great importance for identifying a lack of certain clotting factors. With Hemophilia, this time is increased, which indicates a decrease in the ability to form a blood clot. Determination of coagulant (clotting) activity of factors VIII, XI and von Willebrand factor to exclude Hemophilia A, C and von Willebrand disease.

In the coagulation laboratory, to determine the level of a deficient coagulation factor, a programmable coagulometer of the Sysmex-CA 660 type was used, which is an analyzer of hemostasis indicators designed to study the plasma hemostasis subsystem by clotting methods (i.e., based on recording the time of formation of a fibrin clot). The device (manufactured by Sysmex LLC, Japan) has 30 programmed methods for determining the parameters of the blood coagulation system. The coagulation link of hemostasis was assessed by the following tests: activated partial thromboplastin time (APTT), deficiency factor activity (f.VIII, IX, XI, XII, FVW), thrombin time (TT), fibrinogen (F), fibrinolytic activity (FA), the level of soluble fibrin-monomer complexes (SFMK).

Clinical case: patient D., 4 years old, first applied to the RSSPMC of Hematology. The clinical picture of the patient is bruising, hemorrhages in the skin, mucous membranes, nasal and gingival bleeding. Consanguineous marriage of parents denies. The family history of bleeding is clear. Two brothers and an uncle (mother's brother) have hemophilia B.

Results and discussion.

Laboratory data before treatment: APTT 91 sec., fibrinogen 5.8 g/l, Quick prothrombin 108%, FVII 102%, FII 98%, FV 100%; FVIII 104%, FIX 4.8%, FX 96%, FXI 95.9%, FW 101%, FXII 103%, factor IX inhibitor-0 BU,platelet aggregation with ristomycin 65%, platelet aggregation with collagen 73%, platelet aggregation with ADP 69%. The absence of an inhibitor to Factor XI made it possible to exclude acquired deficiency of XI.

In the general blood test, the patient's hemoglobin was 97 g/l, erythrocytes 3.1 x 1012/l, platelets 190 x 109/l; leukocytes 9.8 x 109/l; in a biochemical blood test - total protein 69 g/l, albumin 40 g/l, alanine

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aminotransferase 42 U/l, aspartate aminotransferase 29 U/l, creatinine 85 µmol/l.

Laboratory data after treatment: APTT 38 sec. *, fibrinogen 3.4 g/l*, Quick prothrombin 115%, FVII 105%, FII 103%, FV 100%; FVIII 114%, FIX 106%*, FX 106%, FXI 101.0%, FW 105%, FXII 101%, factor IX inhibitor-0 BU, platelet aggregation with ristomycin 68%, platelet aggregation with collagen 78%, platelet aggregation with ADP 69%.

In the general analysis of blood in a patient, hemoglobin rose by 112 g/l, erythrocytes 3.8 x 1012/l, platelets 202 x 109/l; leukocytes 7 x 109/l;

Taking into account the anamnestic, clinical and laboratory data, the patient was diagnosed with Hemophilia B. Replacement therapy was carried out with the drug, ALPROLIX, a recombinant factor of fusogen IX for the treatment of hemophilia type B. This drug is designed to correct blood clotting processes (blood clotting factors). The components present in its composition contribute to the correction of hemostatic disorders associated with a deficiency of these factors. After administration of ALPROLIX, there was a significant increase in factor IX activity to the required hemostatic level from 4.8% to 106%, a shortening of APTT from 91.0 to 38.0 sec, a decrease in fibrinogen from 5.8 g/l to 3.4 g/l . Changes in other indicators of the coagulogram (PTI, TV, FVIII, FX, FXI, F.VWF) were also noted, but they were insignificant.

Thus, the treatment is reduced to stopping the bleeding that has arisen by transfusion of media containing factor IX (plasma and recombinant blood coagulation factors IX, etc.).

Modern replacement therapy with clotting factor IX drugs has led to a decrease in the severity of the clinical symptoms of the disease, as well as an improvement in the patient's quality of life, which reduces the risk of complications.

It was shown that the restoration of factor IX activity in plasma after the administration of ALPROLIX occurs in accordance with the calculated values. The emergence of immune inhibitors in response to the introduction of the drug ALPROLIX was not observed.

The recombinant factor ALPROLIX is a highly effective hemostatic drug in the treatment of hemophilia B by increasing the level of the deficient factor.

References

1. Voitsekhovsky V.V., Landyshev Yu.S., Yesenina T.V. Treatment of bleeding of various etiologies with recombinant activated factor VII preparations. Medical Bulletin of the North Caucasus, Scientific and Practical Journal. 2008. No. 2. C138-141.
2. Davydkin I.L., Kosyakova Yu.A., Gusyakova O.A., Zubova I.A., Evseeva T.Yu. Features of the hemostasis system in hemophilia. Kazan Medical Journal. 2010. Volume 91, No. 4, P 438-441.
3. Ivashkina E.P., Vorozhtsova S.I., Ignatiev S.V., Tarasova L.N. Hemostasiological parameters in patients with hemophilia during hemoctin replacement therapy. Bulletin of the blood service of Russia. 2012. №3. C-53-56.
4. Shutov S.A., Danishyan K.I., Karagyulyan S.R., Vasiliev S.A., Kopylev K.G. Bulletin of the blood service of Russia. 2015. №2. C-68-73.5. Andreeva T.A., Selivanov E.A. Recombinant drugs and their role in the modern treatment of hemophilia - M., 2010. - No. 1. - C. 32-41.
5. Srivastava A., Brewer A.K., Mauser-Bunschoten E.P., Key N.S., Kitchen S., Llinas A., et al. Treatment Guidelines Working Group. The World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 2013; 19(1): e 1–14.
6. Sakurai Y., Takeda T. Acquired hemophilia: a frequently overlooked autoimmune hemorrhagic disorder. //Journal of Immunology Research. Vol. 2014. Article ID 320674. 10 pages.