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MODERN POSSIBILITIES FOR THE USE OF EMICIZUMAB IN HEMOPHILIA A: MECHANISM OF ACTION, CLINICAL EFFICACY AND SAFETY

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Abdumajidov Hamidulla Amanullaevich
Doctor of Medical Sciences, Professor, Professor of the 3rd Department of Surgical Diseases of the 3rd Medical Faculty of Tashkent State University, cardiovascular surgeon of the highest category, laureate of the State Prize.
Abdumajidova Nozima Hamidullaevna
Assistant of the Department of Clinical Pharmacology, Tashkent State Medical University, Tashkent, Republic of Uzbekistan.

Abstract

Hemophilia A is a hereditary coagulopathy associated with either quantitative deficiency or functional insufficiency of blood coagulation factor VIII, which leads to impaired formation of a stable fibrin clot and the development of hemorrhagic syndrome of varying severity. Although replacement therapy with factor VIII concentrates has long been the basis of pathogenetic treatment of this disease and has significantly improved patient survival, its clinical effectiveness remains limited in some cases due to the development of inhibitor forms, the need for repeated intravenous administration, variability of the hemostatic response, and insufficient control of spontaneous and recurrent bleeding episodes.

The development and introduction of emicizumab (Hemlibra) marked a qualitatively new stage in the evolution of prophylactic therapy for hemophilia A. Emicizumab is a humanized bispecific monoclonal antibody whose mechanism of action is based on functional mimicry of the cofactor activity of activated factor VIII through simultaneous binding of factors IXa and X, thereby restoring key components of the intrinsic coagulation pathway. During treatment with this drug, a sustained reduction in the frequency of hemorrhagic episodes is achieved, the need for bypassing hemostatic agents decreases, and the effectiveness of long-term prophylaxis improves both in patients with inhibitors to FVIII and in those without inhibitors.

This review systematizes current data on the molecular and pharmacological mechanism of action of emicizumab, its clinical efficacy, safety profile, therapeutic advantages compared with traditional replacement therapy, and the significance of the drug in the context of modern personalized management strategies for patients with hemophilia A.

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Keywords

hemophilia A, emicizumab, Hemlibra, factor VIII, inhibitor form of hemophilia, prophylactic therapy, monoclonal antibodies, coagulopathies, hemorrhagic syndrome.

Introduction

Hemophilia A is one of the most significant hereditary disorders of the hemostatic system and represents an X-linked recessive disease, the pathogenetic basis of which is deficiency or functional insufficiency of coagulation factor VIII. This defect is accompanied by impairment of the intrinsic coagulation pathway, reduced thrombin generation, insufficient formation of a stable fibrin clot, and, consequently, an increased tendency to spontaneous, post-traumatic, and postoperative bleeding. The clinical picture of the disease varies depending on the level of residual FVIII activity and may include hemarthroses, intramuscular hematomas, prolonged bleeding after invasive procedures, and, in severe cases, life-threatening hemorrhagic complications.

Epidemiologically, hemophilia A occurs in approximately one in 5,000 newborn boys, which determines its high medical and social significance. The chronic recurrent course of the disease leads to the gradual development of disabling musculoskeletal lesions, primarily hemophilic arthropathy, limitation of physical activity, decreased quality of life, and a substantial increase in the burden on the healthcare system.

Traditionally, the basis of hemophilia A treatment has been replacement therapy with plasma-derived or recombinant factor VIII preparations. The use of prophylactic FVIII administration regimens has significantly reduced the frequency of bleeding episodes and improved long-term prognosis. However, this therapeutic strategy has a number of fundamental limitations. The most significant of these is the development of inhibitor antibodies that neutralize the coagulation activity of the administered factor VIII. According to various data, inhibitor formation occurs in 25–30% of patients with severe hemophilia A and represents one of the most complex clinical problems in modern hematology, substantially complicating the achievement of effective hemostatic control.

Additional disadvantages of classical replacement therapy include the need for frequent intravenous administration, technical difficulties in ensuring venous access, especially in young children, marked dependence of efficacy on the pharmacokinetic characteristics of the drug and the individual patient response, as well as the persistent risk of breakthrough bleeding even during regular prophylaxis. In this regard, the development of alternative approaches aimed at

restoring hemostatic potential without direct FVIII replacement has become one of the priority areas of modern hematology.

The most significant achievement in this field has been the development of emicizumab, an innovative drug with a unique mechanism of action distinct from classical replacement therapy. Its clinical introduction has not only expanded the possibilities for treating inhibitor forms of hemophilia A, but has also generally transformed the concept of prophylactic management of this category of patients.

Mechanism of Action of Hemlibra — Emicizumab

Emicizumab (Hemlibra®) is a recombinant humanized bispecific monoclonal antibody developed to functionally reproduce the cofactor activity of activated factor VIII. Under physiological conditions, FVIIIa acts as a cofactor for FIXa, ensuring effective activation of factor X on the phospholipid surface, which is a key stage in the amplification of thrombin generation. In hemophilia A, this mechanism is impaired, resulting in a significant reduction in the efficiency of the coagulation cascade.

Emicizumab is capable of simultaneously binding activated factor IX and factor X, bringing them into spatial proximity and thereby creating conditions for a reaction analogous to the physiological function of FVIIIa. Thus, the drug does not replace the quantitative deficiency of factor VIII itself, but provides functional compensation for its cofactor activity, restoring impaired coagulation amplification.

A fundamentally important feature of emicizumab is the absence of structural homology with factor VIII, due to which the drug is not recognized by inhibitor antibodies to FVIII and retains clinical efficacy in patients with the inhibitor form of the disease. This circumstance determines its exceptional importance in the treatment of patients in whom traditional replacement therapy is ineffective or significantly limited.

Another important advantage of emicizumab is its pharmacokinetic profile. The drug is administered subcutaneously, is characterized by a long half-life averaging approximately 28 days, and allows the use of different maintenance dosing regimens — weekly, every two weeks, or every four weeks. These pharmacological characteristics provide a more stable hemostatic effect, reduce fluctuations in coagulation response activity, and improve adherence to therapy.

Clinical Efficacy of Emicizumab

The clinical efficacy of emicizumab has been convincingly confirmed in a series of multicenter international studies of the HAVEN program, the results of which have essentially formed the modern evidence base for its widespread use in prophylactic treatment of hemophilia A.

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The HAVEN 1 study was of particular importance, as it investigated the use of emicizumab in adults and adolescents with hemophilia A complicated by the presence of inhibitors to factor VIII. The data obtained demonstrated a statistically and clinically significant reduction in the annualized bleeding rate compared with the absence of prophylaxis. During emicizumab therapy, a marked decrease was observed both in the total number of hemorrhagic episodes and in the number of bleeding episodes requiring emergency hemostatic treatment.

The HAVEN 2 study confirmed the high efficacy and acceptable safety profile of the drug in children with the inhibitor form of the disease, which was of particular clinical importance given the difficulty of long-term intravenous prophylaxis in pediatric practice. The HAVEN 3 study demonstrated a pronounced reduction in bleeding frequency in patients without inhibitors, thereby expanding the clinical niche of emicizumab far beyond inhibitor hemophilia alone. In turn, HAVEN 4 confirmed that even when the drug is administered once every four weeks, a sustained prophylactic effect comparable to more frequent dosing regimens is maintained.

It is important to emphasize that the clinical efficacy of emicizumab is not limited solely to a quantitative reduction in hemorrhagic episodes. During its use, patients demonstrate significant improvements in quality-of-life indicators, reduced chronic pain syndrome, decreased anxiety associated with the risk of bleeding, increased physical activity, and better social adaptation. These effects are especially important in the context of the long-term chronic course of hemophilia A, in which the goal of treatment goes beyond laboratory correction of hemostasis and includes preservation of the patient's functional status.

From a practical point of view, a fundamentally important aspect is also the reduction in the frequency of hemarthroses and, consequently, slowing of the progression of chronic hemophilic arthropathy. This circumstance substantially increases the long-term value of emicizumab as a drug capable not only of preventing acute bleeding but also of modifying the course of the disease by preventing disabling complications.

Safety and Tolerability

Based on the combined data from clinical studies and post-marketing surveillance, emicizumab is characterized by a favorable safety profile and high overall tolerability. The most common adverse events are mild or moderate local reactions at the injection site, headache, arthralgia, and asthenic manifestations. In most observations, these adverse effects are transient, do not require discontinuation of therapy, and do not significantly affect overall adherence to treatment.

The issue of thrombotic complications deserves particular attention. The most serious adverse events, including thrombotic microangiopathy and thrombosis, were reported extremely rarely and mainly in patients who simultaneously received high cumulative doses of activated prothrombin complex concentrate (aPCC) during emicizumab therapy. This fact indicates not so much the independent prothrombotic activity of the drug, but rather the need for strict adherence to protocols of concomitant hemostatic treatment, especially in situations of breakthrough bleeding.

A significant advantage of emicizumab is the absence of induction of an inhibitor response, as well as preservation of therapeutic activity regardless of previously formed antibodies to FVIII. Clinically, this means the possibility of long-term effective use of the drug in the most complex category of patients, for whom standard replacement therapy is often ineffective, technically difficult, or economically excessively burdensome.

It is also important that the subcutaneous route of administration makes it possible to avoid complications associated with the need for permanent venous access, including infectious risks, catheter thrombosis, and pronounced psychological discomfort, especially in the pediatric population.

Significance of Emicizumab for Clinical Practice

The introduction of emicizumab into clinical practice has become not merely the appearance of a new medicinal product, but an actual revision of the traditional paradigm of prophylactic treatment of hemophilia A. While the classical model of therapy was based primarily on replacing deficient factor VIII and overcoming the limitations of this strategy, the use of emicizumab demonstrated the possibility of effective disease control based on an alternative hemostatic correction that is not based on FVIII replacement.

The clinical value of the drug is determined by several aspects. First, a marked reduction in the frequency of spontaneous, post-traumatic, and intra-articular bleeding is achieved. Second, patients' quality of life improves due to a reduced therapeutic burden and simplification of the treatment regimen. Third, high efficacy is ensured in patients with inhibitors, who represent one of the most problematic categories in hematological practice. Fourth, the risk of progression of chronic hemophilic arthropathy decreases, which is of fundamental importance for the prevention of early disability.

The use of emicizumab appears especially promising in pediatric and adolescent populations, where frequent intravenous infusions are associated with significant organizational, technical, and psychological difficulties. Subcutaneous

administration and infrequent dosing intervals substantially optimize long-term treatment and increase the real feasibility of prophylactic programs.

In addition, the use of emicizumab has pronounced organizational and economic significance. Despite the high cost of innovative therapy, its use may potentially be accompanied by a reduction in the total costs of the healthcare system due to a decrease in hospitalizations, emergency hemostatic interventions, orthopedic complications, surgical operations, and long-term rehabilitation. Therefore, the drug may be considered not only a highly effective clinical agent, but also a component of a rational resource-saving strategy for managing patients with chronic coagulopathies.

Prospects for Further Research

Promising areas of emicizumab research are associated with the accumulation of long-term data on its efficacy and safety, optimization of individualized dosing regimens, clarification of its use in various age and clinical subgroups, and investigation of its role in combined therapeutic approaches. Of particular interest is the possibility of integrating emicizumab into personalized patient management models, taking into account inhibitor status, phenotypic severity of the disease, bleeding frequency, joint status, and concomitant pathology.

Additional scientific and practical significance is attached to the study of the potential combination of emicizumab with innovative strategies, including gene therapy technologies, the use of new hemostatic molecules, and improved methods for monitoring the coagulation response. In the context of the rapid development of personalized medicine, emicizumab is regarded as one of the key elements of future multicomponent therapy for hemophilia A.

Conclusion

Thus, emicizumab (Hemlibra) should be regarded as one of the most significant innovative achievements of modern clinical hematology, which has fundamentally changed approaches to the prophylactic treatment of hemophilia A. Its unique mechanism of action, based on functional mimicry of the activity of activated factor VIII through bispecific binding of factors IXa and X, ensures restoration of a critically important component of the coagulation cascade regardless of the presence of inhibitor antibodies to FVIII.

The results of large international studies convincingly demonstrate the high clinical efficacy of the drug, expressed in a substantial reduction in bleeding frequency, decreased need for additional hemostatic therapy, prevention of hemarthroses, slowing of the progression of hemophilic arthropathy, and improvement in patients' quality of life.

A favorable safety profile, absence of the need for frequent intravenous administration, the possibility of infrequent subcutaneous dosing, and high therapeutic acceptability make emicizumab especially important in the treatment of children, adolescents, and patients with the inhibitor form of the disease. From clinical, pathogenetic, organizational, and pharmacoeconomic points of view, the drug represents a justified and promising alternative to traditional replacement therapy.

Consequently, the introduction of emicizumab into broad clinical practice reflects the formation of a new concept for the management of patients with hemophilia A, based on the principles of long-term prophylaxis, individualization of therapy, minimization of complications, and maximal preservation of the patient's functional status. In this context, emicizumab may be considered not only an effective medicinal product, but also a crucial element of the modern personalized model of medical care for patients with hereditary disorders of hemostasis.

REFERENCES:

1. Oldenburg J., Mahlangu J.N., Kim B., et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors // New England Journal of Medicine. — 2017. — Vol. 377, No. 9. — P. 809–818. — DOI: 10.1056/NEJMoa1703068.
2. Mahlangu J., Oldenburg J., Paz-Priel I., et al. Emicizumab Prophylaxis in Patients Who Have Hemophilia A without Inhibitors // New England Journal of Medicine. — 2018. — Vol. 379, No. 9. — P. 811–822. — DOI: 10.1056/NEJMoa1803550.
3. Young G., Liesner R., Chang T., et al. A multicenter, open-label phase 3 study of emicizumab prophylaxis in children with hemophilia A with inhibitors // Blood. — 2019. — Vol. 134, No. 24. — P. 2127–2138. — DOI: 10.1182/blood.2019001869.
4. Pipe S.W., Shima M., Lehle M., et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study // The Lancet Haematology. — 2019. — Vol. 6, No. 6. — P. e295–e305. — DOI: 10.1016/S2352-3026(19)30054-7.
5. Callaghan M.U., Negrier C., Paz-Priel I., et al. Long-term outcomes with emicizumab prophylaxis for hemophilia A with or without FVIII inhibitors from the HAVEN 1–4 studies // Blood. — 2021. — Vol. 137, No. 16. — P. 2231–2242. — DOI: 10.1182/blood.2020009217.

6. Yoneyama K., Schmitt C., Kotani N., et al. Approach to substitute for a conventional dose-finding study in rare diseases: example of phase III dose selection for emicizumab in hemophilia A // Clinical Pharmacokinetics. — 2018. — Vol. 57, No. 9. — P. 1123–1134. — DOI: 10.1007/s40262-017-0616-3.

7. Retout S., Schmitt C., Petry C., et al. Population pharmacokinetic analysis and exposure–response assessment of emicizumab in people with hemophilia A // Clinical Pharmacokinetics. — 2020. — Vol. 59. — DOI: 10.1007/s40262-020-00904-z.

8. Mancuso M.E., Booth J., Buckner T.W., et al. Health-related quality of life and caregiver burden of emicizumab in children with haemophilia A and factor VIII inhibitors: results from the HAVEN 2 study // Haemophilia. — 2020. — Vol. 26, No. 6. — P. 1009–1018. — DOI: 10.1111/hae.14183.

9. Srivastava A., Santagostino E., Dougall A., et al. WFH Guidelines for the Management of Hemophilia, 3rd edition // Haemophilia. — 2020. — Vol. 26, Suppl. 6. — P. 1–158.

10. Rodriguez-Merchan E.C., Valentino L.A. Emicizumab: review of the literature and critical appraisal // Haemophilia. — 2019. — Vol. 25, No. 1. — P. 11–20.

11. Andrade P.E.A., Mahlangu J.N., Pipe S.W., et al. Emicizumab: the hemophilia A game-changer // Haematologica. — 2024. — Vol. 109.

12. Chowdary P. Haemophilia // The Lancet. — 2025. — Review article on modern approaches to hemophilia management, including emicizumab.