The Importance of Endothelial Dysfunction in The Development of Disorders of The Hemostasis System in Patients with Rheumatoid Arthritis

Musaeva N. B.

Tashkent Medical Academy

ABSTRACT

The article contains information about the physiology of the hemostatic system and its components, and discusses the connection between the hemostatic system and inflammation. The physiology of normal hemostasis, the interaction of platelets with endothelial cells and leukocytes, as well as with von Willebrand factor and the complement system and their role in rheumatoid arthritis are described.

Keywords: blood coagulation system, venous thromboembolism, inflammation, rheumatoid arthritis, thrombosis, blood clotting factors, complement, cytokines.

Introduction

Hemostasis is one of the body's defense systems, ensuring, on the one hand, the preservation of blood in the bloodstream in a liquid aggregate state, and on the other, the formation of blood clots when the vessel wall is damaged to stop bleeding and prevent blood loss. At the same time, this is one of the "problem" systems of the human body. The terms "hemostasis" and "coagulation" are often used interchangeably, but this is not entirely correct [1]. Hemostasis is a complex and complex process that requires the interaction of numerous physiological mechanisms. It is divided into primary (endothelial cells and platelets) and secondary (plasma factors). The corresponding cellular and molecular mechanisms are aimed at "sealing" damaged vessels with local formation of clots that prevent bleeding [2]. As soon as the integrity of the vessel is restored, the thrombus is destroyed and normal hemostasis is resumed.

Materials And Methods

Conventionally, the blood coagulation system can be divided into three components: coagulation, anticoagulation and fibrinolysis [3]. Conditionally, since in reality these systems are closely interconnected, and their separation is only a way of presenting the material.

There are several theories of blood coagulation: classical coagulation theory; waterfall theory, or cascade theory; revised theory of coagulation; cellular model of hemostasis [1, 2].

The blood coagulation system includes platelets, plasma coagulation factors and plasma coagulation inhibitors. The liver synthesizes many coagulation factors: fibrinogen (factor I), prothrombin (factor II), factors V, VII, IX, X, XI, XII, XIII, as well as coagulation and fibrinolysis inhibitors. The rough endoplasmic reticulum of hepatocytes is the main site of synthesis of proteins of the coagulation system [3, 4].

Results And Discussion

The main inducers of platelet activation and aggregation are von Willebrand factor, collagen, thrombin, adenosine diphosphate. The plasma membrane of platelets contains several types of von Willebrand factor receptors. This factor, by binding to receptors, acts on platelets through the inositol phosphate signal transduction system. As a result, platelets acquire a spiky-spherical shape, facilitating their interaction with each other and with the surface of the damaged endothelium. The most important primary inducers of platelet activation are thrombin and collagen. The interaction of these proteins with specific receptors of the plasma membrane of platelets leads to the mobilization of Ca2+ from the dense tubular system into the cytoplasm, which leads to their adhesion and aggregation.

metabolism and release of biologically active substances. These substances cause morphological changes, adhesion, platelet aggregation and participate in the formation of a blood clot.

Disruption of the functional activity of platelet receptors and the system of secondary messengers is associated with changes in their function and can cause a number of diseases accompanied by thrombosis or bleeding. Platelets, accumulating at the site of injury, form a platelet plug, which can stop bleeding from small vessels. Stabilization of thrombi depends on the appearance of thrombin, which causes the formation of fibrin threads that stabilize platelet aggregates in the arteries and are the main component of venous thrombi. The formation of thrombin occurs as a result of a series of sequential reactions in which 12 proteins - coagulation factors, Ca2+ ions and phospholipids - participate. All factors of the hemostasis system in their activated form are specialized enzymes – serine proteases, and factor XIII is a transglutaminase. The coagulation process is usually divided into successive stages, each of which consists of converting a specific component into its active form.

The cellular model of blood coagulation is intended to describe the processes of hemocoagulation in vivo and explain the limitations that must be taken into account when interpreting the results of laboratory coagulation tests:

- in vivo, the blood coagulation process is uniform and is associated with hemostatic reactions of platelets. Platelets not only participate in the activation of coagulation factors, but also perform the function of regulating the entire process of blood coagulation;
- coagulation process under physiological conditions;

yah is localized by the area of the vessel defect. Its non-proliferation is facilitated by the anticoagulant system and normally functioning endothelial cells;

- excess thrombin in the human body is inactivated by antithrombin III, which is also active against factors XIIa, XIa, IXa, Xa

Conclusion

According to a number of authors, methotrexate, the most commonly used in the treatment of RA, leads to a significant reduction in the number of cases of myocardial infarction (MI) and the total number of cardiovascular diseases. Treatment with TNF inhibitors helps to reduce the level of CRP, as well as two recognized predictors of cardiovascular risk – PAI-1 and PAI-1/t-PA. It also allows for significant improvements in endothelial function. According to V. Zoller et al., the risk of PE and DVT may be higher in the early stage of RA, for example in the first year after starting treatment with disease-modifying anti-inflammatory drugs (DMARDs) or establishing a diagnosis of RA, which may be associated with uncontrolled inflammatory activity before achieving positive effect of antirheumatic therapy. However, the use of nonsteroidal anti-inflammatory drugs and glucocorticoids (GCs) to relieve the inflammatory process is known to increase the risk of VTEC. It is also known that GCs increase the levels of blood clotting factors, which increases the risk of VTEC. S.C. Kim et al. found a higher risk of VTEC in patients receiving TNF-α inhibitors compared to patients treated with DMARDs, in particular methotrexate.

References

1. Reshetnyak VI, Zhuravel SV, Kuznetsova NK, Pisarev VM, Klychnikova EV, Syutkin VE, Reshetnyak TM. The hemostasis system is normal and during liver transplantation (review). General resuscitation. 2018;(5):85-96.
2. Strukova SM. Fundamentals of physiology of hemostasis. 2nd ed. Moscow: Moscow State University Publishing House; 2013. Strukova SM. Osnovy fiziologii gemostaza
3. Aksu K, Donmez A, Keser G. Inflammation-Induced Thrombosis: Mechanisms, Disease Associations and Management. Curr Pharm Des. 2012;18(11): 1478-93.
4. Levi M, van der Poll T, Buller HR. Bidirectional relation between inflammation and coagulation. Circulation. 2014 Jun 8; 109(22):2698-704. doi: 10.1161/01.CIR. 0000131660.51520.9A.