CHANGES IN COAGULATIVE HEMOSTASIS IN PATIENTS WITH LIVER DISEASE

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Abstract. The liver plays a key role in primary and secondary hemostasis, being the site of synthesis of all coagulation factors and their inhibitors. Liver diseases lead to complex changes in hemostasis, while maintaining a balance between the coagulation and anticoagulation systems, but with a reduced reserve. There is increasing evidence that thrombosis of the portal and hepatic veins underlies disease progression in patients with cirrhosis and aggravates hemostasis disorders.

Keywords: liver diseases, method, treatment, hemostasis.

INTRODUCTION

The liver plays a key role in primary and secondary hemostasis. It is the site of synthesis of all coagulation factors and their inhibitors with the exception of von Willebrand factor and is responsible for the elimination of activated factor-inhibitor complexes. Liver diseases lead to complex complex disorders in the hemostatic system, but at the same time a balance is maintained between the coagulation and anticoagulation systems with a reduced reserve, and this balance is easily disturbed in one direction or the other, so patients with severe liver damage may develop not only bleeding, but also thrombosis (Table) [40]. In liver cirrhosis, platelet function is impaired, and thrombocytopenia develops due to secondary splenomegaly and decreased thrombopoietin synthesis.

MATERIALS AND METHODS

Table

Hemostasis disorders in liver diseases

Promotes bleeding	Способствует тромбозу

1. Thrombocytopenia 2. Platelet dysfunction 3. Increased platelet inhibition by nitric oxide (NO) and prostacyclin 4. Low level of factors II, V, VII, IX, X, XI 5. High quality and quantitative fibrinogen disorders 6. Low level α2-antiplasmin, thrombin-activated fibrinolysis inhibitor (TAFI)	1. Elevated levels of factor VIII and von Willebrand factor 2. Low levels of protein C, protein S, antithrombin III, α2-macroglobulin 3. Low plasminogen levels 4. Low cofactor II levels

All of the above hemostasis disorders do not always lead to spontaneous bleeding. Infection (sepsis) is one of those factors that shifts the balance towards hypocoagulation, significantly impairing coagulation, and thereby triggering the development of bleeding from varices.

RESULTS AND DISCUSSION

Procoagulant factors

The liver is the site of synthesis of fibrinogen and factors II, V, VII, IX, X, XI and XII. Von Willebrand factor is synthesized by the endothelium, and factor VIII is synthesized by both hepatic and extrahepatic sinusoidal endothelial cells, therefore the plasma concentration of factor VIII does not decrease in liver diseases, and may even be increased [30].

Von Willebrand factor

Plasma concentration of von Willebrand factor increases both in acute liver failure and in chronic liver diseases [2]. A correlation has been proven between the severity of liver disease and the level of von Willebrand factor in plasma.

Fibrinogen

Fibrinogen is an acute phase protein of inflammation, and its concentration remains normal or increases in liver diseases. Low concentrations (below 1 g/l) are observed only with very severe liver damage due to reduced synthesis. It is worth noting that high concentrations of fibrinogen in patients with chronic hepatitis, cholestatic jaundice and hepatocellular carcinoma do not lead to increased clot formation, since most of it is non-functional [20].

Platelets

In liver diseases, the functional activity of platelets is often impaired and their number decreases, which leads to disruption of primary hemostasis. About one third of patients with chronic liver diseases have thrombocytopenia (70–90 109/l), which increases in parallel with the progression of the disease and the development of hypersplenism. Thrombopoietin levels increase in thrombocytopenia, but to a lesser extent than in patients with normal liver function.

Pre-hepatic period

The first stage of the operation is characterized by great trauma due to the dissection of adhesions and the intersection of many collateral vessels. As a rule, moderate coagulation disturbances and moderate blood loss are observed, which correlates with the complexity of hepatectomy and the severity of hypocoagulation before surgery. The etiology of liver disease influences blood loss and, accordingly, the need for transfusion. In hepatocellular carcinoma, cholestatic liver lesions (primary sclerosing cholangitis, primary biliary cirrhosis), there is a tendency to hypercoagulation, determined by thromboelastogram, and fibrinolytic activity is less pronounced, therefore antifibrinolytic drugs are not prescribed. During transplantation in children for biliary atresia, coagulation disturbances are not as significant as in cirrhosis of other etiologies.

CONCLUSION

Liver diseases lead to complex complex disorders in the hemostatic system, while a balance is maintained between the coagulation and anticoagulation systems with a reduced reserve, and this balance is easily disturbed in one direction or the other, so patients with severe liver damage may develop not only bleeding, but also thrombosis. Thus, during surgery, patients with cirrhosis often experience increased bleeding, and bleeding from esophageal varices is the main cause of death. On the other hand, evidence is increasingly accumulating that portal vein thrombosis underlies the progression of the disease [47]. Preliminary results of a study on the progression of fibrosis after liver transplantation for hepatitis C (WACT-F trial) showed that the administration of warfarin can significantly slow down this process

in the graft [8]. Recently, there has been increased interest from researchers in the endothelium and the study of its role in the local regulation of hemostasis.

Thus, at the moment, many questions remain unanswered, and it is too early to say that we have a complete understanding of hemostasis disorders in liver diseases.

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