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tytuł pracy: **„Zaburzenia hemostazy a występowanie krwawień żylakowych z górnego odcinka przewodu pokarmowego u pacjentów z marskością wątroby”**

Summary

Introduction

Bleeding from esophageal varices and gastric varices is one of the most severe complications of liver cirrhosis beside ascites and hepatic encephalopathy. To date, a few predictors of variceal bleeding in patients with liver cirrhosis has been identified. These include: hepatic venous pressure gradient (HVPG), the size of varices and their location, the presence of red signs on varices, the severity of liver failure, hepatocellular carcinoma and a history of variceal bleeding. The association between coagulopathy of liver cirrhosis and the incidence of variceal bleeding remains unclear, and routine correction of hemostasis disturbances in these patients is not recommended due to the lack of data confirming the effectiveness of such proceedings. It is also known that the results of routine coagulation tests such as prothrombin time (PT) and activated partial thromboplastin time (APTT) do not correlate with the occurrence of bleeding after invasive procedures in patients with liver cirrhosis. The results of previous studies showed also no effect of prolonged PT and APTT on the occurrence of bleeding from the gastrointestinal tract. The usefulness of these tests in the assessment of the bleeding risk in cirrhotic patients, is most likely limited by the inability to assess compensatory mechanisms occurring in the hemostasis system in liver cirrhosis. These disorders include e.g. the decreased activity of natural anticoagulants and increased activity of von Willebrand factor. The results of these tests do not reflect the influence of platelets number and platelets function disorders on clot formation, as well as fibrinolysis disturbances of liver cirrhosis.

Aim

The aim of the study was to compare the hemostatic abnormalities found in patients with liver cirrhosis and a history of variceal bleeding, at least three weeks before with the hemostatic abnormalities found in patients with cirrhosis and medium-large esophageal or gastric varices who has never had symptoms of acute bleeding from the upper gastrointestinal tract.

Patients and methods

The study included 58 patients – 23 women and 35 men with liver cirrhosis who were diagnosed on the basis of clinical symptoms and laboratory tests. Basic laboratory tests were performed in all patients, including routine coagulation tests. Thromboelastometry (Rotem Gamma®) with the activation of intrinsic (INTEM) and extrinsic (EXTEM) coagulation pathway in whole blood was performed in each group. The effectiveness of plasma hemostasis was evaluated by thromboelastometry after inactivation of platelets with

cytochalasin D (FIBTEM). In addition, to evaluate the activity of endogenous heparinoids there was performed heparinase modified thromboelastometry (HEPTEM). A tranexamic acid modified thromboelastometry (APTEM) was performed in case of results indicating excessive fibrinolysis, to confirm this disorder. Platelet aggregation test was performed on the Multiplate® analyzer with adenosine diphosphate (ADP) as a platelet activator. Thrombin generation assay (Trombopath®) before (ThP-B) and after the activation of protein C (ThP-A) was also performed. In addition, in both groups the activity of selected coagulation factors and antithrombin was measured.

Results

The study included 58 cirrhotic patients (n = 32, group without previous bleeding; n = 26, group with a history of variceal bleeding). The results of routine coagulation tests (PT, APTT, fibrinogen level, platelet count) and factor VII activity differ significantly between these two groups, suggesting the existence of a pro-hemorrhagic profile in patients with a history of bleeding. Moreover, in FIBTEM test (thromboelastometry with inhibition of platelet activity) lower values of MCF (maximum clot firmness) and A (amplitude) were observed in patients with a history of variceal bleeding. However, the effectiveness of hemostasis and physical properties of the clot, assessed by thromboelastometry in INTEM and EXTEM tests in both groups were comparable. This demonstrates the compensatory role of platelets in cirrhotic patients with a history of variceal bleeding. The results of aggregometry in both groups were also comparable despite the lower platelet count in Group 2, indicating a greater efficiency of platelet aggregation in this group. The results of thromboelastometry after the inactivation of platelets also confirmed their greater proportion in the clot in patients with a history of variceal bleeding.

The reduced activity of factor VII was accompanied by a significant decrease of antithrombin activity and significantly increased activity of factor VIII and von Willebrand factor. The results of coagulation factors and natural anticoagulants activity measurement indicated the existence of rebalanced state of hemostasis system. This finding was confirmed by the results of thrombin generation assay (Trombopath®) after activation of the protein C indicating comparable values of Th-P A.

The activity of natural anticoagulants correlated with the severity of liver cirrhosis according to Child-Turcotte-Pugh score and MELD value.

Conclusion

The results of this study do not confirm the influence of hemostasis disturbances on the incidence of variceal bleeding in patients with liver cirrhosis. The study showed the complex nature of coagulation mechanisms in these patients. The rebalanced state of hemostatic system in cirrhotic patients may result either from the simultaneous reduction of the activity of clotting factors and natural anticoagulants in plasma and the compensatory role of platelets.