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METHODS OF PREDICTING THE RELAPSING HEMORRHAGE

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Abstract. Methods of predicting relapsing hemorrhage. Trofimov M.V., Kryshen V.P., Gaponov I.V. *In this article the authors presented their own original methods for predicting ulcerous gastroduodenal bleeding defended by Patent of Ukraine. The implementation of these procedures led to substantial lowering of recurrent hamorrhage rate – more than twice. All methods have pathogenetic foundation and are based on ulcerogenesis mechanisms revealed during the longlasting complex clinical and experimental research. In such a way surgeons obtain some possibilities of early diagnostics of bleeding relapses and adequate treatment and effective hemorrhage prevention accordingly.*

Реферат. Методи прогнозування рецидивної кровотечі. Трофімов М.В., Кришень В.П., Гапонов І.В. *У цій статті автори презентували власні оригінальні методи прогнозування рецидиву виразкової гастро-дуоденальної кровотечі, захищені патентом України. Реалізація цих методів сприяла суттєвому зменшенню кількості рецидивних кровотеч - більше ніж у два рази. Всі методи мають патогенетичну основу і базуються*

на механізмах патогенезу, виявлених під час тривалого комплексного клініко-експериментального дослідження. Таким чином, хірурги отримують можливість ранньої діагностики рецидивів кровотечі і відповідно адекватного лікування та ефективної профілактики крововтрати.

Complex observation of 143 patients with bleeding gastroduodenal ulcer was conducted. Pathophysiologically grounded principles of predicting relapsing hemorrhage have been developed by us based on data of pathomorphological, immunohistochemical and microbiological research of the ulcer substrate in case of active bleeding, at stopped bleeding with signs of unstable local endoscopic hemostasis and high risk for manifestation of relapsing hemorrhage in the clinic.

MATERIALS AND METHODS

According to our data, the main chain of pathogenesis of appearing relapsing hemorrhage is the increase in blood filling of the periulcerous area and especially blood deposition in dilated vessels of submucosal vascular plexus directly under the ulcer defect. For predicting relapsing bleeding, as a basis we used research of indices, which are directly connected with the increase in blood filling of the periulcerous area. Local increase in activity of i-NOS due to leucocyte infiltration of the mentioned area causes the increase of blood filling in the periulcerous area. Finding out the level of activity of i-NOS in periulcerous area on the third day of staying in the hospital in cases of unstable local endoscopic hemostasis will enable doctors to apply some measures for preventing this severe complication.

The suggested method (Patent of Ukraine for the useful model #59395 "Way of defining the risk of relapse of gastroduodenal hemorrhage of ulcer genesis" is carried out in the following way. The patient with the arrested bleeding by conservative and endoscopic means, while carrying out endoscopic monitoring has local hemostasis defined by Forrest and targeted biopsy of mucous of stomach and duodenum is carried out near the area of the defect (1-1.5 mm). After that, immunohistochemical research is carried out to define the activity of inducible NO-synthase using Scarpelli method. High risk of hemorrhage relapse is determined by the presence of more than 5 cells colored in blue within the field of the view, low risk – from 3 till 5 cells, absence – less than 3 cells.

Upon carrying out clinical researches we revealed the correlational connection between the character of microbe semination of the periulcerous area and local level of i-NOS activity and stage of the local endoscopic hemostasis. In case of impossibility to carry out specific immunohistochemical

research, we developed a method of indirect estimation of risk of relapsing hemorrhage (Patent of Ukraine for the useful model #59731 "The method of endoscopic diagnostics of relapsing stomach-intestinal hemorrhage."

The suggested method includes selection of mucous biopsy materials around the hemorrhage area (around 2 mm) and microbiological research. The character of bacterial semination, its qualitative and quantitative analyses enable researchers to conclude the possible threat of relapsing hemorrhage and effectiveness of the carried out endoscopic hemostasis and conservative therapy. High risk for relapsing hemorrhage is set when the level of microorganisms of type *Klebsiella pneumoniae* and *Streptococcus* β -haemolyticus are present in biopsy materials of mucous of stomach and esophagus in the amount of over 10^6 – 10^7 , and low level of relapsing hemorrhage – if semination of microorganisms of type *Klebsiella pneumoniae* and *Streptococcus* β -haemolyticus in samples is 10^4 – 10^5 . The absence of relapsing hemorrhage is defined if concentration of microorganisms of type *Klebsiella pneumoniae* and *Streptococcus* β -haemolyticus in those samples is 10^2 – 10^3 .

The mentioned method is carried out in the following way. The patient with signs of unstable endoscopic hemostasis or with the arrested hemorrhage by endoscopic ways, esophagogastroduodenal study is carried out for endoscopic monitoring. After that the condition of local endoscopic hemostasis by Forrest is estimated and targeted biopsy of mucous of stomach or duodenum is taken at the distance of 1-1.5 mm from the side of the ulcerous defect. Selection of biopsy material is carried out using biopsy pincers FB-IF. While taking samples of biopsy of mucous of stomach and duodenum for microbiological research it is essential to exclude the possibility of contaminating the studied material by outside micro flora.

The given above ways of predicting relapsing hemorrhage are quite invasive for patients and require application of special tools and laboratory equipment. Due to that, it is essential to develop such a method of predicting relapsing hemorrhage which would be mini-invasive, available, quick and simple with application of technique, acceptable price and mainly precision of diagnostics which could be considered as a screening method.

Therefore based on carried out experiments and clinical researches we developed our own way of

defining the risk of gastrointestinal hemorrhage relapse of ulcerous genesis (Patent of Ukraine on the helpful model # 59730 “Way of defining stomach-intestinal relapsing hemorrhage”). The essence of the suggested approach is in sampling venous blood from the patient on arrival at the hospital and determination of stable metabolites NO in serum. On the third day of treatment the sample of venous blood is taken repeatedly, with further definition of stable metabolites of NO in serum. The increase in level of stable metabolites NO is caused by the increase of i-NOS activity in periulcerous area, which can be explained by the expressed leukocyte infiltration with preference of the lymph chain. At increase in NO production, manifested vasodilatation, blockage of vasoconstriction, depression of clot formation are observed. These changes cause the blood filling of the periulcerous area that could lead to development of bleeding and create some conditions for recurrent hemorrhage.

The suggested method is carried out in the following way. During the esophagogastroduodenoscopy the presence, localization and character of ulcer defect of mucosa are defined along with the local hemostasis by Forrest. At that the sampling of

5 ml of blood from the peripheral vein is carried out. The blood sample is centrifuged for taking serum.

On the third day of stay the patient underwent repeated definition of stable metabolites of NO in blood serum according to the methodology mentioned above. The high risk of relapsing hemorrhage is defined using the following criteria: if the level of stable metabolites NO increases 70% and more compared with the previous – high level; low level of relapsing hemorrhage – if the level of stable metabolites NO increases not more than 35-70% compared to the previous one; absence of relapsing hemorrhage – if level of stable metabolites NO increases less than 35% compared to the previous level.

CONCLUSION

The implementation of the presented methods of defining the risk for gastrointestinal relapsing hemorrhage of ulcerous genesis can be used in every hospital, besides it does not require expensive and sophisticated equipment and trained personnel. High precision of diagnostics, rapid results (within 2-3 hours) and low price are significant in the screening procedure. The application of elaborated techniques has been allowed to decrease the rate of recurrent bleeding from 10,5% to 4,2%.

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