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FEATURES OF THE TREATMENT OF ULCER BLEEDING FROM THE UPPER COMPARTMENTS OF THE GASTROINTESTINAL TRACT IN ELDERLY PATIENTS

Abstract. Features of the clinical course of ulcer bleeding from the upper parts of the gastrointestinal tract in elderly patients are determined. Changes in homeostasis and reserve capabilities of the body depending on the amount of blood loss are studied. Suggested ways to improve the results of treatment of these patients.

Keywords: gastrointestinal tract; ulcer bleeding, elderly patients, features of treatment.

Gastrointestinal bleeding is an important problem in urgent abdominal surgery. A special category of patients consists of persons with a high operational risk. It includes patients with acute and chronic cardiovascular pathology, after coronary artery bypass grafting, renal artery bypass grafting, as well as patients with acute cerebrovascular accident [1]. According to various authors, their number is 20-50%. Recurrence of bleeding in these patients is the most common cause of death. Today, a partial solution to the problem of gastroduodenal bleeding has become possible with the development of endoscopy. It allows you to quickly identify the location of the source of bleeding, determine its size and endoscopic characteristics, perform hemostasis with the subsequent control of its effectiveness. In addition, the endoscopic method is minimally invasive and effective in the treatment of

gastroduodenal ulcers, which is able to reduce the number of open operations at the height of bleeding. However, the postoperative mortality rate remains high among patients with cardiovascular disease [2]. Indications for surgical intervention depend on the prognosis of recurrence of bleeding and assessment of the vital functions of the patient's body. Severe co-morbidity forces a cautious decision to be made about the necessity of performing operations for recurrent bleeding. In this case, repeated endoscopic gastro-duodenoscopy (EGD) under the conditions of local hemostasis has the advantage, and provides an opportunity to operate in a delayed period, after the normalization of indicators of vital functions.

Resection methods are the majority in the structure of operative interventions. At the same time, palliative methods are not used due to the lack of possibility of radical elimination of the morphological substrate of the disease and the threat of postoperative complications, which cause an increase in postoperative mortality.

The aim of the study. To increase the effectiveness of treatment of elderly patients with ulcerative gastrointestinal bleeding through the study of the dynamics of immune system indicators and their relationship with local endoscopic hemostasis.

Research materials and methods. A retrospective analysis of the treatment of 73 elderly patients with myocardial infarction and acute coronary syndrome, in whom cardiac pathology was complicated by gastric and duodenal ulcer bleeding, was performed. An analysis of the treatment of 35 elderly patients (according to the WHO classification - 61-90 years) was carried out. 19 (54%) of them were men, 16 (46%) were women. The average age was 76.3 years. Patients were divided into groups: A – patients who received therapy according to the standard scheme of treatment of cardiovascular pathology (n=20), B – "double" therapy (n=15). 5 patients with concomitant neurological pathology (acute cerebrovascular disorder) and severe endocrine pathology (decompensated diabetes mellitus) were excluded from the study. A category of 50 people - relatively healthy patients (donors) who were similar to the experimental group in terms of age, sex, and the method of determining the main indicators - was selected as a control.

The following cytokines were studied: interleukins (IL-4, IL-6) and tumor

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necrosis factor (TNF α). Processing of laboratory data was carried out using laboratory methods, as well as determination of the main indicators of the immune system -IL-6, IL-4. At the same time, all patients underwent esophagogastroduodenoscopy to determine the localization, size of the ulcer defect and the state of local endoscopic hemostasis. Venous blood, which was taken from the elbow vein during hospitalization, as well as on the third and seventh days of hospital stay at the same time for the correctness of the results, was used as the material for the study of immunological parameters. Qualitative determination of the concentration of IL-6, IL-4 in blood serum was carried out with the help of immunoenzymatic analysis using test systems of ZAO "Vektor-best" (Novosibirsk) according to the manufacturer's recommendations. The content of these indicators in the experimental samples was determined using calibration curves with optical density values of standard samples in the laboratory of the medical university [3].

All ascending data that were obtained during the research, in order to optimize mathematical processing, were entered into a database built using Microsoft Excel spreadsheets. Statistical processing of the research results was carried out using the methods of variational statistics implemented by the standard package of Statistica for Windows 6.0 applications.

Research results and their discussion. Retrospectively, it was determined that in the period from 2017 to 2020, there was an increase in the number of patients with peptic ulcer bleeding from the stomach and duodenum and concomitant pathology of the cardiovascular system - acute myocardial infarction and acute coronary syndrome (n=73). In 28 patients, which are 38.4% of the total number of patients with acute myocardial infarction, the latter developed against the background of coronary heart disease, and in 45 patients (61.6%) acute coronary syndrome (ACS) was diagnosed, indicating a severe course the main disease.

It was established that a relatively mild course of the disease was observed when receiving standard hypotensive therapy (n=541). Blood loss of small and medium volume prevailed - 228 ($42.14\pm2.12\%$) and 126 ($23.29\pm1.82\%$) cases, respectively. Regarding local endoscopic hemostasis, the percentage of cases with signs of absence of recent bleeding (Forrest III) has increased over the past 3 years,

from 13.5% to 19.7%. However, during the reception of "double" therapy (n=68), a severe course was observed and blood loss of a large volume and massive blood loss prevailed - 19 (27.94 \pm 5.44%) and 28 (41.18 \pm 5.97%) respectively. The proportion of patients with active bleeding (Forrest I) was 38.5% (p<0.05).

In the structure of operative interventions, a decrease in the percentage of radical methods compared to conditionally radical and palliative methods was determined in the ratio of 1:4, and the postoperative mortality rate was 30%. The total mortality was 8.4%. We analyzed the mortality in patients with gastric and duodenal ulcers on the background of cardiovascular pathology with various degrees of blood loss and found that even with a small form of blood loss, 5 (0.8%) deaths were recorded. With an average degree of blood loss, 4 (0.7%) fatal cases were found. With severe forms of blood loss, the number of fatal cases increases sharply to 22 (3.6%) - with a small form of blood loss and 20 (3.3%) - with a massive form of blood loss [4].

A number of studies have shown that elevated IL-6 has a more important prognostic value than C-reactive protein for the occurrence of cardiovascular death and other cardiovascular complications. We found an increase in acute-phase C-reactive protein and interleukins in both categories of patients. On the first day of hospital stay, C-reactive protein was 3.7 times higher and interleukin-6 was 4 times higher in group B compared to group A, 75.60±1.86 and 19.95±4.09, respectively. The level of interleukin-4 was reduced in both groups during the first day and was 2.08 ± 0.36 in group A and 2.28 ± 0.33 in group B. On the third and seventh days in group A at the level of C-reactive protein 16.00±1.58 and 19.70±2.24 levels of interleukin-6 and interleukin-4 were 6.68 ± 0.61 and 8.54 ± 0.93 and 2.73 ± 0.86 and 2, 14±0.6, respectively. In group B, when the level of C-reactive protein on the third and seventh days was 66.33±4.24 and 44.53±5.89, respectively, interleukin-6 and interleukin-4 were 27.88±2.46 and 19.65± 1.99 and 1.95±0.19 and 1.83±0.2, respectively (p<0.01). Therefore, in groups F and B, we can claim a strong correlation between interleukin-6 and C-reactive protein r=+0.97 and r=+0.94, respectively (p>0.05).

At the same time, a significant increase in the levels of IL-2, IL-4, IL-6, IL-12

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and IL-18 was determined in patients with coronary heart disease compared to healthy individuals, and the level of IL-6 was even higher in patients with myocardial infarction . An increase in the concentration of IL-6 was noted during an exacerbation of peptic ulcer disease, pancreatitis, gluten enteropathy, Crohn's disease, nonspecific ulcerative colitis, viral hepatitis, and primary biliary cirrhosis of the liver. TNF α has mainly immunomodulatory and anti-inflammatory effects. The concentration of the circulating marker TNF α is usually very low, but it increases significantly (maximum in 1.5 hours) if an acute situation occurs. Determination of TNF α and IL-6 levels plays a significant role in the diagnosis of congestive heart failure. During periods of exacerbation, the amount of IL-4 increases almost 3 times compared to the norm, and during remission, its level decreases, especially against the background of the duration of treatment.

As a result of the release of TNF, the permeability of capillaries increases, the endothelium of vessels is damaged, and intravascular thrombosis occurs. The concentration of circulating TNF α is usually very low (<5 pg/ml), but it increases sharply (maximum in 90 min.) after LPS administration and returns to normal within 4 h. High levels of TNF α (>300 pg/ml) are found during septic shock. The maintenance of high levels indicates the possibility of the development of undesirable consequences.

In our studies, it was determined that IL-6, depending on the state of local endoscopic hemostasis at the time of hospitalization, was higher than the control group, but no significant difference between the indicators was found. In the case of a high risk of recurrence of bleeding (Forest II) on the 7th day, the normalization of the indicator was not determined. In patients with stable hemostasis (Forest III), IL-6 approached the normal value (p>0.05). A sharp increase in IL-6 was determined depending on the state of local endoscopic hemostasis, especially during active bleeding (Forest I) up to 36.54 ± 1.61 and also at a high risk of recurrence of bleeding (Forest II) - up to 33.87 ± 2 .01 with a gradual decrease until the 7th day, however, the normalization of the indicator was not observed (p<0.01).

The IL-4 indicator behaves somewhat differently. A sharp decrease in the content of IL-4 was noted during the high risk of recurrence of bleeding under

conditions of stable hemostasis, which did not normalize on the 7th day of the patient's stay in the hospital (p>0.05). In addition, a reduced level of IL=4 was observed during active bleeding (Forest I). Under conditions of high risk of recurrence of bleeding (Forest II), a reduced level of it was also noted to 2.34 ± 0.47 and 2.23 ± 0.5 s with a further decrease to 2.02 ± 0.32 and 1.67 ± 0.26 on the first and seventh days, respectively (p>0.05).

The analysis of the results of the study showed that in patients of group B, there was a 6-fold increase in the level of IL-6 in the blood serum during active bleeding and a 5-fold increase during the high risk of recurrence of bleeding (p>0.05). A different situation was observed in the case of studying the level of IL-4. The latter was reduced almost 3 times in group A and 4 times in group B compared to the control group (p<0.01).

A high level of pro-inflammatory cytokines IL-6 and low activity of the antiinflammatory mediator IL-4 determine the activity of the process, their long-term circulation in patients with ulcer bleeding from the upper gastrointestinal tract is associated with an unfavorable prognosis. With an imbalance of pro- and antiinflammatory mediators in favor of the former, the risk of recurrence of bleeding in the second group increases. Changes in the number of IL-6 pro-inflammatory cytokines in peripheral blood should be the cause and one of the mechanisms of recurrence of bleeding.

To characterize the correlation of C-reactive protein and Troponin-E, we need to determine the level of the latter in patients of both groups. We have the opportunity to separate this group of patients with acute myocardial infarction into a separate group (n=5). As a result of the study, it was possible to determine an increase in C-reactive protein in patients of this group by 16 times on the first day and almost 13 times on the seventh day of hospital stay (p<0.01). Regarding Troponin-T, it increased by 32.5 times on the first day and by 23.5 times on the seventh day. In this case, a moderate correlation between Troponin-T and C-reactive protein can be claimed.

We constructed an approximate analytical dependence of the probability of recurrence of bleeding on the level of C-reactive protein and the state of local endoscopic hemostasis, which allows us to obtain the degree of the possibility of recurrent bleeding. On the first day, this analytical dependence looks as follows: $y_1=-2.3818 \times 1+86.672$, where y_1 is the probability of recurrent bleeding, and x_1 is the level of C-reactive protein on the first day. On the third day - $y_3=-1.7426 \times 3+68.938$, where y_3 is the probability of recurrent bleeding, and x_3 is the level of C-reactive protein on the third day. On the seventh day - $y_7=-0.2431 \times 7+34.719$, where y_7 is the probability of recurrent bleeding, and x_7 is the level of C-reactive protein on the seventh day.

The considered patients belong to the group of high operational risk. Therefore, radical and conditionally radical methods of operative interventions should not be used due to the possible decompensation of cardiovascular pathology both in the intra- and postoperative period. When conservative therapy and methods of local endoscopic hemostasis were ineffective, surgical intervention was used. We have developed a method of surgical treatment of a bleeding ulcer of the pylorobulbar part of the stomach and received Patent for a utility model No. 139011 dated 10.12.2019. This surgical method with the use of tissue flaps to close the ulcer defect can be used in emergency surgery in the treatment of the category of patients with cardiovascular pathology. This method makes it possible to eliminate the need for the formation of a gastropyloroduodenal joint, thereby increasing the effectiveness of medical care due to the improvement of blood supply (microcirculation), reducing the risk of ischemia and necrosis, especially in this category of elderly patients. As a result of the use of the latter, there is a reduction in the duration of the operation by 42.4±2.43 minutes (p<0.05) compared to the use of the standard method. The advantages of this method are related to the possibility of stitching a bleeding vessel at the bottom of the ulcer with simultaneous tamponade of the mucous membrane. This surgical method made it possible to significantly reduce the risk of recurrence of bleeding in the postoperative period. A decrease in total mortality from 8.4% to 2.8% was noted. A relatively short-term operation with elements of radicalism makes it possible to minimize the processes of decompensation of the pathology of the cardiovascular system, because this category is patients with a high operative and anesthetic risk.

Conclusions. An important aspect when choosing treatment and diagnostic tactics and the method of surgical intervention is the presence of cardiovascular system pathology in patients. The determined changes in the cytokine profile make it possible to carry out a qualitative analysis of the state of local hemostasis and to determine adequate treatment tactics for this category of patients.

When analyzing the state of local endoscopic hemostasis, it was determined that the rate of unstable hemostasis with a high risk of recurrence of bleeding in patients of group A is higher than in group B by 17% due to an increase in the number of patients with active bleeding in the latter. The rate of stable F III hemostasis in group A was 30%, which was not observed in group B (p < 0.05). These results play an important role in the choice of treatment tactics. As for active bleeding, there was no active bleeding in group A, and it was 47% in group B (p<0.05). In the group of patients who had a recurrence of bleeding and who received "double therapy", the indicators of the body's immunoreactivity in comparison with the group of patients who received standard hypotensive therapy and had a lower of recurrence of bleeding indicate percentage a more pronounced immunosuppression.

Modifications in the operative treatment of ulcerative gastrointestinal bleeding in patients with acute cardiovascular pathology make it possible to perform operations with elements of radicalism, while reducing the duration of the operation itself and the development of postoperative complications, as well as postoperative mortality.

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