Research Article

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Restoration of Intestinal Propulsion in Patients with Severe Acute Pancreatitis in the Conditions of the Resuscitation and Intensive Care Unit

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RELEVANCE The intestine plays an important role in the processes of systemic inflammation, sepsis and multiple organ dysfunction, in the course of hemorrhagic shock, trauma, burns, pancreatitis, extensive abdominal surgery and in seriously ill patients in intensive care units (ICUs). One of the leading causes affecting the outcomes of treatment of surgical patients after interventions on the abdominal organs continues to be the syndrome of intestinal insufficiency developing in the early postoperative period, which important pathogenetic aspect is impairment of the propulsive function of the intestine.

AIM OF THE STUDY Improving treatment outcomes in patients with severe acute pancreatitis by restoring propulsive bowel function.

MATERIAL AND METHODS The study included 94 patients with severe acute pancreatitis (67 (71.3%) men and 27 (28.7%) women) admitted to the ICU in the first 24–72 hours from the onset of the disease (abdominal pain syndrome). The mean age was 48.2 ± 12.5 years, the patients were divided into two study groups: patients of the comparison group (n=40) received standard therapy in the ICU, patients of the study group (n=54) described treatment was supplemented with the use of saline enteral solution and early start of enteral nutrition in order to restore the functional activity of the intestine.

RESULTS Extended therapy with the inclusion of saline enteral solution made it possible to correct the manifestations of intestinal failure syndrome 2.4 times faster, to start enteral nutrition on day 2.1±0.8 of dynamic observation in the ICU in patients of the study group, which contributed to leveling the manifestations of intestinal failure syndrome, prevention and treatment of nutritional deficiencies. At the same time, effective intestinal peristalsis, confirmed by ultrasound, was determined in 57.4% of patients on day 2.1±1.6, in 35.1% on day 3.6±2.0, in 7.4% of patients on day 4.8±1.7 of stay in the ICU. While in the comparison group, peristalsis was determined in 37.5% of patients in 4.4±2.3 days, in 30% of patients in 6.2±1.1 days, in 27.5% in 8.1±3.6 days, in 5% of patients in 10.4±2.2 days and in 6.7% of patients it was not possible to restore effective peristalsis.

CONCLUSION Enteral solution in the treatment regimen for patients with a diagnosis of "Acute severe pancreatitis" contributed to a more rapid recovery of the effective motor-evacuation function of the intestine and made it possible to reduce the number of purulent-septic complications 1.4-fold, cases of multiple organ failure 1.7-fold, and mortality 1.6-fold.

Keywords: intestinal failure syndrome, acute pancreatitis, multiple organ failure

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IAH – intra-abdominal hypertension
IAP – intra-abdominal pressure
IL – intestinal lavage
AP – acute pancreatitis
ICU – intensive care unit
MOF – multiple organ failure
IF – intestinal failure
SES – saline enteral solution
SAP – severe acute pancreatitis
EGIS – esophagogastrointestinoscopy

INTRODUCTION

Intestinal failure is a combination of violations of the motor, secretory, digesting, absorption and barrier functions of the intestine due to various reasons, leading to ascending contamination of opportunistic microflora from its distal to proximal sections, the development of uncontrolled translocation of microbes and their metabolites into the blood , which leads to the exclusion of the small intestine from interstitial metabolism, creates the prerequisites for irreversible disorders of the main indicators of homeostasis [1].

In the early phase of acute pancreatitis (AP), an important role is played by microcirculation disorders that occur in the course of inflammation and a decrease in capillary blood flow in the tissues of the pancreas. Hypotension associated with systemic inflammatory response syndrome leads to centralization of blood circulation due to shunting of blood from peripheral vessels to the main circulation. Microcirculatory disturbances in the intestine lead to neuroendocrine dysregulation, dysfunction of intestinal epitheliocytes, impaired motor and evacuation functions of the intestine. The intestine plays an important role in the processes of systemic inflammation, sepsis and multiple organ dysfunction (MOF), associate with hemorrhagic shock, trauma, burns, pancreatitis, extensive abdominal surgery and in seriously ill patients in intensive care units (ICU) [2, 3]. One of the leading causes affecting the outcomes of treatment of surgical patients after interventions on the abdominal organs continues to be developing in the early postoperative period, IF, which important pathogenetic aspect is the disturbed propulsive function of the intestine [4–8].

Despite the fact that IF often occurs in ICU patients, it is usually underestimated, since the pathophysiological aspects associated with it are not well understood, and its clinical significance remains controversial to this day and raises a number of questions from specialists dealing with this issue [9–11].

The mucous membrane of the small intestine is an epithelial surface ranging from 150 to 300 m^2 and consists of a continuously renewing epithelium. It is important to note that its function is not limited to the digestion and absorption of nutrients, but is also responsible for many immune responses against toxins, microorganisms, etc. [12–14].

Intestinal failure is characterized by a significant decrease in the mass of intestinal epitheliocytes and their acute dysfunction associated with the loss of the intestinal barrier function [15].

Bacterial translocation is defined as the process by which bacteria or other antigenic macromolecules (such as lipopolysaccharide and peptidoglycan), which are normally found in the lumen of the gastrointestinal tract, spread across the intestinal mucosal barrier into normally sterile tissues, where they can either cause infection or activate the immune system [16, 17].

Gastrointestinal motility, usually controlled by a complex mechanism consisting of intermuscular and submucosal plexuses, the autonomic nervous system, hormones, neurotransmitters, and tissue myostimulators, is often affected in severely ill patients, which can lead to impaired enteral nutrition and poor outcome [18].

Delayed gastric emptying, gastrostasis, observed in approximately 50% of ventilated patients, leads to nasogastric feeding intolerance, upper gastrointestinal bacterial overgrowth syndrome, gastric colonization, and an increased risk of pulmonary aspiration and nosocomial infection. Abnormal small bowel motility also causes

bloating with the risk of diarrhea leading to hypovolemia, incomplete absorption, and negative nitrogen balance. In addition, digestion and absorption may be further impaired by small intestinal motor dysfunction and damaged mucosal structure [19, 20].

In connection with morphofunctional and hemocirculatory changes in the intestinal wall in IF, the permeability of the intestinal barrier to endotoxin, bacteria and bacterial antigens, toxic substances increases, causing their translocation, which causes the development of systemic infection, sepsis, and multiple organ failure [21].

Prevention of translocation by removing intraluminal flora, predominantly consisting of aerobic gram-negative microorganisms, can be an effective method for preventing infection of necrotic tissues of the pancreas [14]. One of the methods to reduce the bacterial load is the selective decontamination of the intestine with antibacterial drugs. Carrying out such therapy has shown that this method eliminates aerobic gram-negative bacteria from the intestinal tract and reduces the risk of purulent-septic complications in patients with AP who are treated in the intensive care unit [23, 24]. However, in a number of studies, the results obtained did not show a decrease in mortality and still remain controversial [25].

Another method of treating IF is intestinal lavage (IL) using saline enteral solution (SES), isotonic to the chyme of the initial parts of the small intestine [26], in patients with severe acute pancreatitis (SAP) [27]. This method, due to the isoionicity of the solution used, ensures the electrolyte balance of the body, and due to the correspondence between the osmotic pressure of the solution and the colloid-osmotic pressure of the blood plasma, it eliminates unidirectional massive transport of water through the intestinal wall. During the IL, along with the intestinal contents, the part of the intracavitary microflora (P-flora), which is represented mainly by opportunistic and pathogenic strains, is removed, while the M-flora (mucosal) is preserved, since it is protected by a water-insoluble layer of mucous deposits the inner wall of the intestine [28]. The acidic environment of saline enteral solution (SES) reduces the growth of opportunistic and pathogenic flora remaining in the intestine. The described technique was previously used in the treatment of patients with SAP and pancreatic necrosis in the ICU [28, 29]. Intestinal lavage was performed using two methods: 1) patients, under the supervision of medical personnel, independently drank SES, heated to 38 °C, 150–200 ml every 5–10 minutes; 2) patients had their small intestine intubated with a two-channel silicone probe "ZKS-21M" under endoscopic guidance, passing through the ligament of Treitz. The prepared solution was administered through the perfusion channel of the probe at a rate of 20–30 ml per minute, in a volume of 60–63 ml/kg body weight [29].

The disadvantage of this application is that during the IL procedure it is necessary to limit the intravenous administration of solutions to 400-800 ml, to exclude the introduction of hypo- and isotonic saline and glucose solutions. Oral use of SES in critically ill patients is associated with a high risk of aspiration of gastric contents, since almost all patients with SAP have dyspeptic disorders such as nausea or vomiting. A high level of intra-abdominal hypertension (IAH) with a large volume of SES injected into the intestine (4,000-5,000 ml) does not allow the use of this technique, as it can lead to intra-abdominal hypertension (IAH) and the development of compartment syndrome. At the same time, with the introduction of SES through a nasointestinal probe in the group of patients with normal or slightly elevated IAP levels, this technique has proved to be the best way to restore intestinal motility and a detoxification method in the complex treatment of patients with destructive pancreatitis in the toxemia phase.

Thus, the need to find a method for treating IL in patients with SAP was the reason for conducting this study.

The purpose of the study: to improve the results of treatment of patients with SAP by restoring the propulsive function of the intestine.

MATERIAL AND METHODS

The study included 94 patients with SAP (67 (71.3%) men and 27 (28.7%) women (Table 1)) admitted to the ICU within the first 24–72 hours from the onset of the disease (abdominal pain syndrome). Mean age 48.2±12.5 years; The patients were divided into two study groups: patients of the comparison group (n = 40) received standard therapy in the ICU, the treatment of patients of the study group (n = 54) was supplemented with SES and early enteral nutrition in order to restore the functional activity of the intestine.

Inclusion Criteria:

1. Admission to the ICU 24–72 hours after the onset of abdominal pain.
2. The presence of a diagnosis of SAP.
3. Age 18–70 years.
4. *APACHE* II over 10 points.
5. *SOFA* over 2 points.
6. The degree of IF 2nd and higher.

Exclusion Criteria:

1. The agonal state of the patient.
2. Unstable hemodynamics (increasing dosages of vasopressor and inotropic support).
3. The presence of competing diseases that cause the severity of the condition.
4. Long-term use of anticoagulants in history.
5. The presence of cancer.
6. The presence of autoimmune diseases.
7. Severe liver dysfunction.
8. Injuries or surgical interventions in the area of the central nervous system, organs of vision and hearing.
9. Syndrome of disseminated intravascular coagulation as part of heparin-induced thrombocytopenia.
10. Acute bacterial endocarditis and protracted endocarditis.
11. Organic disorders with an increased risk of bleeding (active peptic ulcer, hemorrhagic stroke, cerebral aneurysm or cerebral neoplasia).
12. Refusing treatment.

All patients were standardized for age, gender and comorbidities. The severity of the condition in the study groups was assessed using the *APACHE* II, *SOFA* , *MARSHALL* , *Ranson* scales and amounted to 16.6±4.0, 3.42±1.25, 2.7±0.75, 3.6±0.46 points in patients of the 1st group and 16.4±3.8, 3.51±1.32, 2.6±0.64, 3.4±0.42 points in patients of the 2nd group, respectively (Table 2). Statistical analysis was performed using *Statistica* 10.0 and *MS Excel software*. For each variation series, the mean value (*M*) and standard deviation (σ) were calculated.

All patients of the study groups in the first 24 hours of stay in the ICU underwent instrumental research methods, including:

1. Ultrasound examination of the abdominal organs.
2. Plain radiography of the abdominal organs.

Additionally, to assess the functional state of the intestine, laterography and a survey radiograph of the abdominal cavity were performed.

3. Esophagogastrointestinoscopy (EGIS).

When analyzing the data obtained using EGIS, a visual picture of the state of the examined intestine was evaluated.

Table 1

The distribution of patients by gender

Floor	Number of patients	Share of total number of patients, %
Women	27	28.7
Men	67	71.3

Table 2

The assessment of the severity of the condition of patients with severe acute pancreatitis

Scale	1st group	2nd group
APACHE II	16.6±4.0	16.4±3.8
SOFA	3.42±1.25	3.51±1.32
MARSHALL	2.7±0.75	2.6±0.64
Ranson	3.6±0.46	3.4±0.42

In group 2, in addition to routine research methods, intra-abdominal hypertension (IAH) was also assessed by measuring intra-abdominal pressure (IAP). The interpretation of the results was carried out according to the scale proposed by *the WSACS* :

I degree IAH, 12–15 mm Hg;

II degree IAH, 16–20 mm Hg;

III degree IAH, 21-25 mm Hg;

IV degree IAH, over 25 mm Hg.

The result is recorded at the end of the patient's exhalation. The result obtained is considered the value of IAP in centimeters of the water column (1 cm of water column \u003d 0.74 mm Hg).

In order to stimulate intestinal motility and enteral correction of the microbiota, the patients of the study group were injected into the nasointestinal probe, installed through the endoscope channel into the jejunum behind the ligament of Treitz, for enteral infusions, containing inulin and L-glutamine (2.5 g and *15* g respectively). The introduction of SER was carried out at a rate of 6–10 ml per minute in a volume of 1500 (±400) ml under the control of IAP, which should not exceed 16–20 mm Hg.

In case of IAP III degree (over 21 mm Hg), the volume of SES administration should not exceed 500 ml. At the same time, cleansing enemas (3-4) are performed with SES, and 100 ml of Lactulose is added. In the case when IAP is more than 25 mm Hg (Grade IV), enteral correction was not performed, and the decision to conduct enteral infusion is possible only after determining the surgical tactics for resolving the abdominal compartment syndrome. Recovery of effective intestinal peristalsis was assessed by ultrasound.

RESULTS

In the course of the study, it was found that in the comparison group, where standard conservative therapy was carried out, effective intestinal motility, confirmed by ultrasound, was determined in 37.5% of patients after 4.4±2.3 days, in 30% of patients after 6, 2±1.1 days, in 27.5% after 8.1±3.6 days, in 5% after 10.4±2.2 days, and in 6.7% of patients it was not possible to restore effective peristalsis (Fig. 1*A*). The independent stool was observed in 52.5% of patients by 8.2±1.9 days, in 30% by 9.6±2.8 days of observation in the ICU; in 17.5% of patients, independent stools were not recorded (Fig. 2A*)* . The development of purulent-septic complications was observed in 47.5%. The development of MOF was observed in 30%. The mortality in the comparison group was 27.5% (Fig. 3).

When measuring IAP in the study group, IAH degree I was observed in 53.7%, IAH degree II was observed in 9.3%, IAH degree III was seen in 5.5%, IAH degree IV was observed in 1.8% of patients, in 22.2% of cases IAH was not was determined (Table 3).

In the study group, where SES was included in complex therapy, effective intestinal motility, confirmed by ultrasound, was determined in 57.4% of patients by 2.1±1.6 days, in 35.1% by 3.6±2.0 days and in 7.4% of patients for 4.8±1.7 days of stay in the ICU (Fig. 1*B*). While spontaneous stool was observed in 66.7% of patients after 180.5±23.4 minutes, in 24.1% of patients after 260.8±32.2 minutes and in 9.3% after 340, 5±19.6 minutes from the start of SES administration (Fig. 2*B*).

The development of purulent-septic complications was observed in 33.3%. The development of MOF was registered in 18.5%. The mortality in the study group was 16.7% (Fig. 3).

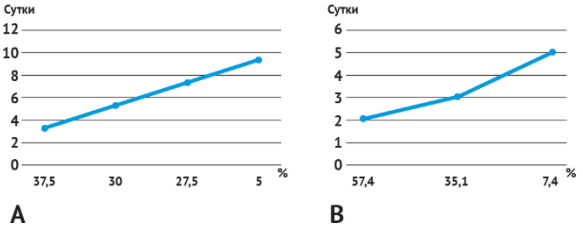

Fig. 1. The restoration of intestinal propulsion in patients. A — comparison group; B — study group

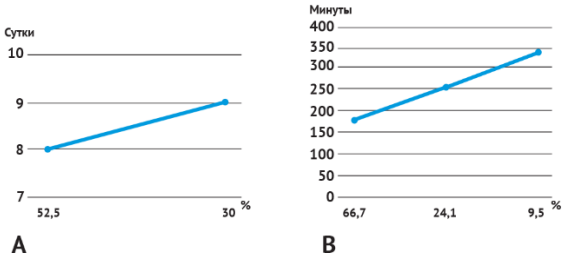

Fig. 2. The restoration of independent bowel movement in patients. A — comparison group; B — study group

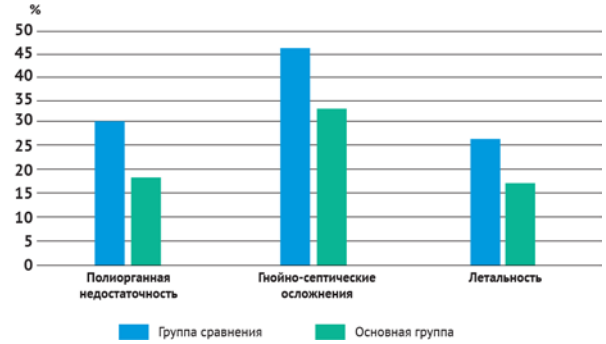

Fig. 3. Results of treatment

Table 3

The degree of intra-abdominal hypertension in patients of the study group

Share of total number of patients, %	Degree of intra-abdominal hypertension
53.7	I
9.3	II
5.5	III
1.8	IV
22.2	–

CONCLUSION

In the course of this study, it was noted that there is a direct relationship between ultrasound changes, determined by examining the intestines of patients with severe acute pancreatitis, the degree of intra-abdominal hypertension and the incidence of purulent-septic complications, multiple organ failure, and the level of mortality in patients of this category. Obviously, in addition to assessing effective peristalsis using ultrasound, it is necessary to monitor the severity of intestinal failure syndrome using the following ultrasound criteria: small intestine lumen diameter, thickness, presence of wall edema, differentiation of intestinal wall layers, severity of folds, pathological changes in the mesentery of the small intestine intestines, the amount and nature of fluid in the abdominal space.

The inclusion of enteral infusion of saline enteral solution into the treatment regimen for patients with a diagnosis of "Acute severe pancreatitis" contributed to a more rapid recovery of effective motor-evacuation function of the intestine and reduced the number of infectious complications 1.4-fold, cases of multiple organ failure 1.7-fold, and the mortality 1.6-fold.

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