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Management of Severe Acute Pancreatitis

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Abstract **Objective.** Improvement the effectiveness of treatment of patients with severe acute pancreatitis. **Material and methods.** The experience of the treatment of 87 patients with severe acute pancreatitis is considered. The protocol of therapeutic and diagnostic tactics included active conservative management of patients with a daily overall assessment of the clinical picture according to the Marshal, APACHE II and Ranson scales, the dynamics of laboratory changes, combined with the instrumental research data (ultrasound, CT and MRI) and the use of delayed surgical interventions. **Results.** In 54 (62%) patients, the therapy led to recovery without surgical treatment, 33 (38%) were operated for purulent-septic complications. The overall mortality in the study group was 18.4%. Satisfactory outcomes were achieved in 71 patients (81.6%). Mortality among operated patients was 48.5%. **Conclusion.** The use of the developed protocol led to a decrease in overall and postoperative mortality, the number of systemic complications and a significant increase in survival in severe acute pancreatitis.

Keywords Severe acute pancreatitis, Pancreas necrosis, Treatment, and diagnostic protocol

1. Introduction

Acute pancreatitis (AP) continues to be among the most common emergency pathologies of the gastrointestinal tract and is characterized by a high percentage of disability and mortality in its destructive forms. Studies conducted under the auspices of WHO have noted a steady increase in the annual incidence of AP, which ranges from 200 to 800 cases per 1 million of the world's population [1-7].

Of all forms of AP, severe acute pancreatitis (SAP) develops the most significant level of mortality, developing in 20–30% of cases. In addition, the number of patients who develop infected pancreatic necrosis, late multiorgan failure (MODS) and other severe purulent-destructive complications of AP - arrosive bleeding, duodenal fistula, small and colonic fistulas, pancreatic fistula increases [4, 5, 6]. According to various studies, despite the general decrease in the incidence over the past decade, the death rates of AP vary from 10% to 85% [2, 8-10].

According to many authors, the complexity of managing patients with SAP is a limited understanding of the pathogenesis, uncertainties in predicting certain complications and outcome of the disease, and the choice of effective methods of treatment [5, 11, 12]. The solution to this problem implies a significant reduction in mortality and the frequency of severe, first of all, infectious-septic and respiratory complications of this disease, a decrease in the duration and cost of treatment, and an improvement in the quality of the further life of patients. The results of a complex of measures depending on the time of treatment, the adequacy of its volume, the availability of appropriate life-support technologies, a clear definition of indications and contraindications, the interaction of specialists [5, 6, 9, 10, 12-15].

In order to develop an optimal algorithm for the complex treatment of SAP, which allows reducing mortality and the frequency of complications, an attempt was made to create such a protocol in the context of the ICU. It includes the algorithm of collectively coordinated actions of the resuscitator and surgeon when the patient enters the hospital, determines the main elements of the conservative and surgical treatment tactics. Further, the use of this protocol allowed to achieve satisfactory results in 81.2% of patients with SAP.

2. Material and Methods

We analyzed the data of 87 patients with SAP were treated for the period from 2008 to 2018. The average age was 55.5 (38.0-73.0) years. Acute destructive pancreatitis was diagnosed in 63 patients (72.4%), complicated forms of severe destructive AP - in 24 (14.6%).

The work used the criteria for diagnosis and determination of the severity of the AP, based on paragraphs of the Atlanta-92 international classification of the second and third revision (2012). The main type of treatment for SAP was intensive conservative therapy, which includes the following points:

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- infusion therapy in a volume of not less than 40 ml/kg of body weight with a ratio of colloid and crystalloid solutions of 1: 4;
- multimodal analgesia: epidural analgesia (continuous infusion of 0.2% lidocaine solution with a speed of 6-12 ml / h); nonsteroidal anti-inflammatory drugs (dexketoprofen 50mg 3 times a day); opioid analgesics (promedol 1-2% to 20 mg / day);
- antisecretory therapy: suppression of the secretion of the pancreas (somatostatin selection drug 100 mcg 3 times per day subcutaneously); suppression of gastric secretion (rabeprazole up to 40 mg/day i.v.);
- rational antibacterial therapy: the use of drugs that create maximum concentrations in pancreatic tissues that are in excess of the minimum inhibitory concentration for the majority of infectious agents in case of pancreatic necrosis (piperacillin and mezlocillin; third-generation cephalosporins (cefotaxime, ceftazidime); imipenem and metronidazole).
- extracorporeal methods in the absence of endotoxin shock: low-flux ultrafiltration (with persistent oliguria less than 500 ml/day, hyperkalemia more than 6.5 meq / l, glomerular filtration rate less than 20 ml/min and an increase in creatinine level).
- respiratory support in the development of pancreatitis-associated acute respiratory distress syndrome (ARDS). Indications for intubation - respiratory index (PaO_2/FiO_2) below 200. The principle of "safe ventilation" is used: peak pressure less than 35 cm of water, FiO2 not more than 60%, respiratory volume less than 6-8 ml/kg. The criterion of adequacy is the following indicators: PaO_2/FiO_2 more than 300, a decrease in infiltration on the chest radiograph, an increase in static compliance (Cst).
- nutritional support is provided by parenteral administration of fat emulsions, amino acids in the first 24 hours of the disease with the transition to enteral administration of balanced mixtures on the 5-7th day of the favorable course of the disease, trying to ensure 25-30 kcal/kg per day.

Indications for surgical interventions are lack of effect from conservative intensive care, the progression of peritoneal phenomena, sequestration of the gland, development of suppurative complications of pancreatitis (suppuration of pancreatic necrosis, abscess of the omental bursa) usually for 7-15 days; the occurrence of arrosive bleeding.

Laparoscopy is carried out as the first stage of surgical treatment with an inconclusive diagnosis of pancreatitis, clarification of the form of the disease, in order to remove peritoneal exudate, drainage of the abdominal cavity. When combined with AP and destructive cholecystitis (progressive biliary hypertension with hyperbilirubinemia more than 100 μmol/l), cholecystectomy with choledochus drainage is indicated.

The main tasks of delayed open operations are the mobilization of all foci of necrotic destruction in the retroperitoneal space, complete necroectomy or sequestrectomy, delimitation of all necrotic zones from the free abdominal cavity, ensuring adequate drainage of exudate with the planning of subsequent intervention in a certain period.

3. Results

The main etiological forms of SAP in the studied group of patients were biliary in 50.6% (n=44), alcoholic (including alimentary-toxic) - 32.2% (n=28) of observations, less frequent traumatic pancreatitis (including cases after endoscopic interventions) - 17.2% (n=15) of observations.

Among the purulent-septic complications in the operated patients with destructive SAP, infected postnecrotic pancreatic cysts, as well as retroperitoneal phlegmon, and purulent peritonitis were observed in 59.6% and 38.6% of cases, respectively. Less common: abscess stuffing bags - 27.4% of cases and pancreatic abscesses - 11.5%, respectively. Moreover, more than 50% of patients with SAP had 2 or more purulent-septic complications.

The most unfavorable for prognosis systemic complications of SAP were: ARDS, MODS, sepsis. At the same time, 100% mortality was observed in postoperative patients with infected forms of pancreatic necrosis with an increase in APACHE II indices above 20 points, Ranson - above 6.

In 7 patients, extracorporeal detoxification methods were applied in a complex of therapeutic measures. The severity of intoxication syndrome decreased according to the clinical picture and laboratory research methods. 33 (38%) patients underwent various types of surgical interventions. 12 patients underwent drainage of the omentum bag under ultrasound control, 10 patients underwent laparoscopy, laparotomy, drainage of the omentum bag and abdominal cavity, in one - choledocholithotomy, cholecystectomy, choledoch drainage. In 10 patients (four of them after minimally invasive medical operations), despite the ongoing therapy, signs of septic sequestration developed that required performing a laparotomy, necrotomy, sequestrum and pancreatic contraction, drainage of the abdominal cavity and retroperitoneal space. Repeated surgical interventions were performed in 14 patients, of which patients take repeated necro- and sequestrectomy, six - laparotomy, sanation of the abdominal cavity, necro- and sequestrectomy after minimally invasive surgical interventions.

Upon detection of pancreatic destructive peritonitis, at the first stage, surgical treatment of 6 patients selected laparoscopic sanation and drainage of the abdominal cavity, which, in combination with complex intensive therapy, led to abortive peritonitis in 83.3% of cases, relief of pancreatic necrosis - in 59.4%. However, in 40.6% of cases after laparoscopy, a transformation of sterile pancreatonecrosis into an infected one was observed. In 16 patients in the postoperative period, despite ongoing therapeutic measures,

death occurred, the cause of which was progressive MODS in the background of purulent-septic complications of SAP. Mortality among operated patients was 48.5%.

Thus, intensive conservative therapy without the use of surgical methods led to the recovery of 54 (62%) patients, of whom 69.2% were initially diagnosed with a sterile form of AP. The overall mortality in the study group was 18.4%. Satisfactory results were achieved in 71 patients (81.6%) with AP. When analyzing the main causes of deaths in the dead with destructive pancreatitis from 1998 to 2017. It was found that increasing liver failure was detected in 28.8% of patients, respiratory failure (ARDS), renal and cardiovascular failure in 42.5%, 40.5% and 33.2% of cases, respectively. Much less common: disseminated intravascular coagulation, which is set in 14.2%, metabolic syndrome and sepsis - in 12.8% of cases, septic (infectious-toxic) shock - in 9.5%, profuse arrosive bleeding - 8.3 %, profuse gastroduodenal bleeding - in 3.5% of cases, respectively; 56 (83.6%) patients had more than two fatal complications.

4. Discussion

One of the main criteria that characterize various forms of SAP in the early stages of its development is the degree and scale of the initial pancreas damage. This is what determines the pattern of development of the pathological process, allows you to predict the outcome, predict the nature and timing of the development of complications, apply for standardized treatment programs from the time of verification of the diagnosis [4, 13, 18, 26, 28].

During the past, more than 20 years, some important points of the Atlanta-92 classification [16] revised in accordance with the deepening of knowledge about pathophysiology, morphology, course of AP, and taking into account the emergence of new diagnostic capabilities. In 2007, on the initiative of M.G. Sarr (USA) once again set up an international working group on the 3rd revision of the Atlanta 1992 classification. For 5 years, experts have studied international experience in the diagnosis and treatment of AP in large-scale studies, and in 2013 the text of the third revision of the classification of AP was published and recommended for use [17].

The conservative treatment of AP is still mostly symptomatic. There are no specific medications affect the cause of the disease. There are two main areas of basic therapy for patients with SAP. The purpose of the first is to prevent specific complications that may arise in a given patient and to carry out maintenance therapy. The second goal is to limit the severity of inflammation and pancreas necrosis, preventing the pathogenesis of SIRS [18, 19, 20].

SAP has a significant depletion of the body and usually occurs with symptoms of acute paralytic intestinal obstruction. In this regard, the organization of clinical nutrition is an important component of intensive care AP. In patients with SAP, the maintenance of the pancreas at rest is mandatory; therefore, nutritional support should be started with parenteral access [21]. In this case, the minimum input volume should provide a positive nitrogenous balance in the first 72 hours from the onset of the disease [22].

Early enteral nutrition is indicated after compensation for hemodynamic disorders. If the volume of enteral nutrition tolerated by the patient is insufficient to achieve adequate caloric content, it is necessary to introduce a combined parenteral and enteral nutrition.

The goal of antibiotic prophylaxis is the prevention of superinfection in necrotic tissues. The tactics of antibiotic use in acute pancreatitis should include their early adequate use, and local data on hospital flora should be taken into account. Late organ dysfunction, which most often occurs between the second and third weeks of the development of SAP, is most likely a consequence of secondary infection and peripancreatic necrosis due to bacterial translocation from the gastrointestinal tract to the necrotic tissue of the pancreas fluid [4].

There are a large number of published studies with questionable constructs and conflicting results, which can be explained by the inclusion of heterogeneous patients, different antibiotic regimens and different research goals [19]. Several randomized controlled studies indicate the effectiveness of prophylactic antibiotics in reducing septic complications and mortality in patients with necrotizing pancreatitis [23]. The American Gastroenterology Association recommends initiating antibiotic prophylaxis in cases of advanced necrosis, which includes more than 30% of the pancreas based on CT. It should be prescribed for no more than 14 days, as long-term antibiotic therapy increases the incidence of fungal infections. The role of prophylactic antifungal agents has not been fully defined [19, 24].

Pancreatitis-associated ARDS, as one of the common and early terrible complications of SAP, is responsible for 60% of all deaths during the first week of the disease [25]. The use of modern technologies of respiratory support with the possibility of selecting the optimal modes of ventilation at each stage of the intensive treatment of SAP allows reducing the number of infectious and inflammatory complications in patients associated with mechanical ventilation.

As a rule, sterile pancreatic necrosis can be maintained conservatively, and in most cases, low mortality is recorded (12%) [5, 11]. However, an infected form of pancreatic necrosis is observed in 25-70% of patients with SAP. More than 80% of deaths, in this case, are associated with the development of infected pancreatic necrosis and septic complications [18, 19, 20]. Today, with infected forms of pancreatic necrosis, the indications for surgical treatment are beyond doubt. It is generally accepted that in order to prevent sepsis, infected non-viable tissue should be removed [2, 4, 12].

Randomized controlled studies have demonstrated that the effectiveness of delayed necrotomy is higher than early [27]. It has also been proven that relaparotomy increases the proportion of local intra-abdominal and systemic organ lesions and has a negative hemodynamic and systemic inflammatory response, causing the progression of MODS, uncontrolled hemorrhagic complications, and sepsis.

Therefore, at the present stage, surgical interventions in this pathology should be considered as forced [5, 6, 9, 29].

5. Conclusions

A comprehensive diagnostic and treatment protocol with the full use of intensive care in the early phases of the disease is of great importance in reducing the likelihood of infection of sterile pancreatic necrosis and the occurrence of purulent complications.

Actively expectant tactics with the phased use of surgical methods for treating SAP allows stabilizing patients, reducing endogenous intoxication, interrupting complications of pancreatic necrosis, reducing the risk and volume of delayed open surgery with an increase in survival to 81.6% and a corresponding decrease in mortality to 18.4%.

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