Modern Therapeutic Approach of Acute Severe Forms of Pancreatitis. A Review of the Literature and Experience of Surgical Department No III Cluj

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Abstract
The title of "the great abdominal drama" attributed to acute pancreatitis is fully justified by the impressive clinical presentation, the deep consumptive characteristics of physio-pathological processes taking place, the severity of the complications and the complexity of the treatment.

Materials and methods: The aim of our study was to analyze the results on a number of 81 consecutive patients hospitalized in...
the Surgical Clinic III Cluj during 28 months, all diagnosed with severe forms of acute pancreatitis. There were two groups of patients, non-surgical (43 cases) and surgical cases (38 cases), respectively. The diagnosis and forms of the disease took into account the clinical picture, serum amylase, CPR and Balthazar procalcitonine, together with the classification of the lesions on CT scan.

Results: All patients were admitted to the intensive care unit and received supportive treatment such as antibiotics, pancreatic exocrine secretion inhibitors and proton pump inhibitors. The surgical act in the 38 cases was indicated by septic intra-abdominal pressure or high functionality threatening vital viscera. Intraoperatively the abscesses were drained, the necrotic areas were removed and cholecystectomy was performed in patients with biliary etiology. Statistically, we obtained significant differences in the incidence of complications between the group of patients operated and those not operated (p = 0.000048), but not in what concerns the length of hospitalization (p = 0.99999) and the number of deaths (p = 0.2102). The overall mortality was 14.41%, comparable to that found in the literature. In none of the patients CT-guided drainage of collections was performed prior to surgery, which was a major drawback of the treatment.

Conclusions: Our results support the importance of an early diagnosis and medical treatment, the delayed surgery being required in high intra-abdominal pressure or SEPS.

Key words: acute pancreatitis, severe form, medical treatment, late surgery

Introduction

Acute pancreatitis reports an incidence varying from one country to another, between 5-100 cases/100,000 population (1,2,3,4,5), explainable by the unequal distribution of the principal risk factors of the disease, such as gallbladder stones and excessive consumption of alcohol.

20% of the patients with acute pancreatitis develop severe forms of the disease, characterized by local evolution of the disease towards necrosis and superinfection, and systemic through the appearance of multiple organ failure. The mortality in this severe form of acute pancreatitis is 7-15% (6,7). This percentage increases substantially with the presence of multiple organ failure. In this way, the mortality rate of patients with severe acute pancreatitis accompanied by respiratory, renal and hepatic insufficiency is 43%, 63% and 83%, respectively (8).

The prognosis of the patients depends mainly upon introduction of an early and correct treatment. Hospitalization in an intensive care unit is mandatory along with monitoring and sustainance of vital parameters, broad spectrum antibiotic therapy, inhibition of exocrine pancreatic secretion and proton pumps, keeping a constant view that the surgical intervention is only indicated when the ultrasound-guided or CT-guided percutaneous drainage of the peripancreatic fluid collection is inefficient and when raised intrabdominal pressure poses a threat to the normal function of kidneys, lungs and heart. (9)

All these therapeutic measures are meant to prevent complications. Modern treatment strategies have the goal to modulate the exaggerated inflammatory response and the CARS syndrome (anti-inflammatory response syndrome), by acting at the biological and physiological level of the cell, and improving the methods which allow us to identify potentially unfavourable evolution of the patient as early as possible.

Material and Method

Our study includes a number of 81 patients (24 female, 57 males; median age: 55.3 years, ranging within 19-90 years), admitted to the Surgical Clinic No. III Cluj from January 2009 to April 2011, and diagnosed with severe acute pancreatitis. Out of all these patients, 38 (46.91%, 6 females, 32 males; median age 56.63, within the range 25-90 years), needed surgical intervention because of the evolution of the disease towards sepsis. The diagnosis was based upon the clinical finding supported by paraclinical investigations, serum and urinary levels of amylase and the imaging aspect (Ultrasound and CT). Severe acute pancreatitis was defined according to the Atlanta criteria (10). The CT results were included in the Balthazar classification (11). The etiology of pancreatitis was found to be biliary in 35 cases (43.20%), alcoholic in 30 cases (37.04%), metabolic in 10 cases (12.35%) and the rest were found to be a mixed etiology like post-ERCP or idiopathic (7.41%). (Table 1)

Statistics

The data were analysed from the statistical point of view and the results were expressed as a numerical form and as percentage, mean and standard deviation were utilised for continuous variables. Fischer test was utilised for the analysis of the data and a p-value lesser than 0.05 was considered to be statistically significant.

Results

All the patients with severe forms of acute pancreatitis were admitted to the intensive care unit. Daily monitoring of the

Table 1. Demographic data of the patients included in the study

<table>
<thead>
<tr>
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<th>Cases of acute pancreatitis (81)</th>
<th>Cases of operated acute pancreatitis (38)</th>
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<tbody>
<tr>
<td>Females</td>
<td>24(29.62%)</td>
<td>6(15.78%)</td>
</tr>
<tr>
<td>Males</td>
<td>57(70.37%)</td>
<td>32(84.21%)</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>55.3</td>
<td>56.63</td>
</tr>
<tr>
<td>with limits between (yrs):</td>
<td>19-90</td>
<td>25-90</td>
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general status, temperature, diuresis, intestinal transit, biochemical and hematologic parameters were performed. Imagistic investigations were performed whenever considered necessary. The CRP and procalcitonine levels were assayed dinamically.

The initial treatment was conservative and included reestablishing hydroelectric balance, antibiotics (Tienam or Cephalosporines with Metronidazol), inhibitors of the exocrine pancreatic secretion (Sandostatin), inhibitors of the proton pumps. The patients were given both enteral and parenteral nutrition.

The surgical intervention was decided when the general status of the patient got altered by the appearance of sepsis, confirmed through increased leucocytes level, CRP and procalcitonine in the presence of an intraabdominal fluid collection found on CT or when the increased intraabdominal pressure threatened the functioning of the vital organs. The earliest surgical intervention was performed on day 6 and the latest was on day 22 during the evolution of the disease.

Intraoperatively there were performed necrosectomy, evacuation of the intraabdominal abcesses, peritoneal lavage and placement of the multiple intraperitoneal drainage tubes. In the case of the patients where the etiology was found to be biliary, colecistectomy accompanied other surgical manoeuvres (17 cases). Choledocotomy and external biliary drainagof the common bile duct were performed in case of these patients having hepatobiliary lysis and in whom sfincterotomy and endoscopic drainage could not be performed earlier (5 cases) or were proven to be ineffective (3 cases). The latter were patients who required an early surgical intervention to remove the causing factor. An open surgical method was used in all the cases because or the presence of multiple intraabdominal abcesses and the altered clinical status of the patients.

Postoperatively, the general status of the patients was monitored clinically and paraclinically, providing sustainance of the vital functions and antibiotherapy according to the antibiogram. A number of 16 patients out of the total who underwent the first surgical intervention had a favourable evolution, however 22 had complications, out of which 8 needed reintervention.

The most frequent complications were pancreatic fistulas (15 cases) and septic shock (4 cases), 6 patients (13.95%) of the group who did not undergo surgical intervention developed complications like MSOF.

Statistics obtained a significant difference between the group of patients who underwent surgery and the ones who did not have a surgical intervention. The median duration of hospitalization was 11.48±9.43 days for the unoperated cases and 30.89±23.38 days for the operated cases, respectively. We did not observe any significant difference in duration of inhospital stay (p=0.2102) and the mortality rate between the operated and non-operated patients (p=0.99999). (Table 2)

**Discussions**

Nowadays, acute pancreatitis is considered to be a systemic disease, as after activation of intraglandular pancreatic proteasis, followed by destruction of cellular membranes of the acins and liberation of the enzymes in the peripancreatic tissues, the body activates local protective mechanisms, like inflammatory reaction and activation of cytokines, events which can get out of the local control, resulting in uncontrolled, excessive activation of inflammatory cells and mediators, situation that is defined as SIRS (systemic inflammatory response syndrome) (12). Proinflammatory cytokines like TNF-α and IL-β are released in the circulation, through the portal vein (13), increasing the inflammatory response, and IL-6 stimulates the hepatic synthesis of acute phase proteins (CRP, procalcitonine) (14). Proinflammatory cytokines increase the capillary permeability of the entire organism, amplifying fluid loss and favouring intratissular migration of leucocytes (12), with the activation of neutrophiles and monocytes, which liberate the proteolitic enzymes and free radicals, destroying the vascular endotelium as well as the parenchimal cells (15). This phenomenon, accompanied by the deficiency of cellular oxygen, leads to the disfunction of vital organs, followed by their failure, most affected being those having rich capillar capital, like the lungs and the kidneys (15,16,17). Progression of events explains the early deaths in acute pancreatitis (12).

Concomitantly along with SIRS, with a role of controlling its magnitude, mechanisms of CARS (compensatory anti-inflammatory response syndrome)are occuring, but its exacerbation leads to immunosupression and an increased risk of infectious complications, in this way a characteristic feature of the later phase of the evolution of patients having acute severe pancreatitis (12,18). The most powerful anti-inflammatory cytokines are IL-10, responsible for the decreased monocyte HLA-DR expression (19). Along with the IL-10, in response to the immunosupression IL-1
Acute pancreatitis represents one of the most severe abdominal pathologies, having a potential lethal evolution in a large number of cases, and with a serious consumption of human and financial resources. The results of the treatment can be improved by knowing the physiopathological phenomenon behind this pathology, early diagnosis of the form of the disease and a rapid initiation of the maintenance therapy.

Patients who need a surgical intervention will be postponed until the sepsis given by the superinfection of the necrotic zones or until abdominal compartment syndrome will appear leading to dysfunction of the intra-abdominal organs.
Minimally invasive techniques like the imaging or endoscopic guided drainage proved themselves to be useful in gaining time and postponing the surgical moment and sometimes to be sufficient enough as therapeutic gestures.

References


