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• BRIEF REPORTS •

Clinical characteristics and management of patients with early acute severe pancreatitis: Experience from a medical center in China

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Abstract

AIM: To study clinical characteristics and management of patients with early severe acute pancreatitis (ESAP).

METHODS: Data of 297 patients with severe acute pancreatitis (SAP) admitted to our hospital within 72 h after onset of symptoms from January 1991 to June 2003 were reviewed for the occurrence and development of early severe acute pancreatitis (ESAP). ESAP was defined as presence of organ dysfunction within 72 h after onset of symptoms. Sixty-nine patients had ESAP, 228 patients without organ dysfunction within 72 h after onset of symptoms had SAP. The clinical characteristics, incidence of organ dysfunction during hospitalization and prognosis between ESAP and SAP were compared.

RESULTS: Impairment degree of pancreas (Balthazar CT class) in ESAP was more serious than that in SAP (5.31±0.68 *vs* 3.68±0.29, $P<0.01$). ESAP had a higher mortality than SAP (43.4% *vs* 2.6%, $P<0.01$), and a higher incidence of hypoxemia (85.5% *vs* 25%, $P<0.01$), pancreas infection (15.9% *vs* 7.5%, $P<0.05$), abdominal compartment syndrome (ACS) (78.3% *vs* 23.2%, $P<0.01$) and multiple organ dysfunction syndrome (MODS)(78.3% *vs* 10.1%, $P<0.01$). In multiple logistic regression analysis, the main predisposing factors to ESAP were higher APACHE II score, Balthazar CT class, MODS and hypoxemia.

CONCLUSION: ESAP is characterised by MODS, severe pathological changes of pancreas, early hypoxemia and abdominal compartment syndrome. Given the poor prognosis of ESAP, these patients should be treated in specialized intensive care units with special measures such as close supervision, fluid resuscitation, improvement of hypoxemia, reduction of pancreatic secretion, elimination of inflammatory mediators, prevention and treatment of pancreatic infections.

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INTRODUCTION

Despite considerable improvement in the treatment of severe acute pancreatitis (SAP), the mortality of the disease still ranges between 15-25%[1-3]. Multiple organ dysfunction syndrome (MODS)[4-7], the extent of necrotic pancreatic parenchyma and the presence of bacterial infection have been identified as major determinants for death[8,9]. A number of such patients developed pancreatitis-associated intractable organ failure during the early course of SAP, and no effective treatment methods were available, the mortality was up to 40-60%[3,10,11]. For the purpose of assessing the clinical course and management of these specific severe pancreatitis, we defined these severe acute pancreatitis with presence of organ dysfunction within 72 h after onset of symptoms as early severe acute pancreatitis (ESAP)[12]. In this paper, we analyzed the clinical features of 69 cases of ESAP and discussed the key of ESAP management.

MATERIALS AND METHODS

Clinical data

From January 1991 to June 2003, a total of 297 patients with SAP were treated in our hospital, including 140 males and 157 females (average age 58.53, from 15 to 79 years). Among them 69 cases were with organ dysfunction within 72 h after onset of symptoms, and 228 cases without organ dysfunction.

SAP and organ dysfunction definitions were adopted from the Atlanta Classification System for SAP[13]. All patients received standardized intensive care treatment as the following: (1) Supportive care including maintaining circulation volume, nutritional supplements, prophylactic antibiotics for pancreatic infection, oxygen supplementation, and mechanical ventilation, as well as monitoring for respiratory, cardiovascular and renal insufficiency and correcting them early. (2) To ' rest the pancreas' by fasting with nasogastric drainage to remove gastric secretions and by using anticholinergic agents or H_2-blocking agents and somatostatin to inhibit pancreatic secretion. (3) Multiple measures were taken early for accelerating the recovery of gastrointestinal function. (4) Infectious necrosis of pancreas was identified by dynamic contrast-enhanced CT. (5) Oddi' s sphincterotomy and nasobile drainage were performed for biliary pancreatitis accompanied by bile duct obstruction. (6) Surgical treatment (necrosectomy with drainage and continuous postoperative lavage of the lesser sac) was performed if infected pancreatic necrosis was identified or if the patient did not respond to maximal intensive care treatment over a period of more than 72 h.

Patients were divided into two sub-groups: ESAP with organ dysfunction and SAP without organ dysfunction within 72 h after onset of symptoms. APACHEII score, Balthazar CT class, number of organ dysfunction and rate of pancreatic infection in both groups were analyzed retrospectively.

Statistical analysis

Measurement data was expressed as mean±SD, the difference between the groups was analyzed with Student' s *t* test. Quantitative data was analyzed with Chi-square test. To identify the risk factors for ESAP, multiple logistic regression analysis with backward elimination was used. The level of significance was $P<0.05$.

RESULTS

ESAP characteristic

Data of 297 SAP are given in Table 1. The mean time between onset of symptoms and hospital admission was 25.64 h. Mortality of ESAP was higher than that of SAP, early death rate (within 1 wk) was 53.3%(16/30) in ESAP and 33.3%(2/6) in SAP respectively. Pulmonary failure was the most frequent organ dysfunction in ESAP. Compared with SAP group, the different types of organ dysfunction were observed more frequently in the ESAP group. The hospital course of patients with ESAP was characterized by a high incidence of progressive MODS (Table 2).

Table 1 Comparison of clinical characteristics between ESAP and SAP

Factor	ESAP group	SAP group
Age (year)	58.95±5.51[a]	60.12±5.16
Sex (M / F)	38 / 31[a]	102 / 126
Hours between onset and admission	24.72±5.21[a]	26.04±4.03
APACHE II at admission	16.6±0.72[b]	9.4±0.45
Impairment degree of pancreas (Balthazar CT class)	5.31±0.68[b]	3.68±0.29
Hypoxemia (%)	59(85.5)[b]	57(25)
ACS (%)	54(78.3)[b]	53(23.2)
Fever (T>38.5 °C)(%)	38(55.1)[b]	55(24.1)
Pancreas infection (%)	11(15.9)[a]	17(7.5)
Other infections (%)	40(57.9)[b]	41(17.9)
Non-effective after 48 h ICU treatment (%)	42(60.8)[b]	27(11.8)
Surgical treatment (%)	18(26.1)[b]	15(6.5)
Death (%)	30(43.4)[b]	6(2.6)
Death within 3 d	7	1
Death within 1 wk	16	2
Death after 1 wk	14	4
Mean hospitalization (d)	44.72±42.15[1]	21.26±23.66

[1]$P>0.05$, [a]$P<0.05$, [b]$P<0.01$, *vs* SAP group, ACS: abdominal compartment syndrome.

Table 2 Incidence of organ dysfunction during hospitalization in patients with ESAP and SAP (%)

Factor	ESAP group	SAP group
Single organ dysfunction	15(21.7)[a]	25(10.9)
MODS	54(78.3)[b]	20(10.1)
Pulmonary insufficiency	59(85.5)[b]	27(11.8)
Hepatic dysfunction	14(20.3)[b]	17(7.5)
Renal insufficiency	28(40.6)[b]	9(3.9)
GI dysfunction	24(34.8)[b]	16(7.0)
Shock	29(42.0)[b]	10(4.4)

[a]$P<0.05$, [b]$P<0.01$, *vs* SAP group.

Table 3 Features of victim in ESAP group

Factor	Death group (n=30)	Cure group (n=39)
Numbers of organ dysfunction	3.33±0.25[b]	2.27±0.21
APACHE II score	16.1±1.12[b]	14.2±1.09
Balthazar CT class	5.69±0.62[b]	4.47±0.43
Hypoxemia (%)	30(100)[b]	27(69.2)
Abdominal compartment syndrome (%)	27(90)[b]	22(56.4)
Pancreas infection (%)	8(26.7)[1]	4(10.3)
Other infections (%)	16(53.3)[1]	24(61.5)

[1]$P>0.05$, [b]$P<0.01$, *vs* cure group.

Features of victim in ESAP

Table 3 shows the features of death cases of ESAP. Multiple logistic regression analysis with backward elimination revealed that hypoxemia, higher APACHE II score, MODS and the extent of pancreatic necrosis were high risks for ESAP death.

DISCUSSION

With the advance in SAP study over the years, that the occurrence of early organ dysfunction is correlated with cascade response which gives rise to inflammatory mediators such as cytokine has been recognized gradually[14-16]. The effect of cytokine on the early stage of SAP should be emphasized. In fact, ESAP, a special critical type of SAP, is manifested as sharp changes during the early stage of SAP of non-stable vital signs and early organ dysfunction. Isenmann and Beger reported a group of SAP cases admitted to hospital within 72 h after onset of abdominal pain with organ dysfunction, which was defined as ESAP, and the mortality rate was up to 42%[12]. According to Mckay' s data[11], 40% of all death occurred within 3 d in SAP. In our data, the mortality rate was 23.3% (7/30) in ESAP group within 3 d and 53.3%(16/30) within 1 week. This indicated that ESAP was the higher risk group of acute pancreatitis death. Therefore it is very important to understand the characteristics of ESAP, which were mainly summarized as: a short disease course with progressive multiple organ dysfunction; early hypoxemia; a higher incidence of abdominal compartment syndrome; a higher incidence of infected pancreatic necrosis; and higher CT score of pancreatic changes. ESAP is a critical type of SAP with a high early mortality rate and poor prognosis. High-risk factors of mortality in ESAP group are early hypoxemia and multiple organs dysfunction.

Because there is an extremely high risk of progressive MODS, as well as an extremely high mortality rate in ESAP, ESAP patients should receive maximal intensive care treatment for organ dysfunction. First of all, our data showed that hypoxemia occurred in 85.5% ESAP. For correcting hypoxemia, all patients were given positive end-expiratory pressure (PEEP) early. Respirator respiration through tracheal intubation should be used if hypoxemia can not be improved after 4-6 h. The principle of respirator use is ' to use early and to stop early' , the oxygen concentration should be lower than 40%. The most important change of respiration system is ARDS. Pulmonary infection may be present due to ARDS, and even pulmonary infection may become the main reason for deterioration in ESAP. Monitoring of occurrence and progression of ARDS should be emphasized. Secondly, abdominal compartment syndrome (ACS) will be established if intra-abdominal pressure is higher than 15 mmHg (2kPa) with low cardiac output and progressive oliguria, and hypoxia occurred even if the airway peak value is normal or higher. Our result showed that higher pressure of abdominal cavity was presented in 78.3% ESAP. Higher pressure of abdominal cavity may damage the function of lung, heart, kidney and liver, inducing or exacerbating organ dysfunction. Abdominal decompression is the only way treating ACS. ACS can be divided into two types: one is present as ascites, peritoneal lavage or drainage can not only reduce the higher intra-abdominal pressure by using laparoscope but can also reduce systemic inflammation by diluting and draining abdominal exudates which contained pancreatic juice and cytokines. Another type of ACS is the result of enteroparalysis and gastrointestinal (GI) pneumatosis. Recovery of GI function is very important. We usually use purgative agents such as magnesium sulfate or Dahuang decoction (TCM) for accelerating GI function. These agents can promote GI peristalsis, decrease the intra-abdominal pressure, combat bacteria infection, protect the barrier function of GI tract, decrease translocation of bacterial and endotoxin and accelerate

the ascites absorption. Also, magnesium sulfate can reduce the opportunity of bacterial infection by promoting bile excretion and pancreatic juice excretion. Additionally, Pixiao can draw ascites out of peritoneal cavity. Our results indicated that the earlier the ACS was relived, the better the prognosis was. Thirdly, most ESAP cases had systemic inflammatory response syndrome (SIRS), which is the result of interaction of multiple inflammatory cytokines and has no specific therapeutic treatment modality. Hemofiltration has the effect of stabilizing hemodynamic and homeostasis, cleaning excess inflammatory factors such as cytokines, improving the function of heart, lung and kidney, and reducing the degree of illness[17-20]. We treated 25 ESAP patients with SIRS by hemofiltration at the early stage and obtained satisfactory (Data not shown). Fourthly, our data showed that the prognosis of early non-organ dysfuncion group was satisfactory based on the same treatment principle and themortality rate was just 2.6%. In the absence of evidence for pancreatic necrosis, SAP should be treated by non-surgical treatment if the condition is stable[21-25]. Owing to the unstable condition in ESAP, the mortality rate may increase because of operation[26]. Surgical treatment would be considered when: (1) Higher intra-abdominal pressure is not resolved or ascites is increased after 8-12 h' therapy. (2) Dynamic CT examination indicates the evidence of severe pancreatic lesion or inflammatory necrosis. As conventional operation may make patient' s condition worse at this stage, we proposed the method with minimal interruptions on body function such as peritoneal lavage under laparoscope, posterior peritoneal or paracolici sulci drainage to avoid systemic circulation or metabolism disturbances. The emphasis of surgery is peritoneal drainage and relief of intraabdominal pressure. Our data indicated that the outcome was better than simple conservation group and the mortality rate was reduced. Fifthly, prophylactic antibiotic was used early. All patients were given antibiotics once SAP was diagnosed. Antibiotics which can pass the blood-pancreas barrier and have effect on normal gut bacteria were first of choice. In general, Tienam or third generation cephalosporin with flagyl was applied. Sometimes, antibiotic was given by using arterial catheterization so that the pancreas could encounter higher drug concentration. Sixthly, low molecular weight heparin and Alprostadil can improve the microcirculation in pancreas[27,28]. We usually used these agents early. Lastly, nutritional support should be applied under the circumstance of stable systemic condition[29,30]. In general, we used parenteral nutrition (PN) at early stage. Enteral nutrition (EN) was used through jejunum once gut function recovered. EN can maintain gut mucosa barrier function, prevent or reverse the damage of gut mucosa barrier.

As our knowledge about the pathogenesis of systemic complications of ESAP is limited, patients with early organ dysfunction still remain a serious problem. The mechanism of ESAP and effective therapy still pose a challenge for future study.

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