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• CLINICAL RESEARCH •

Factors predisposing to severe acute pancreatitis: evaluation and prevention

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Abstract

AIM: To analyze factors predisposing to the infections associated with severe acute pancreatitis (SAP) and to work out ways for its prevention.

METHODS: Total 208 cases of SAP treated in this hospital from Jan. 1980 to Dec. 2001 were retrospectively analyzed.

RESULTS: Statistical difference in the incidence of the aforementioned infections was found between the following pairs: between the groups of bloody or non-bloody ascites, paralytic ileus lasting shorter or longer than 5 days, Ranson scores lower or higher than 5, hematocrit lower or higher than 45 %, CT Balthazar scores lower or higher than 7 and between 1980.1-1992.6 or 1992.7-2001.12 admissions (χ^2>3.84, P<0.05), while no statistical difference was established between the groups of biliogenic and non - biliogenic pancreatitis, serum amylase <200 U/L and ⩾200 U/L, serum calcium <2 mmol /L and ⩾ 2 mmol/L or groups of total parenteral nutrition shorter or longer than 7 days (χ^2<3.84, P>0.05).

CONCLUSION: Occurrence of infection in patients with SAP is closely related with bloody ascites, paralytic ileus ⩾ 5 days, Ranson scores ⩾5, hematocrit ⩾45 % and CT Balthazar Scores ⩾7, but not with pathogens, serum calcium and total parenteral nutrition (TPN). Comprehensive prevention of pancreatic infection and practice of individualized therapy contribute to reducing the incidence of infection.

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INTRODUCTION

Severe acute pancreatitis (SAP) characterized by atrocious progression, multi-complications and unquenchable mortality rate is a very dangerous acute abdomen[1-3]. SAP progresses in two consecutive stages: the earlier stage marked by serious physiological disorder and the later stage presenting with necrosis and infection. The earlier-stage mortality mainly caused by hypovolaemia, shock, adult respiratory distress syndromes (ARDS) and cardiac or renal insufficiency has been remarkably lowered as a result of the improvement on intensive care for severe diseases in recent years, however the later-stage mortality as a consequence of pancreatic or peri- pancreatic infections and their complications is still above 50 %[4-6]. Though the primary choice for pancreatic infection was surgery, surgical intervention can not obviously bring down the formidable mortality, thus rendering it extremely valuable to study the predisposing factors and to work out ways for effective prevention.

MATERIALS AND METHODS

Clinical data

Total 208 SAP cases treated in this hospital since Jan. 1980 to Dec. 2001 were selected, which consisted of 112 males and 96 females with an average age of 49 ranging from 18 to 82 years old. All the patients were diagnosed by clinical presentations, biochemical findings and CT scanning on pancreas according to the universal standard for SAP diagnosis in China. Among these 208 cases, 68 were diagnosed as secondary pancreatic infection and the other 114 non-infections. 94 cases admitted between Jan. 1980 and June. 1992 underwent operations in the earlier stage, while the other 114 cases between July 1992 and Dec. 2001 were treated by the principle of "Individualized therapy", which, with emphasis on conservative management in the earlier stage, exploited comprehensive individualized treatments to prevent secondary pancreatic infection. Preventive measures include: (1) volume supplementation, shock correction and protection against multiple organ dysfunction syndrome (MODS); (2) improving pancreatic micro-circulation; (3) decontamination of intestinal tract to facilitate the recovery of gastrointestinal function; (4) preventive prescription of antibiotics; (5) nutritional support; (6) peritoneal lavage or drainage in case of retention with a great amount of exudates in the abdominal cavity. The criteria for diagnosis of pancreatic infection are: (1) body temperature continuously ⩾38.5 ℃, white blood cell count (WBC)⩾ 20×10^9/L and signs of peritoneal irritation in more than 2 quadrants; (2) air bubbles in necrotic tissue of the pancreas by enhanced CT scanning; (3) bacteria found by culture or smear examination on fine needle aspirate.

Statistical analysis

All the data was analyzed by chi-square test.

RESULTS

Analysis of factors inducing pancreatic infection

Table 1 shows that statistical difference existed between the groups of bloody and non-bloody ascites, paralytic ileus lasting shorter or longer than 5 days, Ranson scores lower or higher than 5, hematocrit lower or higher than 45 %, CT Balthazar scores lower or higher than 7 and between 1980.1-1992.6 or 1992.7-2001.12 admissions (χ^2>3.84, P<0.05), while no statistical difference was found between the groups of biliogenic and non - biliogenic pancreatitis, serum amylase <200 U/L and ⩾200 U/L, serum calcium < 2 mmol /L and

⩾2 mmol/L or groups of total parenteral nutrition shorter or longer than 7 days (χ^2<3.84, *P*>0.05).

Table 1 Factors predisposing to infections associated with SAP

Factors	Total cases	Incidence of infections			*P* values
		cases	%	χ^2	
Admission					
1980.1-1992.6	94	40	42.6	7.58	<0.01
1992.7-2001.12	114	28	24.6		
Ascites					
Non-bloody	156	40	25.6	14.1	<0.01
Bloody	52	28	53.8		
Paralytic ileus					
<5 days	150	43	28.7	3.96	<0.05
⩾5 days	58	25	43.1		
Ranson Scores					
<5	144	40	27.8	5.14	<0.05
⩾5	64	28	43.8		
Hematocrit					
<45 %	128	35	27.3	4.33	<0.05
⩾45 %	80	33	41.2		
CT Balthazar Scores					
<7	138	38	27.5	4.95	<0.05
⩾7	70	30	42.9		
Etiology					
Biliogenic SAP	90	35	38.9	2.77	>0.05
Non-biliogenic SAP	118	33	28.0		
Serum amylase					
<200 U/L	83	25	30.1	0.41	>0.05
⩾200 U/L	125	43	34.4		
Serum calcium					
<2 mmol/L	88	34	38.6	2.45	>0.05
⩾2 mmol/L	120	34	28.3		
TPN					
<7 days	126	37	29.4	1.61	>0.05
⩾7 days	82	31	37.8		

DISCUSSION

More than 80 % of mortality in SAP is related with infection, mainly the secondary infection in the tissues[7-9]. Secondary pancreatic infections including infective pancreatic necrosis, pancreatic abscess and infective pancreatic psudocyst are responsible for more than 90 % of systematic infections and predispose to acute injury of gastric mucosa, hemorrhage in the abdominal cavity, fistula of digestive tract and multiple organ failure. Baron *et al* deemed that the morbidity of secondary infection was 30-70 %[10], while a morbidity of 32.7 % was demonstrated in this study. The mechanisms of secondary infection have not been fully elucidated yet. Gastrointestinal paralysis and edema of the intestinal mucosa caused by pancreatic enzymes and many other bioactive and toxic substances released in the acute stage give rise to disorder and translocation of bacterial clusters as well as atrophy of the intestinal mucosa lack of stimulus from food as a result of long-term (more than 1 week) gastric decompression. TPN impairs the mononuclear phagocytic system and thus weakens the intestinal immunity, which in turn promotes intestinal bacteria translocation making secondary infection inevitable[11-13]. In our experience the main cause of mortality in the later stage of SAP (after 2 weeks) was pancreatic infection or multiple organ system failure (MOSF). To prevent secondary pancreatic infection is essential to reducing the mortality of SAP. Therefore it is of chief importance to understand the factors related to pancreatic infection before any prevention is undertaken against it[14,15].

Our data did not indicate obvious relationship between the incidence of secondary infection and etiology of pancreatitis, serum amylase, serum calcium and TPN. Biliogenic pancreatitis is generally considered as a high risk factor to pancreatic infection, since it is always accompanied by biliary tract infection. However such consequence is not confirmed by our data, which may be that the secondary infection of SAP is mainly entero-genic. Whether TPN increases the incidence of secondary infection is still controversial[16-18], but there is an evidence that long-term central venous catheter deposit, tedious intubating manipulation and improper nursing of catheter lead to certain catheter-related infections, which are proved to give priority to G^- bacteria, whereas in our study, to G^+ bacteria instead. Accordingly, it may be concluded that TPN has no marked relationship with infections caused by intestinal bacteria translocation.

According to our data, bloody ascites, paralytic ileus ⩾5 days, Ranson scores ⩾5, hematocrit ⩾45 % and CT Balthazar scores ⩾7 predispose to secondary pancreatic infection. Great amount of bloody ascites indicating severe hemorrhage and necrosis of the pancreas and dissemination of inflammatory mediators throughout the abdominal cavity can not be absorbed in most cases if not timely eliminated, and it acts as an important initiator giving rise to or worsening the ongoing intra-peritoneal infection. The relationship between pancreatic infection and the extent of pancreatic or peri-pancreatic necrosis graded by CT Balthazar scoring has been confirmed by many investigations[19,20], but intestinal malfunction as an initiative to bacteria translocation and pancreatic infection has been ignored although the latter two are being investigated more deeply, producing the concept of preventive prescription of intra-intestinal antibiotics in view of pancreatic infection. Recently, some traditional Chinese medical doctors, who have achieved prominent efficacy using prescriptions emphasized on Tungli (an acupoint) and purgation, found the earlier the intestinal malfunction corrected, the lower the incidence of secondary pancreatic infection in the later stage was, otherwise the high incidence of both MOSF in the earlier stage and secondary pancreatic infection in the later stage persists. Ranson' s grading system as a standard to evaluate the severity of acute pancreatitis and to determine its prognosis went into practice in 1974 and has been proved efficient ever since by both domestic and foreign researchers. In our study, the coincidence of secondary infection with the Ranson' s score of SAP was established.

Recently, some scholars pointed out that pachyhemia poses threat in the earlier stage of SAP, as Hayakawa demonstrated that apparent reduction of circulation volume and pachyhemia existed in patients with SAP and suggested hemoglobin >150 g/L as a preliminary indicator to pachyhemia[21]. Baillargeon' s study demonstrated that pachyhemia with hematocrit ⩾47 % at admission or HCT staying high in 24 hours after admission points to SAP and helps evaluate the extent of pancreatic necrosis and predict the onset of MOSF[22,23]. In this study, hematocrit was obtained in the earlier stage of SAP before any intervention, which precisely reflected the extent of pachyhemia. Our data further demonstrated that pachyhemia is closely related with secondary infection of SAP, but the mechanism was unknown. We deem it may be that the exudation of large amount of plasma from circulation into the third space through the capillary bed with enhanced permeability by activated pancreatic enzymes and other vaso-active substances produced by SAP results in systemic

pachyhemia, elevated HCT count and deteriorated pancreatic micro-circulation and eventually leads to pancreatic infection. We also found that the incidence of pancreatic infection in the group admitted in 1992-07/2001-12 was significantly lower than that in the group of 1980-01/1992-06 admission. The reasons were: (1) application of "individualized therapy" on SAP; (2) adoption of comprehensive prevention against secondary pancreatic infection. The patients admitted during 1980-01/1992-06 underwent operations in the earlier stage, which as a matter of fact, not only aggravated the instability of circulation in the earlier stage or even caused shock rather than reduced the incidence of MOSF, but also destroyed the integrity of the pancreas, hampered its self-healing process, gave rise to further ischemia and necrosis after the operation and rendered it a site vulnerable to bacteria translocation increasing the incidence of pancreatic infection.

While in recent years, as to the patients admitted in 1992-07/2001-12 "Individualized therapy" was adopted, which with emphasis on conservative management in the earlier stage employs comprehensive individualized treatments to prevent secondary pancreatic infection and alternates to surgical operations if failed. Comprehensive preventions include: (1) blood volume supplementation, shock correction and especially preventions against multi-organ low perfusion injury and MOSF in the earlier stage of SAP. Ischemia and anoxia are responsible for pancreatic necrosis, damage to gastrointestinal mucosal barrier, bacteria translocation and even malfunction of the heart, the kidneys or the lungs; (2) to improve the microcirculation: by decreasing the fragility of RBC and lowering blood viscosity, the combined administration of Dextran, Saliva miltorrhiza, Ca^{2+}-blocker and large dosages of dexamethason maintains hyperdynamic circulation, which is efficient in oxygen transportation. Therefore, pancreatic and systemic micro-circulation is protected and intracellular Ca^{2+} overload prevented, resulting in alleviated necrosis of the pancreatic acinar, suppression of various imflammatory mediators and lowered incidence of micro-thrombocytosis; (3) intestinal decontamination to facilitate the recovery of gastrointestinal function: traditional Chinese cathartic herbs including castor oil and magnesium sulfate were early administrated to achieve decontamination, which not only decrease the population of intestinal bacteria but also promote gastrointestinal peristalsis eliminating "dead cavities". Translocation of intestinal bacteria as the principal cause of secondary infection is thus constrained. Moreover, physical therapy targeted at the gastrointestinal tract is helpful for the recovery of its function; (4) preventive administration of antibiotics: the antibiotics against G^- bacilli especially those capable of passing through the blood-pancreas barrier such as third generation cephalosporin, imipenem, tinidazole, etc are effective, while other antibiotics such as first generation cephalosporin, ampicillin, amikacin, etc have been proved ineffective thus improper for prescription[24,25]. (5) nutritional support: enough energy should be supplemented by means of EN (enteral nutrition) or TPN (total parenteral nutrition) to stop self burning, potentiate resistance against infection and accelerate tissue healing[26]. Recent study shows that pure TPN reduces the production of saliva, gastric juice, intestinal juice and bile, which are essential to the integrity of gastrointestinal barrier and function. Though a necessary part of the therapeutic planning, single application of TPN can not reverse hypercatabolism in the earlier stage but together with fasting, enhances the permeability of the intestinal mucosa. It is suggested that TPN should give way to EN when the digestive tract restore the ability to bear food load; (6) peritoneal lavage and drainage of effusion[27]: Beger argued that severe intraperitoneal hyperbaric status might lead to the death of patients with SAP[28,29]. When large amount of ascites develops in SAP patients, active peritoneal lavage or ultrasonic B or CT guided drainage through a small abdominal incision should be employed to eliminate activated inflammatory mediators and toxic peritoneal exudates, so that toxin intake and intraperitoneal hyperbaric status can be alleviated. By these measures certain cases, on which conservative treatment is ineffective, avoid the operations aimed at establishing peripancreatic drainage in the earlier stage and the incidence of secondary pancreatic infection is thus reduced.

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