

Management of severe acute pancreatitis

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Severe acute pancreatitis is associated with organ failure and/or local complications as necrosis, abscess and fluid collections and pseudocysts. Shock, gastrointestinal bleeding, renal insufficiency, severe metabolic disturbance are common complications whereas adult respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC) and pancreatic encephalopathy are most serious. The degree of lesions varies in different individuals, therefore treatment should be individualized. In recent years, we managed such patients by combined traditional Chinese and western medicine according to Balthazar and Ranson's CT grading^[1] with great success, no death occurred in cases with CT grade E and D, and many serious complications have become preventable. The essentials of this management are depicted below.

Inhibiting pancreatic enzyme secretions and activities and decrease of exudation into pancreatic substance, abdominal cavity and retroperitoneal space

Severe acute pancreatitis is often caused by hemorrhage and necrosis and less commonly by interstitial edema, however, the treatment is similar. The pancreatic fluid is rich in pancreatic lipase, trypsin, chymotrypsin, elastase, phospholipase A₂, RNAase and kallikrein and the exudative fluid in the abdominal cavity contained protease, bradykinin, histamine, complement component, phospholipase A₂ and prostaglandins, which can destroy pancreatic tissues and damage the abdominal organs and tissues. Release of cytokines such as IL-1, TNF, PAF, and TXA₂ ET, can cause serious damages to blood vessels with consequent increase of vascular permeability and loss of plasma.

Octreolide can inhibit pancreatic exocrine secretion and gastrointestinal hormones, reduce intraductal pressure, diminish pancreatic autodigestion, decrease PAF activity and reduce exudation from microvessels. It was administered at dosage of 0.1 mg in 20 ml 25% glucose intravenously and followed by 0.5 mg in 1000 ml glucose in saline for 24 hours continuously for 5 - 7 days. Decocting of Rhubarb mixtures (Bupleuri radix 10 g, White peony 10 g, Scutellaria 10 g, Unripe bitter orange 10 g, Magnolia bark 10 g, Refine mirabilite 10 g, Rhubarb 10 g) was used concomitantly twice a day, for most serious cases, once every six hours. Rhubarb stabilizes the lysosomal membrane, inhibits secretion and activities of pancreatic lipase, trypsin, chymotrypsin, elastase, kallikrein-kinin relaxes Oddi's sphincter; promotes colonic peristalsis, contraction and emptying, besides, it has broad

antibiotic spectrum. Bupleuri radix, Unripe bitter orange 枳实 and Refined mirabilite enhance the small intestinal propulsive function, white peony inhibits pancreatic amylase, Bupleuri radix and Scutellaria lower the elevated temperature due to necrosis. The overall action of this prescription is to promote the drainage of pancreatic fluid and retroperitoneal exudation along the pathway to pancreatic duct and intestinal tract and pass out from the anus. Rhubarb mixture and octreotide potentiate each other in inhibiting the enzymatic activities, the former also alleviates the abdominal distention and pain.

Replenishing the diminished blood volume and correcting the hypoalbuminemia

Loss of plasma into peritoneal cavity and retroperitoneal space due to increased vascular permeability leads to hypotension and even shock, this requires early replenishment of blood volume. We infused 400 ml - 600 ml of plasma instantly and 200 ml everyday afterwards till the general condition became stable. Rhubarb can decrease vascular permeability and arrest the exudative process. In fluid replacement, colloidal and crystalline solution should be given in proper proportion, human serum albumin at a dose of 10 g given everyday and balanced solution is preferred in addition to Ringer's solution, glucose in saline and glucose water with supplements of potassium chloride to maintain water electrolyte balance at an optimum level. We give 3000 ml - 4000 ml of fluid every day and keep the urinary output over 1000ml, depending on the moistening degree of the surface of tongue, which indicates the normalization of gastrointestinal function and adequate hydration.

Improving intestinal ileus and restoring absorptive and motility function of gastrointestinal tract

Rhubarb mixture is useful in intestinal ileus patients even when peristaltic sound is diminished or nearly absent. When the ventral surface of tongue become moistened, it indicates that the absorptive and motility function of gastrointestinal tract have been restored, then the velocity and fluid volume infusion should be reduced to avoid overloading of the heart and circulation, particularly in the elderly. We do not advocate the use of atropine or gastric decompression.

Total parenteral nutrition and maintenance of intra and extracellular ionic balance

Rhubarb has inhibitory effect on Na⁺, K⁺, -ATPase. ATP consumption is lowered and body catabolism is kept at a lower level. When general condition is stabilized, early institution of total parenteral nutrition as amino acids mixture and intralipid are imminent sodium, potassium, calcium and magnesium salts should be replenished with sodium potassium phosphate 0.1 mol 200 ml as a loading dose, thereby 100 ml everyday for two days and 100ml once every week to maintain intra and extracellular ionic balance and to correct hypocalcemia concomitantly.

Restoring pancreatic microcirculation and perfusion of vital organs

Pancreatic microcirculatory impairment occurs at the early onset of severe acute pancreatitis with microthrombosis in

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most of the cases, which is synchronous with increment of plasma TXA₂ and TXA₂/PGI₂ ratio. TXA₂ is a potent vasoconstrictor and causes platelet aggregation and constricts the arteriole. Also due to the release of many cytokines and free radicals, the PAF constricts the blood vessels, endothelin lowers the tissue blood flow, free radicals damage the pancreatic tissues, all these augment the ischemic damage on the pancreas. Tetra-methylpyrazine can inhibit TXA₂ synthetase activity, decrease the TXA₂/PGI₂ ratio. PGE₁ can improve pancreatic microcirculation, inhibit platelet aggregation, decrease TXA₂ synthesis, inhibit release of TNF- α , IL-1, IL-6, phospholipase A₂ and the free radicals liberated by neutrophils and macrophages. Exogenous PGE should be given at 300 μ g as a loading dose, and 200 μ g in 250 ml glucose solution daily thereafter for 5-7 days which might arrest further ischemic damage to the pancreas and increase the perfusion of other organs such as kidney, lung and brain. To achieve the optimum effect, whether it should be given at the onset of the disease process on admission or given afterwards for tissue repair would require further cumulation of experience.

Prevention and treatment of pancreatic infection

Pancreatic infection develops in 10%-20% of patients with severe acute pancreatitis, especially in those with multiple organ failure and immunocompromised cases. The organisms frequently isolated from infected necrosis and pancreatic abscess are *E. Coli*, *Klebsiella*, *Enterobacter*, *Enterococcus* and other streptococci, occasionally staphylococcus, pseudomonas, anaerobes or fungus^[3]. Sources of bacteria are mostly from biliary, urinary, respiratory tract or colon, which are mostly hematogenous. Bacteremia often comes from venous or urinary catheterization, so venous catheter placement should not be over one month and urinary catheter should be avoided. On selection of antibiotics, one should choose relatively liposoluble acidic drugs with high penetrability into the necrotic tissues which have a larger distribution volume and stabilized ionization rate in basic pH. Quinolones and metronidazole can pass through blood-pancreatic barrier and by cell to cell communication or via paracellular pathway or via damaged ducts, and enter the hemorrhagic necrotizing tissues. The antibiotic level is low in ischemic tissues, because the quinolones cannot diffuse back into plasma, its concentration is relatively high in pancreatic tissues, repeated administrations maintain high tissue level and enhance the degree of penetration without serum accumulation. Imipenem penetrates into pancreatic fluid, its level is higher in necrotic fluid than in pancreatic tissues^[4]. Aminoglycosides have a low penetrating ability. Metronidazole is a weak base and has a low molecular size and shows a very high rate of penetration. Therefore, clinically we frequently use ciprofloxacin or together with metronidazole or imipenem alone.

Prevention and treatment of complications

Omeprazole 20 mg - 40 mg by intravenous infusion should be given at the beginning to prevent stress ulcer bleeding and acidification of duodenum which might further lead to secretion of pancreatic fluid. Release of myocardial suppressive

factor by the pancreas would produce tachycardia and negative effect on the heart which can be abolished by naloxone 0.4 mg intramuscularly or 0.06 mg/kg in divided doses intravenously. Naloxone can enhance cardiac contractility and cardiac output.

Adult respiratory distress syndrome is one of the most severe complications, it often arises from delayed correction of shock. Via the circulation, the phospholipase A₂ and trypsin disrupt type II alveolar cell with defective production of surfactant, at the same time vacuolation of macrophages affect the defensive clearing mechanism of the lung. Furthermore, the accumulation of neutrophils produce large amounts of free radicals, TXA₂, TNF- α , fibrin and its degraded product, inflammatory mediator as leukotrienes, all participate in the damaging effect on the lungs, resulting in increased vascular permeability and exudation, interstitial pulmonary edema with early hypoxemia and late carbon dioxide retention. Once the diagnosis of ARDS is established, bronchoalveolar lavage is carried out, first on one side then the other, instill dexamethazone 40 mg and aspirate at the same time, this procedure can washout the inflammatory mediators, complement component, coagulation-fibrinolytic products as well as vascular amines. Corticosteroid inhibits IL-1, IL-6, TNF- α , PAF and inflammatory mediators. Serum albumin should be kept at the lower limit of normal. With diffuse interstitial lung edema, PEEP should be used. Early institution of PGE₁ and cytosine diphosphocholine 30 mg/kg in glucose water can inhibit phospholipase A₂ and prevent ARDS.

DIC is another serious complication, small dose of heparin in the dosage 75 mg/d - 100 mg/d in divided doses can be given every six hours, anti-thrombin III concentrates 3000 μ /60 ml can be given in half an hour, then 1000 μ every six hours^[5]. FDP and D-dimer would decrease, platelet count and fibrinogen increase and bleeding usually ceases.

Obstructive jaundice is usually due to edema of pancreatic head. It will resolve after subsidence of inflammatory edema, only when complicated with common duct stone and deep jaundice, then surgical drainage would be necessary.

Pancreatic encephalopathy is rare, early and energetic treatment at the start can prevent its occurrence.

Due to the damage of pancreatic β cells, insulin supplements should be given. The hypertriglyceridemia and hyperlactic acid dehydrogenase would resolve after recovery.

All twelve cases were managed medically, only one case with subhepatic abscess larger than 3 cm was aspirated by CT guidance. All of these recovered uneventfully in 1 and a half to 2 months without serious complications.

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