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Viewpoint

Nutritional management of severe acute pancreatitis

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Severe acute pancreatitis (SAP) is a common clinical emergency and critical illness. The increases of hyperlipidemic pancreatitis and alcoholic pancreatitis result in the increase of SAP. The SAP mortality is as high as 30% [1]. During the resuscitation and treatment of SAP, the metabolism changes require nutritional support. The individual metabolic status need personalized nutrition approach.

SAP patients are in a state of extreme stress due to inflammation, hemodynamic instability and severe hypoxia [2]. Due to acute respiratory distress syndrome, distributive shock or hypovolemic shock, the cell mitochondria are severely hypoxic. Instead of generating adequate ATP with the tricarboxylic acid cycle, only very limited ATP is produced in the mitochondria through intracytoplasmic glycolysis which also produces a large amount of organic acids such as lactic acid. In addition, patients with SAP encounter impaired insulin secretion, insulin resistance, over productions of glucocorticoids, catecholamines and glucagon, all of which cause hyperglycemia [3]. These patients need to apply insulin to maintain a proper blood glucose level and avoid the drastic fluctuation of blood glucose.

Patients with SAP experience autophagy [4], a phenomenon in which the body catabolizes and metabolizes its own tissue components for the synthesis of inflammatory mediators and cytokines in stress situations, such as IL-1, IL-6, TNF-α, and fibrinogen. At this point, even if nutrients are given, they cannot be utilized.

In addition, continuous renal replacement therapy (CRRT) is often applied in SAP patients to maintain the stability of the internal environment, regulate fluid balance, and remove inflammatory mediators. However, whether it is continuous veno-venous hemofiltration, hemodialysis or plasma exchange in CRRT, nutrients including glucose, amino acids, trace elements, vitamins and electrolytes, will lose from the body [5]. Special attention needs to be paid to CRRT patients to replenish various essential nutrients and maintain the stability of the internal environment.

Once the hemodynamic and internal environments of SAP patients are stabilized, it is necessary to consider the nutritional therapy to meet the metabolic needs of the body and to avoid nutrient deficiencies such as hypoproteinemia, hypophosphatemia, and vitamin B1 deficiency [3]. The nutrients required by the body at this time are mainly glucose, amino acids, various electrolytes and vitamins. Since there are often co-morbidities as hyperlipidemia and liver damage, lipid emulsions should be applied with caution. The total calories (non-protein calories) should be measured by indirect calorimetry or given 25 kcal/kg initially [6], with a larger amount of glucose input to meet the body's energy metabolic requirements, and the insulin dose should be adjusted according to the blood glucose level. The ideal blood glucose level is 7-10 mmol/L. The protein supplement is 1.2-2.0 g/kg per day [7]. CRRT requires more protein supplement (2.5 g/kg per day) [8] and more vitamins and trace elements [9]. The electrolyte supplementation should be adjusted according to the blood electrolyte test results, paying particular attention to blood phosphorus and magnesium to avoid the refeeding syndrome due to the low blood phosphorus [10].

Enteral nutrition is a critical nutritional pathway for the body as it can replenish the nutrients required by the body's nutritional metabolism, and, satisfy the metabolic needs of intestinal microorganisms and maintain the intestinal mechanical, biological, immune and chemical barriers [11,12]. In very critical states such as serious impairment of the body's oxygen metabolism, extreme hemodynamic instability, and severe intestinal ischemia and hypoxia, the nutrition implementation should be hold for SAP patients. However, after the initial improvement of these conditions, the implementation of enteral nutrition should be considered. A small dose of enteral nutrition solution is usually titrated at the early stage of 24-48 h in the disease course [13,14]. And when possible, it is given through the nasogastric tube, with the application of metoclopramide and erythromycin if necessary to facilitate gastric emptying and prevent gastric retention and aspiration. If enteral nutrition is tolerated, the amount of enteral nutrition should be gradually increased to eventually reach 70% of the target caloric and protein amounts [15].

When enteral nutrition is being implemented, parenteral nutrition should be used as a supplement to enteral nutrition and conducted with appropriate quantity of various nutrients in the light of the enteral nutrition and the metabolic status. Particular attention should be paid to whether the enteral nutrition can reach 70% of the target calories and protein when SAP has continued for one week. If not, then parenteral nutrition should be supplemented [16].

For SAP patients, the metabolism of the body is seriously disrupted, and various therapeutic factors would interfere with the metabolism and distribution of nutrients. There are wide vari-

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ety of nutrient requirements and metabolism among individuals in different pathophysiological states, and the gastrointestinal dysfunction affects the digestion and absorption of nutrients. Therefore, in early nutritional support for SAP patients, there should be close monitoring of their nutrition status [2], especially on proteins (amino acids), vitamins, trace elements. It is necessary to avoid both metabolic disorders caused by various nutrient deficiencies, such as phosphorus and thiamine deficiencies leading to refeeding syndrome [17], and nutritional overloads that exacerbate disturbances in the internal environment, such as protein overloads that lead to azotemia. Accordingly, the optimal therapeutic regimen should include early nutrition support while closely monitoring the levels of various nutrients to "make up for the deficiencies and get rid of the excesses" so that the patient can reach an optimal metabolic state for an early recovery.

Potential enteral nutrition intolerance includes, *inter alia*, reflux aspiration, gastric retention, bloating, diarrhea, gastrointestinal bleeding and constipation, and should be monitored during the implementation of enteral nutrition. Patients with SAP are more prone to these intolerances due to serious abnormalities in their pathophysiological status. In this regard, a gradual approach should be adopted in the treatment, striving to start enteral nutrition early but not rushing to reach the full amount, and the nutritional deficiencies can be supplemented with parenteral nutrition to reach the goal, i.e. the so-called "complementary parenteral nutrition" [18].

In order to prevent and reduce the enteral nutrition intolerance, a clinical practice of elevating the head of bed $\geq 30^{\circ}$ and post-pyloric feeding can be used to reduce regurgitation and aspiration. Digestive enzymes help digestion, metoclopramide or erythromycin are helpful for gastric emptying, and neostigmine promotes intestinal peristalsis. Traditional Chinese medical approaches such as dialectical treatment with Chinese herbs (gastric lavage or enema), acupuncture, and mirabilite applied to the umbilicus also have therapeutic effects.

In conclusion, patients with SAP encounter a challenging metabolic state including catabolic and anaerobic processes that requires careful nutritional optimization. After the patient is stabilized, early enteral nutrition and supplemental parenteral nutrition should be initiated and dynamically adjusted according to the specific metabolic demands and gastrointestinal function which is also be influenced by the gut microecology. As the digestive and absorptive capacities improve, the level of nutrition should be increased without further exacerbating the metabolic demands during this state of critical illness.

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