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Review Article

An overview of diarrhea in ICU patients receiving enteral nutrition

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Abstract: Enteral nutrition is accepted as the first choice for critically ill patients. Diarrhea, one of the most common complications, tends to prolong the time of reaching the target nutrient, or even interrupt the intake of nutrients. Consequently, it may not only reduce the therapeutic effect and prolong the length of stay in the hospital, but it also may induce electrolyte disturbance, internal environment changes, and may even be life-threatening. Therefore, doctors and nurses must pay attention to the occurrence of diarrhea. The present study briefly reviews the causes, prevention, and treatment of enteral nutrition-related diarrhea.

Keywords: Enteral nutrition, diarrhea, antibiotics, probiotics, prebiotics

Introduction

Nutritional support therapy has received an increasing amount of attention in intensive care units (ICU). Enteral nutrition is increasingly and widely used in clinics in view of its safety, effectiveness, convenience, and conformity to physiological modes. Studies have shown that enteral nutrition protects the integrity of gastrointestinal mucosa, decreases the occurrence of toxins from the intestinal tract entering into the circulation, thus reducing the incidence of sepsis and multiple organ failure, and is associated with a reduced length of stay in the hospital and reduced mortality [1, 2]. However, critically ill patients often suffer from intolerance during the implementation of enteral nutrition, such as abdominal distension, diarrhea, reflux and constipation, especially diarrhea, which is the most common gastrointestinal symptom with an incidence of 14-36% [3-5]. Simultaneously, continuous diarrhea may further increase the workload of nurses and the cost of ICU hospitalization. Meanwhile, it damages perianal skin, reduces enteral nutrition intake, causes wound contamination, dehydration and the disturbance of water and electrolyte balance, and thus increases the mortality of patients [6-8]. Therefore, treating diarrhea should be considered a highly important task by medical staff in clinical practice. This article reviews the related risk factors, prevention, and treatment of enteral nutrition-related diarrhea in ICU patients during hospitalization.

Definition

Diarrhea refers to the abnormal increase in intestinal peristalsis and stool frequency. Annika et al. suggested that it should be divided into two pathophysiological mechanisms of permeable and secretory diarrhea [9]. However, the definition of diarrhea has not yet been unified. The World Health Organization recommends that it be defined as ≥3 defecations per day and sparse feces. For critically ill patients, some experts suggest that diarrhea should be defined as increased defecation frequency (≥3 times/d), increased defecation volume (> 200 g/d), pasty or watery stool (refer to Bristol Stool Scale type 5-7), while meeting the above conditions [9].

Enteral nutrition-related diarrhea

Formulation of nutrient solution

Nasointestinal/gastric tube feeding can affect the original physiological state of the intestinal

cavity by changing the time of nutrient delivery, intestinal secretion/absorption capacity, and intraluminal microenvironment, interfering with intraluminal microflora metabolism, thus leading to diarrhea. In this regard, the formulation, supply and speed of enteral nutrition, the beginning and duration of enteral nutrition are all related factors associated with the occurrence of diarrhea.

Different formulations of enteral nutrition can increase or decrease the incidence of diarrhea. As evidenced by prior research, the supplementation of fiber in the nutrient solution can reduce the gastric emptying rate, improve the barrier function of the intestinal cavity, enhance the regeneration of epithelial cells, increase the absorption of liquids and electrolytes in the colon, and then reduce the incidence of diarrhea [10]. However, hypertonic nutrient solution may result in the development of diarrhea and gastrointestinal intolerance through osmotic action [11]. FODMAPs are a type of food rich in oligosaccharides, disaccharides, monosaccharides, and polyols which are difficult to absorb. The rapid fermentation of this food in the intestinal tract causes an increase in the osmotic pressure in the intestinal cavity, which induces the increase of gas production and causes diarrhea, abdominal pain, abdominal distension and other related symptoms easily. Accordingly, a nutrient solution containing low FODMAPs can reduce the incidence of diarrhea [12]. In addition, the high nutritional value of nutrient solution makes it an excellent growth and reproduction medium for microorganisms. Hence, the contamination of the nutrient solution or of a nutrient delivery device (nasointestinal tube, etc.) can increase the risk of developing diarrhea. With respect to the above, nurses handling the daily infusion of enteral nutrition should pay attention to the fresh preparation of the nutrient solution and ensure low temperature preservation to prevent contamination.

Quantity of supply and the infusion rate of the nutrient solution

The presence of a period of fasting before enteral nutrition in critically ill patients can easily lead to intestinal dysfunction, and the patients are in a state of stress. Therefore, an overload of nutrient solution supply and a too fast infusion speed will lead to faster gastrointestinal peristalsis and even intolerance in patients. For example, a study performed by Ronan showed that a target of over 60% nutrient solution supply increased the incidence of diarrhea [13]. Therefore, enteral nutrition should start with a low dosage and infusion speed, and gradually increase to the level that patients can adapt to, avoiding diarrhea. In this regard, in the process, the principle of gradual progress should be followed and the enteral nutrition infusion should be performed in a mode from low to high concentration, from small to large doses, and from slow to fast with a 24 h uniform infusion, so that patients have a gradual adaptation process. Furthermore, although there is no strong medical evidence to support the different roles of continuous and intermittent enteral nutrition in the reduction of diarrhea, a single-center trial has suggested that continuous enteral nutrition can reduce the incidence of diarrhea [14, 15].

Time of enteral nutrition

For critically ill patients, enteral nutrition should be given 24-48 h after admission as long as intestinal function exists. Early enteral nutrition can not only provide energy to enhance the body's resistance, but it can also protect the integrity of the intestinal mucosal structure and barrier function through the intestinal absorption of nutrients, reducing intestinal flora translocation. A prior retrospective study showed that patients with acute shock who received enteral nutrition within 24 h exhibited a lower risk of developing diarrhea than those who received enteral nutrition within 74-96 h [16]. There is a positive correlation between fasting time with the occurrence of malabsorptive diarrhea and osmotic diarrhea after enteral nutrition. In addition, in a previous study involving 130 acute shock patients who received enteral nutrition, the corresponding results suggested that when enteral nutrition lasted over 7 days, it was related to diarrhea. In other words, the longer the duration, the higher the incidence of diarrhea [17].

It is speculated that diarrhea may also be related to the temperature of nutrient solution, fat content, calorie density, the location of nutrient tube and the source of protein. However, there is insufficient evidence to prove any such direct

relationship with diarrhea, which remains to be confirmed by further research [18].

Prevention of enteral nutrition-related diarrhea

Diarrhea in ICU patients is a common complication of enteral nutrition. In order to prevent diarrhea, the following should be noted in addition to dealing with the causes of diarrhea: avoid unnecessary fasting; correct hypoproteinemia in time; avoid the long-term use of antibiotics and gastrointestinal prokinetic drugs as much as possible; pay attention to the low temperature preservation of nutrient solution, avoid contamination and heating during feeding, and control the infusion rate, etc. It can also be prevented by adding cellulose, probiotics, prebiotics and lactoferrin.

Fiber-rich nutrient solution

Cellulose can reduce diarrhea, as mentioned above. A meta-analysis of 51 studies found that fiber-rich enteral nutrients reduced the incidence of diarrhea [19]. In critically ill patients, mixed fibers can not only reduce the incidence of diarrhea in antibiotic-treated patients, but they can also increase the concentration of short-chain fatty acids (SCFA). Furthermore, cellulose can not only prevent the occurrence of diarrhea, but it can also have certain anti-inflammatory effects. It can increase the growth and reproduction of anaerobic bacteria in the intestinal tract to avoid the over-proliferation of pathogenic bacteria and the subsequent occurrence of diarrhea. Therefore, ASPEN suggests that fiber-rich enteral nutrition should be considered for critically ill patients with diarrhea [15].

Probiotics and prebiotics

Probiotics are a category of active microorganisms beneficial to the host, which mainly include the three categories of lactobacillus, bifidobacteria and gram-positive cocci. Probiotics can directly act on the intestinal microenvironment, which can produce digestive enzymes to realize better digestion and absorption of nutrients, but they also can inhibit the growth of harmful bacteria, adjust and correct the imbalance of various flora, promote the growth of intestinal mucosa, enhance intestinal immune function, and prevent diarrhea. However, there have been some controversies about the application of probiotics in recent decades [20, 21]. For instance, it has been reported that the use of probiotics may increase the mortality of patients with pancreatitis [22]. A randomized controlled study also found that lactobacillus exhibited no significant effect on improving the course and condition of diarrhea in critically ill patients [23]. Therefore, high-quality research is needed to further explore the value of probiotics in the prevention and treatment of diarrhea.

Probiotic and prebiotic complexes are reported to be more effective in regulating intestinal flora than probiotics alone [24]. Prebiotics refer to food ingredients that are not easily digested. They can promote gastrointestinal health and effectively solve various intestinal problems by selectively stimulating the growth and activity of one or several beneficial bacteria, such as bifidobacteria and lactobacillus. Prebiotics widely used in clinic include isomaltooligosaccharides, fructooligosaccharides, and xylo-oligosaccharides, which can be decomposed and absorbed by beneficial bacteria in the intestine to promote the growth and reproduction of beneficial bacteria. Many studies have confirmed the beneficial effects of probiotics on the human body [25]. However, a multi-center study of probiotics and prebiotics conducted by the European Society of Pediatric Gastroenterology and Hepatology Nutrition showed that probiotics exerted no preventive role in the development of diarrhea [26]. An animal experiment found that probiotics, including fructose and lactulose, can even increase the possibility of intestinal bacterial translocation [27]. Therefore, the role of probiotics in the prevention and treatment of diarrhea remains to be determined.

Lactoferrin

Lactoferrin is a non-heme iron-binding glycoprotein present in milk and a bactericidal monomer glycoprotein released from neutrophil granules. It not only participates in the transport of iron, but it also has powerful biological functions such as broad-spectrum antimicrobial, antioxidant, anticancer, and immune regulation. Some clinical studies in children have shown that lactoferrin can reduce the duration of diarrhea. Moreover, a recent study also pr-

oved that lactoferrin can reduce the incidence of diarrhea in patients with long-term nasointestinal feeding [28].

Treatment of enteral nutrition-related diarrhea

In the case of diarrhea, one should first determine the cause of the diarrhea, carry out an abdominal examination, observe whether there are signs such as abdominal distension and abdominal pain, and determine whether bowel sounds are hyperactive during auscultation, and collect stool samples right away and send them for examination to exclude infectious diarrhea. Meanwhile, it is necessary to pay close attention to the changes in a patient's intake and output, hematuria and electrolytes, and to correct the imbalance of water and electrolytes at an early stage.

The timely management of diarrhea is essential for critically ill patients. First, it is necessary to review the appropriateness of drug use and adjust the use of drugs, such as antibiotics, discontinue gastrointestinal prokinetic drugs and laxatives; reduce the dosage of the enteral nutrition solution and the infusion rate; replace the nutrient solution (low volume and high calorie nutrient solution or nutrient solution rich in cellulose and low FODMAPs), etc. It is not recommended to discontinue enteral nutrition immediately. Only patients with severe diarrhea should consider parenteral nutrition and then enteral nutrition after improvement [11]. Diarrhea is primarily treated by symptomatic treatment, such as the use of antidiarrheal agents such as loperamide or codeine, but it should be used after the exclusion of infectious diarrhea.

Conclusion

Diarrhea is a common complication of critically ill patients. It not only increases the burden of nursing and reduces the therapeutic effect, but also may increase the length of stay in the ICU and affect the prognosis. Therefore, great importance should be attached to diarrhea in clinical practice. There is a need to clarify the relevant causes of diarrhea immediately after it starts. In addition, the selection, preparation, infusion and nursing of enteral nutrition solution should also be emphasized in clinical practice, so as to reduce the occurrence of nutrition-related diarrhea in ICU patients.

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Disclosure of conflict of interest

None.

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