Progress in Clinical Evaluation of Gut Microbiota in Critically Ill Neurological Patients

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Abstract: In recent years, significant progress has been made in the study of gut microbiome. With the development of the Human Microbiome Project (HMP) and the Human Intestinal Macro Genome Project (Me taHIT), the academic community has gained a deeper understanding of the gut microbiome. This article discusses the advantages of gut microbiome in the treatment of neurological critical care, in order to provide reference for relevant medical personnel.

Keywords: neurological critical illness; intestinal microbiome; imbalance of microbial community; intervention measures

In healthy adults, the gut microbiome maintains dynamic balance through feedback mechanisms. The human gut microbiome is composed of bacteria, archaea, eukaryotes, viruses, and parasites. The gut microbiota is mainly divided into three types: symbiotic microbiota, conditional pathogenic microbiota, and pathogenic microbiota. Among healthy individuals, symbiotic bacteria dominate, mainly including Bacteroides, Bifidobacterium, Clostridium, and others. The dominant microbial community plays an important role in nutrition, metabolism, and immunity. In certain pathological conditions, the conditional pathogenic bacterial community or even the pathogenic bacterial community may transform into dominant bacterial communities, which have adverse effects on metabolism, immunity, and other aspects of the body [1-3].

The composition of gut microbiota in critically ill neurological patients is different from that of healthy individuals. Xu et al. [4] found through analysis of the gut microbiota of 98 critically ill patients with neurological disorders that the abundance of Proteobacteria, Deferroobacteria, and Verrucobacteria in the gut microbiota significantly increased, and significant dynamic changes also occurred during hospitalization. The changes in gut microbiota are closely related to the state of the body and are easily influenced by various factors. Understanding the changes in gut microbiota, the structure and abundance of the microbiota, and the relationship with clinical outcomes will help healthcare professionals regulate the homeostasis of the patient's gut microbiota, and have a positive impact on patient treatment and care. This article aims to provide a review of the latest research on changes in gut microbiota in critically ill patients, revealing the causes and effects of gut microbiota changes in critically ill patients, and elucidating methods for regulating gut microbiota homeostasis.

1 Changes in gut microbiota in critically ill patients with neurological disorders

The gut microbiota of critically ill patients shows significant changes, with a significant decrease in the abundance and diversity of gut microbiota and a tendency towards a single microbial structure. Research has found that a single microbial community in the microbiome of critically ill patients can account for over 70%, mostly belonging to the family Enterococcaceae or Enterobacteriaceae. The composition of gut microbiota in critically ill patients with neurological disorders exhibits significant individualized differences, and its changes are influenced by multiple internal and external factors. Changes in the microbiome also have an impact on the responsiveness of clinical intervention measures, the occurrence and development of complications, and the prognosis of patients. The diverse structure and abundance of gut microbiota play an important role in maintaining the body's homeostasis and immune defense. In critical situations, the structure of the human gut microbiota tends to be singular, which can easily lead to exacerbation of steady-state imbalances.

1.1 The pathological and physiological processes of severe neurological disorders

There is an interaction between the nervous system and the gut in pathophysiology, and an increasing number of studies have revealed multiple pathways that mediate bidirectional communication between the gut and central nervous system, collectively known as the gut brain axis, involving the nervous, immune, and endocrine systems

[5-7]. Neurological severity significantly alters the patient's physiology, thereby altering the growth and survival conditions and community structure of intestinal microbiota. The interaction between gut microbiota and the gut immune system plays a crucial role in the occurrence and development of diseases [8]. Neurocritically ill patients are in a state of stress, with disrupted microbiota and imbalanced intestinal mucosal immune system, resulting in impaired intestinal mucosal barrier function, increased intestinal permeability, motility disorders, intestinal hypoperfusion, and reperfusion injury [8-10]. The disruption of intestinal mucosal integrity will lead to the displacement of intestinal microbiota and dysregulation of inflammatory responses, resulting in impaired intestinal immune defense mechanisms and systemic immune activation, leading to various diseases and accelerating the progression of the disease [10-11].

1.2 Nutritional support

Neurological critically ill patients often suffer from consciousness disorders and swallowing dysfunction. Early nutritional assessment and support are particularly important for reducing complications and improving prognosis. Enteral nutrition in nutritional support is of great significance for maintaining intestinal function, but it inevitably affects changes in gut microbiota [12-14]. The complex pathological and physiological changes during critical illness can easily cause inflammatory reactions and metabolic disorders, leading to changes in gut microbiota. Research has shown that early provision of enteral nutrition support in critically ill patients with neurological disorders results in a higher abundance and structure of gut microbiota compared to the group without enteral nutrition support [15], and reduces the incidence of complications and ICU hospitalization time [16]. This suggests that further research should be conducted on enteral nutrition preparations, providing personalized preparations to patients with different needs through the combination of different components, Maximizing the stability of the patient's gut microbiota, reducing complications, and improving prognosis.

1.3 Intervention measures

Clinical intensive care intervention is also an important cause of changes in gut microbiota [17]. Clinical use of drugs such as gastric acid inhibitors, sedatives, opioids, neuromuscular blockers, and antibiotics can lead to imbalanced microbiota homeostasis, greatly altering the composition and abundance of gut microbiota [4]. Research has shown that the use of broad-spectrum antibiotics and the severity of the disease will cause changes in the gut microbiota, which may be related to intestinal dyspepsia, and the progression of intestinal dyspepsia in ICU patients may be related to mortality [18]. For critically ill patients with neurological disorders, various intervention measures may affect the disruption of gut microbiota. Therefore, corresponding methods should be taken to regulate intestinal homeostasis, improve the composition and abundance of the patient's gut microbiota, reduce mortality, and improve prognosis.

2 The clinical impact of microbial community changes

2.1 Prognostic assessment

The pathological and physiological processes of neurological critical illness and the imbalance of gut microbiota caused by intervention measures will affect the prognosis of patients, especially their mortality rate. During hospitalization in the ICU, the patient's gut microbiota shows dynamic changes, and in-depth analysis of the reasons for changes in microbiota is expected to establish a patient prognosis evaluation model. In the study of shock animals, it was found that the composition and abundance of gut microbiota determine the severity of multiple organ failure and the risk of death [17]. Xu et al. [4] analyzed different microbial communities in the gut microbiome and found that changes in the gut microbiome had an impact on the mortality rate of patients at 180 days, with an increase in Enterococcaceae and Enterobacteriaceae independently correlated with the mortality rate at 180 days. Other studies have shown that the degree of decrease in Bifidobacterium abundance performs well in predicting in-hospital mortality, providing higher predictive value for existing scoring systems in the neuro intensive care unit [19]. The dynamic analysis of microbiome composition and monitoring of related biomarkers are helpful for the prognosis evaluation of neurosis patients, but specific predictive models still need to be established.

2.2 The impact on intervention effectiveness

The pathophysiological processes and intensive care interventions of neurological critical illness have greatly altered the composition and abundance of gut microbiota [20]. Animal models and clinical trials have shown that the gut microbiome can also have an impact on clinical intervention measures and drug efficacy. Sivan et al. [21] confirmed by comparing the growth of melanoma in mice with different microbial groups that bifidobacteria are associated with anti-tumor effects. Yoo et al. [22] found through studying the pharmacokinetics of lovastatin in antibiotic treated rats that oral administration of lovastatin is influenced by gut microbiota metabolism, leading to differences in the efficacy of lovastatin. An increasing number of queue research data indicate that the gut microbiome significantly affects the responsiveness and toxicity of various cancer treatment measures. Regulation of the gut microbiome may become an important adjunct to cancer immunotherapy and a predictive indicator of patient susceptibility to disease [23-24].

3 Intervention measures for dysbiosis of microbiota

The gut is home to trillions of microorganisms, and the innate immune system plays an important role in regulating the composition of the microbiome. The gut microbiome also affects the immune function of local and extraintestinal hosts [25-26]. Therefore, targeting the microbiota immune axis for the treatment of critically ill patients is an emerging and exploratory approach, and the steady-state regulation of gut microbiota will become a potential approach for the treatment of critically ill patients.

3.1 Standardized use of antibiotics

The use of antibiotics is particularly common in clinical practice, with significant short-term effects on harmful bacteria. However, long-term and improper use can easily cause dysbiosis of the gut microbiota, altering its composition and function [9,27]. The unreasonable use of antibiotics can cause sensitive bacteria to die in large numbers, while drug-resistant bacteria multiply in large numbers, resulting in a serious imbalance in the proportion of bacterial communities and causing long-term harmful effects on the host. The use of antibiotics requires strict consideration of indications, and the type, administration route, and concentration of antibiotics should be determined based on the specific situation of the patient.

3.2 Microecological modulator

Microecological regulators are live microbial preparations made from normal microorganisms or substances that promote microbial growth, including probiotics, prebiotics, and synbiotics. Research has shown that microecological regulators can effectively regulate gut microbiota, enhance intestinal barrier function, and resist harmful microorganisms [28]. They have great application prospects in today's widely resistant society, but it is necessary to comprehensively consider the patient's condition, type of strain, and dosage. A randomized controlled study of critically ill patients showed that enteral formulas containing probiotics improved diarrhea faster and had a lower incidence compared to standard enteral formulas in nutritional therapy [29]. For critically ill patients with neurological disorders, early enteral nutrition therapy is recommended, so enteral nutrition preparations containing probiotics are expected to become a new choice for treatment.

3.3 Fecal microbiota transfer transplantation (FMT)

The main purpose of FMT is to restore and reconstruct the normal microbiome of the patient's gut. Research has shown that FMT regulation of gut microbiota has a good therapeutic effect in the treatment of recurrent Clostridium difficile, which also proves the therapeutic significance and operability of microbiota in clinical practice [17]. However, the production of FMT preparations should be carried out through standardized procedures to ensure the effectiveness and safety of the donor microbiota to the greatest extent possible, and to avoid situations where harmful microorganisms and pathogens seriously affect patient treatment and even pose a life-threatening risk. Research has shown that the composition and abundance of donor microbiota are related to the success of transplantation therapy [30]. In 2019, the FDA announced that one patient died after receiving FMT treatment, and some patients developed invasive infections, which requires sufficient attention. The clinical application of FMT requires strict adherence to indications and ensuring the safety and effectiveness of the donor microbiota. At present, sterile filtration can be used to remove bacterial components from donor feces, also known as fecal virus transplantation, to reduce the risk of invasive infections caused by bacteria [31], and is also a promising treatment method.

4 Outlook

The gut microbiome is a potential therapeutic direction in the field of neurological critical care, but it is currently necessary to fully understand the internal and external factors that alter the microbiome by various intervention measures, as well as the responsiveness of microbiome changes to intervention measures. For critically ill patients with neurological disorders, the application of microbiome research should be evaluated in conjunction, focusing not only on gut microbiota but also on respiratory microbiota, which is an important influencing factor in disease progression and cannot be ignored. In order to better describe the composition and abundance of microbial communities, research can be conducted from the genus level to the species level. In addition, research areas beyond bacteria, especially viruses, fungi, and bacteriophages, can be expanded to fully understand the importance of the microbiome in influencing neural function. The application potential of gut microbiome is infinite, and it is believed that more research results will be transformed into clinically available technologies and standards in the future.

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