

Effects of Traditional Chinese Medicine on Gastrointestinal Dysfunction in Sepsis from Intestinal Flora

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ABSTRACT

Gastrointestinal dysfunction in sepsis is a key link affecting the prognosis, and its occurrence is closely related to intestinal flora disorders. From the perspective of modern medicine, intestinal flora, this paper discusses the preventive and therapeutic effects of traditional Chinese medicine. The article first combed the understanding of gastrointestinal dysfunction of sepsis in traditional Chinese medicine, which belongs to the category of "intestinal obstruction" and "Guange", and the core of pathogenesis is "toxin damaging intestinal collaterals, fu-organ qi obstruction". The key role of intestinal flora imbalance, barrier function damage and immune inflammatory response out of control in morbidity was elaborated. This paper focuses on the synergistic mechanism of traditional Chinese medicine in multi-target regulation of flora structure, repair of intestinal barrier and inhibition of excessive inflammation through purgative, heat-clearing and detoxifying, spleen-invigorating and blood-activating therapy. The analysis shows that the intervention strategy of TCM based on the principle of "holistic concept" and "strengthening the body resistance and eliminating pathogens" is highly consistent with the inherent requirements of regulating "flora-intestine-axis", which provides a unique way of thinking for clinical prevention and treatment.

KEYWORDS

Intestinal Flora; Traditional Chinese Medicine; Gastrointestinal Dysfunction in Sepsis

1. INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by the disorder of body response to infection, which has become an important challenge in the field of critical care medicine. In its complex pathological process, gastrointestinal dysfunction, as a common and serious complication, is considered to be the key link to promote the deterioration of the disease. In recent years, the role of intestinal flora in sepsis has become increasingly prominent. Intestinal tract is not only a digestive organ, but also a huge immune barrier of human body. Studies have shown that sepsis can lead to significant changes in the structure of intestinal flora, that is, flora imbalance, which will further damage the physical and biological barrier function of intestinal mucosa, lead to increased intestinal permeability, bacterial and endotoxin translocation into the circulatory system, thus activating excessive systemic inflammatory response, forming a vicious circle, and aggravating multiple organ dysfunction [1].

At present, western medicine prevention and treatment strategies such as antibiotics, probiotics and enteral nutrition support have some effects, but they often focus on a single target, and the overall prevention and treatment effect still has room for improvement. Under the guidance of "holistic concept", traditional Chinese medicine has unique advantages in the prevention and treatment of critical illness. According to the theory of traditional Chinese medicine, the gastrointestinal dysfunction of sepsis is classified into the category of "intestinal obstruction" and "Guange", and its

core pathogenesis lies in "deficiency of healthy qi and damage of intestinal collaterals by toxin", and the treatment emphasizes comprehensive therapies such as purging the bowels, clearing heat and detoxifying, and supporting healthy qi. This multi-way and multi-target intervention idea is highly consistent with the inherent requirements of regulating "flora-gut-axis". Therefore, the purpose of this paper is to systematically explore the theoretical basis and mechanism of traditional Chinese medicine in the prevention and treatment of gastrointestinal dysfunction in sepsis from the perspective of modern medicine, and to provide new ideas for enriching clinical treatment strategies.

2. UNDERSTANDING OF GASTROINTESTINAL DYSFUNCTION IN SEPSIS BY TRADITIONAL CHINESE MEDICINE

In traditional Chinese medicine, the gastrointestinal dysfunction of sepsis belongs to the category of "intestinal obstruction" and "Guange", and it is believed that the disease is caused by exogenous warm and epidemic toxin and internal deficiency of healthy qi. The core pathogenesis is "toxic damage to the intestinal collaterals and obstruction of fu-organ qi". The invasion of pestilential toxin stagnates in the stomach and intestines, resulting in the disorder of ascending and descending of qi and the dysfunction of transportation and transformation, manifested as abdominal distension, constipation or diarrhea [2]. Toxic pathogens further damage the intestinal collaterals, and combine with pathological products such as blood stasis and phlegm turbidity to form a vicious circle.

In this pathological process, the function of spleen and stomach is very important. The spleen and stomach are the foundation of the acquired body, governing the transportation and transformation of food essence and ascending the clear and descending the turbid. The healthy function of the spleen and stomach is the basis of maintaining the stability of the internal environment of the human body, which is similar to the concept of intestinal microecological balance in modern medicine. In the case of sepsis, the hyperactivity of toxic pathogens seriously consumes the qi of the spleen and stomach, resulting in the passive generation of qi and blood, and the more deficient the healthy qi is, the more abundant the pathogenic qi is.

Based on the above understanding, the prevention and treatment of traditional Chinese medicine emphasizes the combination of "strengthening the body resistance" and "eliminating pathogens" [3]. The therapeutic method is to purge the bowels, clear away heat and toxic materials, eliminate excess pathogens, invigorate the spleen and stomach, promote blood circulation and remove blood stasis, support healthy qi, and dredge meridians and collaterals, and the idea of overall regulation and multi-target intervention is to restore the ascending and descending of qi in the middle energizer and the normal function of the spleen and stomach, so as to reverse the disease.

3. EFFECTS OF GASTROINTESTINAL DYSFUNCTION ON INTESTINAL FLORA IN SEPSIS

3.1. Imbalance of Intestinal Flora

In the state of sepsis, the intense stress and systemic inflammatory response have a profound impact on the intestinal microecological environment, one of the most significant changes is the serious imbalance of intestinal flora structure. There is a relatively stable dynamic balance among various microorganisms in the intestinal tract of healthy individuals, and the pathological process of sepsis will break this ecological balance. The relative abundance of dominant bacteria, such as some bacteria in Firmicutes, which are usually beneficial to the health of the body, is significantly reduced. Some opportunistic pathogens, such as certain genera belonging to Proteobacteria, may proliferate abnormally. This change in flora composition not only means the decline of microbial diversity, but also leads to the disorder of intestinal microecological function. The reduction of beneficial flora weakens its inherent nutritional, metabolic and immunomodulatory functions, while the excessive

growth of potentially harmful bacteria foreshadows the subsequent destruction of intestinal barrier. This imbalance can be regarded as the concrete manifestation of the imbalance of "healthy qi is stored in the body, and pathogenic factors cannot interfere with it" in the theory of traditional Chinese medicine at the micro level [4]. The function of the spleen and stomach is impaired, and the transportation and transformation are out of order, resulting in the disorder of the internal environment and the growth of pathogenic factors (conditional pathogens). Therefore, intestinal flora imbalance is the initial link and one of the core pathological basis of gastrointestinal dysfunction in sepsis.

3.2. Intestinal Barrier Function Damage

The direct consequence of intestinal flora imbalance is the severe impairment of intestinal barrier function. Healthy intestinal barrier depends on the integrity of mechanical structure, chemical secretion and immune defense, in which intestinal epithelial cells and tight junction proteins constitute the key physical defense line. In the state of sepsis, dysregulated flora, especially over proliferation of potentially pathogenic bacteria, can impair the integrity of intestinal epithelial cells by direct invasion or release of toxins. At the same time, the decrease of beneficial flora leads to the decrease of beneficial metabolites such as short-chain fatty acids, which are essential for maintaining the energy supply of epithelial cells and the normal expression of tight junction proteins. The weakening of this support further aggravates the destruction of the physical barrier, resulting in abnormal increase of intestinal permeability and the formation of the so-called "intestinal leakage" phenomenon. This pathological process is consistent with the state of "unstable barriers" in the theory of traditional Chinese medicine, which indicates that the ability of the body to resist exogenous pathogens has declined significantly. The damage of intestinal barrier opens a channel for intestinal bacteria, endotoxin and other harmful substances to break through the local defense line and enter the circulatory system, which becomes a key link to promote the evolution of local intestinal problems to systemic inflammatory response.

3.3. Uncontrolled Immune Inflammatory Response

The damage of intestinal barrier function directly leads to the uncontrolled immune inflammatory response, which is the core link of the development of gastrointestinal dysfunction to systemic damage in sepsis. When the intestinal physical barrier is destroyed, a large number of intestinal bacteria and their metabolites such as endotoxin can break through the local defense line and enter the portal circulation and systemic circulation. These foreign substances are recognized as danger signals by the body's immune system, which over-activates natural immune cells and triggers a very intense pro-inflammatory response. A large number of inflammatory mediators, including a variety of cytokines, are rapidly released into the blood, forming the so-called "cytokine storm". This excessive inflammatory response not only further damages intestinal tissue remotely, but also attacks organs far away from the intestine, leading to or aggravating systemic complications such as acute lung injury and renal failure. At the same time, the body may turn to an immunosuppressive state after experiencing a strong pro-inflammatory response, which is characterized by increased apoptosis of lymphocytes and depletion of immune cell function, making patients unable to defend against the second attack of infection. This pathological process profoundly reflects the transmission law of "invasion of pathogenic qi from the bowels to the viscera" in traditional Chinese medicine, and the pathological changes of local intestinal tract eventually evolve into systemic decline of healthy qi and imbalance of yin and Yang. Therefore, the uncontrolled immune inflammatory response is the bridge between local intestinal lesions and systemic multiple organ dysfunction, and is the key driving force for the deterioration of the disease.

4. METHODS OF TRADITIONAL CHINESE MEDICINE TO PREVENT AND TREAT GASTROINTESTINAL DYSFUNCTION IN SEPSIS BY REGULATING INTESTINAL FLORA

4.1. Regulate the Flora Structure

One of the core mechanisms of traditional Chinese medicine in the prevention and treatment of gastrointestinal dysfunction in sepsis is that it can effectively regulate the disordered intestinal flora structure and rebuild the microecological balance. This effect is closely related to the fundamental therapeutic principle of "strengthening body resistance and eliminating pathogens" in traditional Chinese medicine. In the early stage of sepsis, pathogenic factors are exuberant, and the treatment is often based on "eliminating pathogenic factors", using the method of purging the bowels and clearing away heat and toxic materials. Purgative drugs can promote intestinal peristalsis and content discharge, directly change the intestinal environment, physically reduce the load of pathogenic bacteria and the accumulation of toxins, and create space for the recovery of beneficial bacteria. Heat-clearing and detoxifying drugs contain a variety of bioactive ingredients, which can selectively inhibit the overgrowth of conditional pathogens, and their effects are different from the indiscriminate killing of broad-spectrum antibiotics, reflecting a more precise regulatory characteristic.

In the late stage of the disease or for patients with obvious deficiency of vital qi, the treatment focuses on "strengthening the body resistance", especially strengthening the spleen and replenishing qi. Traditional Chinese medicine believes that "spleen governing transportation and transformation" is closely related to nutritional metabolism and the generation of grain essence in the body. By improving the functional state of the whole body and the local environment of the intestinal tract, spleen-invigorating drugs are like cultivating a fertile soil, which is conducive to the colonization and reproduction of the beneficial flora inherent in the intestinal tract. Studies have shown that these drugs can promote the growth of probiotics such as Bifidobacterium and Lactobacillus, thereby enhancing the overall diversity and stability of the flora [5]. This two-way regulation of flora structure, that is, the combination of inhibiting harmful bacteria and supporting beneficial bacteria, reflects the synergistic advantages of multi-component and multi-target of traditional Chinese medicine. By reversing the disordered flora structure to the physiological state, traditional Chinese medicine laid a solid foundation for the subsequent repair of intestinal barrier and regulation of immune inflammation, and achieved the purpose of "supporting healthy qi" from the micro-ecological level to resist pathogenic factors.

4.2. Protect the Intestinal Barrier

Based on the preliminary regulation of flora structure, Chinese medicine further plays a role in protecting intestinal barrier function through multiple ways, which is the key link to block the vicious circle of sepsis. The integrity of intestinal barrier depends on the integrity of intestinal epithelial cells and their tight junctions, the mucus layer covering the epithelial surface and the underlying immune defense. Traditional Chinese medicine plays an important role in this link. This treatment can effectively reduce the pressure in intestinal cavity, improve intestinal microcirculation, reduce intestinal wall edema and ischemia-reperfusion injury, and create basic conditions for barrier repair. More importantly, many active ingredients of traditional Chinese medicines for clearing heat and removing blood stasis and strengthening the spleen have been proved to be able to directly up-regulate the expression of tight junction proteins between intestinal epithelial cells, thereby enhancing the compactness of the physical barrier and reducing intestinal permeability.

At the same time, traditional Chinese medicine also pays attention to the strengthening of chemical and biological barriers. Some Qi-benefiting and spleen-invigorating drugs can promote the secretion of mucus by goblet cells of intestinal mucosa, thicken this protective gel layer, and effectively block the direct contact between bacteria and epithelium. In addition, through the optimization of the flora

structure in the early stage, the beneficial flora can restore its metabolic function and produce more beneficial metabolites such as short-chain fatty acids. These metabolites are not only an important energy source for intestinal epithelial cells, but also further strengthen tight junctions and contribute to the maintenance of local intestinal immune homeostasis. This function of indirectly nourishing and repairing the barrier by improving the metabolic function of flora reflects the advantages of the overall regulation of traditional Chinese medicine. This multi-level and multi-target protection of intestinal barrier is not only limited to the repair of physical structure, but also extends to the synergistic improvement of chemical environment and biological function, which effectively curbs the translocation of bacteria and endotoxin, lays a foundation for the control of systemic inflammatory response, and is highly consistent with the therapeutic thought of "protecting the barrier" in traditional Chinese medicine to prevent "invasion of pathogenic factors".

4.3. Inhibit the Excessive Inflammation

The underlying mechanism of TCM in the prevention and treatment of gastrointestinal dysfunction in sepsis lies in its effective regulation of systemic excessive inflammatory response. This effect comes down in one continuous line with the therapeutic principle of "clearing heat and cooling blood" and "promoting blood circulation and detoxification" in traditional Chinese medicine. When the intestinal barrier is damaged and endotoxin is translocated, the inflammatory signaling pathway of immune cells will be over-activated, triggering the cascade release of inflammatory mediators. The intervention strategy of traditional Chinese medicine is not a simple antagonism of a single factor, but a multi-target regulation of key signal nodes such as nuclear transcription factors. Heat-clearing and detoxifying drugs and blood-activating and stasis-removing drugs can effectively inhibit the abnormal activation of these pathways, thus reducing the excessive production of core pro-inflammatory factors such as tumor necrosis factor- α and interleukin-6 at the transcriptional level, and helping to calm the "cytokine storm" that endangers the body.

It is particularly important that the regulatory role of traditional Chinese medicine shows dynamic and balanced characteristics. In the early stage of hyperactive inflammation of the disease, the main treatment is to clear heat and purge fire, aiming at curbing excessive immune activation. With the evolution of pathogenesis, in the late stage of the disease or in the state of deficiency syndrome, the treatment focuses on supplementing qi and nourishing yin, aiming at preventing immune paralysis and promoting the stability and reconstruction of the immune internal environment. This regulation of inflammatory response is not carried out in isolation, but constitutes a synergistic effect with flora regulation and barrier protection. Reconstructed microbiota can produce more anti-inflammatory metabolites, while repaired mechanical barriers can reduce the continuous stimulation of antigens. It can be seen that through the comprehensive network of direct regulation of immune cell function and indirect improvement of intestinal microenvironment, traditional Chinese medicine has achieved precise containment of excessive inflammation, blocked the core driving link of the vicious circle of sepsis, and highlighted its therapeutic advantages under the guidance of holistic view.

5. CONCLUDING REMARKS

To explore the prevention and treatment of gastrointestinal dysfunction in sepsis from the perspective of intestinal flora provides a strong modern scientific basis for explaining the mechanism of traditional Chinese medicine. Guided by the "holistic view", traditional Chinese medicine shows comprehensive advantages in regulating flora ecology, maintaining barrier integrity and balancing immune response through the synergistic effect of multi-components and multi-targets. This dynamic and holistic regulatory strategy is more in line with the complex pathological characteristics of the disease than a single target intervention. Future research can further reveal the material basis and action pathway of pharmacodynamics with the help of modern technologies such as systems biology,

and verify its efficacy through rigorous clinical research, so as to promote the precise application and innovative development of traditional Chinese medicine in the field of critical illness.

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