

Research Progress of Traditional Chinese Medicine in the Treatment of Sepsis Gastrointestinal Dysfunction

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Abstract: Sepsis is a systemic inflammatory response syndrome (SIRS) caused by infection. Further development can lead to severe sepsis, septic shock and multiple organ dysfunction or failure. Gastrointestinal dysfunction is one of the common complications. Reviewing the domestic literature, it is found that in recent years, traditional Chinese medicine has accumulated a large number of clinical research data in the treatment of sepsis gastrointestinal dysfunction, and has achieved good results. This article briefly summarizes the etiology and pathogenesis of gastrointestinal dysfunction in sepsis and the treatment of traditional Chinese medicine, in order to provide reference for further clinical research in the future.

Keywords: Chinese medicine, Sepsis, Gastrointestinal dysfunction.

1. Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. Gastrointestinal dysfunction is an important part of multiple organ dysfunction syndrome (MODS) caused by sepsis, which is one of the important causes of aggravation and death of patients [2]. Some scholars have put forward the theory of "perpetual motion machine" and believed that gastrointestinal tract is the initiating organ and target organ of sepsis [3]. In recent years, gastrointestinal dysfunction caused by sepsis has been paid more and more attention. Some studies [4] have pointed out that the incidence of gastrointestinal dysfunction in sepsis complicated with multiple organ failure can be as high as 78.8%, and its mortality rate can reach 61.7%. Modern medicine believes that the mechanism of gastrointestinal dysfunction in sepsis is related to intestinal barrier damage, intestinal flora imbalance, ischemia-reperfusion injury, insufficient nutritional intake, and neuroimmune system disorder [5]. In the treatment, measures such as protecting gastrointestinal mucosa, restoring gastrointestinal motility, maintaining intestinal microecological balance, actively treating primary diseases, anti-inflammation, and early implementation of enteral nutrition are adopted, but the current treatment plan fails to achieve ideal results in some cases. The field of traditional Chinese medicine has shown unique advantages with its rich treatment methods, significant curative effect and low adverse reaction rate. Many clinical research data show that traditional Chinese medicine has achieved good results in the treatment of sepsis gastrointestinal dysfunction. Based on this, this paper aims to comprehensively review the latest research progress of traditional Chinese medicine in the treatment of gastrointestinal dysfunction in sepsis, in order to provide a useful reference for clinical practice.

2. Etiology and Pathogenesis

Traditional Chinese medicine does not have the name of sepsis gastrointestinal dysfunction. According to its clinical

manifestations, it is similar to "abdominal pain", "abdominal distension", "fullness", "constipation", "diarrhea" in traditional Chinese medicine. About the etiology and pathogenesis of gastrointestinal dysfunction in sepsis, Shi Rong [6] believed that the cause of sepsis complicated with acute gastrointestinal injury was Fu-organ excess and Ying-heat, and the pathogenesis was heat-toxin accumulation, toxin falling into Fu-organs, accommodating Ying-blood, and should be treated with Tongfu Qingying; Mei Manxue [7] believed that sepsis is the syndrome of deficiency in origin and excess in superficiality, and the pathogenesis is related to deficiency, toxin and stasis. "deficiency" is the basis, "stasis" is the real evil, and "toxin" is the inducement, when the lesion involves the gastrointestinal tract, sepsis gastrointestinal dysfunction occurs; "sepsis acute gastrointestinal dysfunction clinical expert consensus of integrated traditional Chinese and Western medicine" [8] on the basis of summarizing and perfecting the thoughts of various doctors, it is proposed that the characteristics of sepsis acute gastrointestinal dysfunction are asthenia in origin and asthenia in superficiality, internal accumulation of stasis and toxin as the basic pathogenesis, spleen and stomach qi deficiency as the pathological basis, according to the process and characteristics of the disease, it is divided into liver and spleen disharmony syndrome, damp heat stagnation syndrome, heat toxin stasis syndrome or fu-organ excess and blood stasis syndrome, yang qi sudden loss syndrome or kidney yin exhaustion syndrome; Recently, some scholars have put forward new insights on the diagnosis and treatment of gastrointestinal dysfunction in sepsis. For example, Liu Zhiliang [9] elaborated Professor Mei Jianqiang's clinical experience in the treatment of gastrointestinal dysfunction in sepsis, professor Mei believes that the root cause of sepsis lies in the deficiency of healthy qi, and the key level of the lesion lies in the damage of collaterals, the core pathological link is collateral stasis. Gastrointestinal dysfunction in sepsis is the key node of the course of sepsis, its core pathogenesis is gastrointestinal yin injury and collateral obstruction, based on this, the treatment of nourishing yin and dredging fu organs and removing blood stasis and dredging collaterals is proposed; Li Xueying [10]

considered that the essential pathogenesis of gastrointestinal dysfunction in sepsis is deficiency of healthy qi and excess of pathogenic qi, obstruction of triple energizer based on the theory of triple energizer membrane and striae, it is a pathological process of triple energizer membrane and striae, deficiency of primordial qi, invasion of pathogenic qi, from light to heavy.

3. Study on the Treatment of Gastrointestinal Dysfunction in Sepsis by Prescription

3.1 Banxia Xiexin Decoction

Banxia Xiexin Decoction (BXD), derived from "Treatise on Febrile and Miscellaneous Diseases", is composed of Pinelliae Rhizoma, Coptis Chinensis Rhizoma, Scutellariae Radix, Zingiberis Rhizoma, Ginseng Radix et Rhizoma, Glycyrrhizae Radix et Rhizoma and Jujubae Fructus, it is mainly used for the treatment of cold and heat mixed Pi syndrome, it has the functions of harmonizing liver and spleen, regulating cold and heat, eliminating Pi and Sanjie, and is widely used in digestive system diseases. Modern studies have shown that BXD has the effects of protecting gastrointestinal mucosa, anti-gastrointestinal tumors, and regulating intestinal flora [11]. Li Guochen [12] observed the clinical efficacy of BXD in the treatment of gastrointestinal dysfunction in sepsis and verified the potential mechanism of its therapeutic effect through clinical research and animal experiments. In the clinical study, the serum diamine oxidase (DAO), D-lactic acid level (D-Lac), TCM syndrome score, APACHE II score, SOF score and gastrointestinal dysfunction score (GIF) in the treatment group treated with BXD on the basis of conventional western medicine were significantly better than those in the control group treated with conventional western medicine ($P<0.01$); animal experiments have shown that BXD treatment can reduce the levels of IL-1 β , IL-6 and TNF- α in serum and small intestine groups, and the high-dose group has better efficacy, the mechanism may be through the regulation of PI3K/Akt/HO-signaling pathway to inhibit sepsis inflammation and reduce intestinal injury in septic rats. In the study of BXD in the treatment of sepsis with multiple organ dysfunction, Shen Yang [13] found that the diagnostic score and incidence of gastrointestinal dysfunction in the traditional Chinese medicine group were lower than those in the control group ($P<0.05$), and the improvement of gastrointestinal function was better than that in the control group ($P<0.05$), this shows that it can regulate gastrointestinal function, reduce the incidence of early gastrointestinal dysfunction in patients with sepsis, and improve gastrointestinal function in patients with gastrointestinal dysfunction. The results of meta-analysis of Wang Shuang [14] showed that the combined use of BXD could improve the total effective rate of patients with sepsis gastrointestinal dysfunction, reduce GIF score, APACHE II score and intra-abdominal pressure level, improve clinical symptoms, and reduce the level of inflammatory indicators. In summary, BXD has a certain therapeutic advantage for sepsis gastrointestinal dysfunction.

3.2 Dahuang Mudan Decoction

Dahuang Mudan Decoction (DMD) is a classic prescription

for the treatment of intestinal carbuncle in "Synopsis of Golden Chamber", the combination of rhubarb, peach kernel, mirabilite, peony bark and wax gourd kernel in the prescription plays the role of purging heat and removing blood stasis, dispersing knots and eliminating carbuncle. Xie Changhui [15] observed the curative effect of DMD addition and subtraction in the treatment of patients with sepsis gastrointestinal dysfunction, the total effective rate of the combined DMD treatment group was higher than that of the control group (94.76% vs 78.95%, $P<0.05$), the levels of CRP, TNF- α , IL-10, D-Lac and intestinal fatty acid binding protein (IFABP) were lower than those of the control group ($P<0.05$), and the citrulline level was higher than that of the control group ($P<0.05$), it was clear that the combined DMD treatment could enhance the curative effect and improve the improvement effect on the body's gastrointestinal function and inflammatory response. The study of Wang Zhuang [16] showed that DMD could significantly reduce the acute gastrointestinal injury (AGI) grade and AGIUS score of patients with sepsis gastrointestinal dysfunction of fu-organ excess and blood stasis type, improve the gastric antrum motility index (MI) of patients, reduce mechanical ventilation time and ICU hospitalization days. Yang Mengxia's team [17] used network pharmacology research to find that the mechanism of DMD in the treatment of sepsis gastrointestinal dysfunction is that this prescription exerts anti-inflammatory and regulating immune system by regulating HIF-1 signaling pathway, PI3K-Akt signaling pathway and IL-17 signaling pathway. It can be seen that DMD has a good effect on gastrointestinal dysfunction in sepsis, especially in patients with intestinal heat and blood stasis.

3.3 Dahuang Fuzi Decoction

Dahuang Fuzi Decoction (DFD), first recorded in "Synopsis of Golden Chamber", is a classic analgesic prescription composed of rhubarb, processed aconite and asarum, it has the functions of warming yang, dispelling cold, relaxing and relieving pain, and mainly treats abdominal pain caused by yang deficiency and cold coagulation. Liu Yongcheng [18] found that compared with the control group, the combined application of DFD group significantly reduced the APACHE-II score, GIF score and the incidence of adverse reactions ($P<0.05$), therefore, the treatment of sepsis patients with Dahuang Fuzi Decoction can significantly improve the gastrointestinal function of patients and reduce the degree of gastrointestinal function damage in patients with severe sepsis. Xu Jieru [19] showed that the levels of WBC, hs-CRP and PCT in the combined DFD group were significantly lower than those before treatment ($P<0.05$), and had anti-inflammatory effect. Liu Jin [20] took elderly patients as the research object, the results showed that Dahuang Fuzi Decoction and Ginseng could improve the gastrointestinal function of elderly patients with acute gastrointestinal injury in sepsis, the mechanism may be through regulating gastrointestinal hormones, reducing intestinal permeability and alleviating inflammation. A meta-analysis [21] showed that DFD is helpful to improve the condition of patients with sepsis gastrointestinal dysfunction, and there is no obvious adverse reaction. In summary, for patients with septic gastrointestinal dysfunction, DFD can inhibit inflammatory response, regulate gastrointestinal function, and improve efficacy.

3.4 Tiaowei Chengqi Decoction

Tiaowei Chengqi Decoction (TCD), derived from "Treatise on Febrile and Miscellaneous Diseases", is one of the main prescriptions for the treatment of Yangming Fu syndrome, it is composed of rhubarb, mirabilite and licorice, which can relieve heat accumulation. In the study of Zhang Xxianjin [22], the indexes of bowel sounds, abdominal circumference and intra-abdominal pressure in the conventional western medicine combined with TCD group were better than those in the control group treated with western medicine alone ($P < 0.05$), and the HLA-DR, total number of lymphocytes, CD3 +, CD4 +, CD8 +, CD4 + / CD8 + and NK cells in the treatment group were higher than those in the control group ($P < 0.05$), it shows that TCD has a benign regulatory effect on the immune status of patients. A recent study [23] also showed that western medicine combined with TCD treatment can also effectively reduce the level of inflammatory factors in the body, which is beneficial to disease control. In summary, TCD improves gastrointestinal function by supporting healthy qi, improving immune function, and controlling the release and level of inflammatory factors.

3.5 Self-made Formula

With the deepening of clinical research, many doctors have also achieved good results in the treatment of this disease through clinical experience. Liu Chao's team [24] self-made Tiaoqi Tongfu Jianpi Recipe (Huangqi, Gualou, Mangxiao, Zhishi, Zhuru, Chenpi, Shanyao, Houpo, Fuling, Baizhu, Gancao) to treat this disease, the results showed that the combination of western medicine and Tiaoqi Tongfu Jianpi Recipe can effectively inhibit the inflammatory response in patients with sepsis gastrointestinal dysfunction, reduce endotoxin levels, promote the repair of intestinal mechanical barrier, and improve gastrointestinal motility. Zhang Liwen [25] treated sepsis patients with gastrointestinal dysfunction of lung-heat and fu-organ excess type according to the self-made prescription of lung-gut combination therapy (almond, aster, trichosanthis pericarpium, fructus aurantii, radix curcumae, peach kernel, black mountain gardenia, xiangdouchi), the results showed that lung-gut combination therapy could effectively reduce the intra-abdominal pressure, gastric residual volume and GIF score of patients, increase the levels of motilin and vasoactive intestinal peptide, reduce the level of gastrin, promote the recovery of gastrointestinal function, and regulate the level of inflammatory factors in the body.

4. Study on the Treatment of Gastrointestinal Dysfunction in Sepsis by Traditional Chinese Medicine Injection Preparation

Traditional Chinese medicine injection preparation directly enters the blood through intravenous injection, according to the characteristics of rapid action and stable curative effect, it has been widely used in clinical practice, especially for acute and critical patients. Zhou Ben [26] explored the effect of Xuebijing injection on patients with gastrointestinal dysfunction in sepsis with blood stasis and fu-organ excess, the results showed that Xuebijing could significantly improve the symptoms of fever, abdominal distension, abdominal pain and ecchymosis, the improvement of inflammation and

prognostic indicators such as hemogram, coagulation function, lactic acid, CRP, PCT, APACHE II score and SOFA score was prominent, which improved the effectiveness of sepsis treatment. Liu Miaokuang [27] observed the effect of Xingnaojing injection on patients with sepsis and gastrointestinal dysfunction, the total effective rate of the treatment group (92.5%) was significantly higher than that of the control group ($P < 0.05$), and APACHE II score, GIF score, DAO, PCT, WBC, CRP and D-Lac levels were significantly lower ($P < 0.05$), suggesting that Xingnaojing injection can significantly improve the serological indicators of patients and promote the rehabilitation of the disease. Zhang Wei [28] suggested that the combination of Shenfu injection can reduce the levels of serum I-FABP, soluble CD14 subtype and malondialdehyde (MDA) in patients with sepsis intestinal mucosal dysfunction, increase the activity of superoxide dismutase (SOD) and reduce the mortality rate.

5. Study on the Treatment of Gastrointestinal Dysfunction in Sepsis by External Treatment of Traditional Chinese Medicine

5.1 Acupuncture

Acupuncture and moxibustion can regulate the function of zang-fu organs and regulate qi movement through meridian acupoint stimulation. Meta-analysis [29] showed that the commonly used meridians for acupuncture and moxibustion treatment were the stomach meridian and Ren meridian of foot Yangming, and the most used degrees were Tianshu, Zusanli and Zhongwan, in the results, the combination of acupuncture and moxibustion on the basis of western medicine treatment can improve the symptom improvement rate and the number of bowel sounds per minute, reduce the 28-day mortality rate, APACHE-II score, CRP and PCT levels, but the improvement of intra-abdominal pressure and gastric residual volume is not obvious. In another study [30], based on the theory of "lung and large intestine are interior-exteriorly related", the experimental group added Chize (bilateral) and Taiyuan (bilateral) on the basis of acupuncture points in the conventional acupuncture group, the results showed that the therapy was more effective than the conventional acupuncture therapy for the gastrointestinal tract. The above all show that acupuncture can effectively alleviate the symptoms of this disease, and the combination of clinical acupuncture and medicine can improve the curative effect.

5.2 Traditional Chinese Medicine Enema

Enema is a treatment method that directly injects drugs into the rectum through the anus, it takes the meaning of "direct access to the disease" and promotes the absorption of inflammatory factors and the excretion of toxins through the absorption of active ingredients of drugs by local intestinal mucosa, the effect is rapid and the curative effect is outstanding. Xu Yonghao [31] retention enema with Dachengqi Decoction, after treatment, the serum APACHE-II score, WBC, PCT and hs-CRP in the observation group were lower than those in the control group, it is suggested that Dachengqi decoction enema can improve gastrointestinal function and reduce inflammatory response in patients with sepsis gastrointestinal dysfunction. Ge Xu [32] used rhubarb enema combined with acupuncture as the observation group.

The study showed that the scores of abdominal distention, hot flashes and delirium, abdominal pain rejection, frequent sagittal rotation, and anal burning in the observation group were significantly lower than those in the conventional group ($P < 0.05$), and the inflammatory index decreased significantly. Hu Naiqiang [33] used self-made enema prescription to treat this disease, the indexes of TNF- α and IL-6 in the treatment group were better than those in the control group, indicating that this self-made enema prescription can better control the inflammatory response.

5.3 Acupoint Application

The acupoint application therapy combines traditional Chinese medicine with acupoints. Through the dual effects of drug drug penetration through the skin and acupoint stimulation, the curative effect is lasting and convenient to use. Studies have shown that acupoint application of traditional Chinese medicine can reduce the probability of gastrointestinal dysfunction in sepsis[34]. Chen Hong [35] study found that the application of cinnamon powder on Shenque, Zhongwan, Guanyuan and Tianshu points can effectively improve the symptoms of gastrointestinal dysfunction in sepsis with spleen and stomach weakness, reduce intra-abdominal pressure and reduce the incidence of MODS. Zhou Boqiao [36] used Sini Decoction (aconite, dried ginger, licorice) powder to apply Zusanli and Shenque, the results showed that the total effective rate of combined treatment was better than that of conventional treatment group.

6. Summary

In summary, gastrointestinal dysfunction in sepsis is a syndrome of deficiency in origin and excess in superficiality, in recent years, clinical research on the treatment of gastrointestinal dysfunction in sepsis with traditional Chinese medicine has achieved certain results. From the perspective of internal treatment, Banxia Xiexin Decoction, Dahuang Mudan Decoction, Dahuang Fuzi Decoction and Tiaowei Chengqi Decoction are classical prescriptions with more clinical application. Many doctors have summarized and put forward their own experience prescriptions according to their long-term clinical experience, and have achieved good curative effect. From the external treatment, acupuncture, traditional Chinese medicine enema, traditional Chinese medicine acupoint application treatment also has more applications, multi-method comprehensive treatment effect is outstanding. Secondly, the traditional Chinese medicine injection preparation based on Xuebijing injection has a prominent effect on inhibiting systemic inflammatory response. Although there are many clinical studies, there is a lack of high-quality multi-center and large-sample studies. In addition, the mechanism of traditional Chinese medicine in the treatment of gastrointestinal dysfunction in sepsis is also worthy of further exploration, in order to provide more valuable reference for the treatment of gastrointestinal dysfunction in sepsis with traditional Chinese medicine.

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