

Research Progress on Diagnosis and Treatment of Diarrhea Predominant Irritable Bowel Syndrome in Traditional Chinese Medicine

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Abstract: *The pathogenesis of diarrhea predominant irritable bowel syndrome has not yet been fully clarified in western medicine, and symptomatic treatments such as spasmolysis and antidiarrheal are generally used in clinic, which lacks systematicness and long-term effectiveness, and the clinical efficacy of some patients is not ideal. Traditional Chinese medicine has significant advantages in improving clinical symptoms, improving body immunity and improving patients' quality of life through syndrome differentiation and treatment. This article mainly summarizes the etiology and pathogenesis of IBS-D, and the treatment methods and prescriptions, in order to provide some ideas and references for the clinical diagnosis and treatment of IBS-D in TCM.*

Keywords: Traditional Chinese medicine, Diarrhea predominant irritable bowel syndrome, Etiology and pathogenesis, Syndrome differentiation and treatment.

1. Introduction

The course of irritable bowel syndrome (IBS) is long, with the characteristics of recurrent and intermittent attacks, which seriously affects the quality of life of patients. According to the Rome IV diagnostic criteria, IBS can be divided into four subtypes based on the difference of stool characteristics when patients have abnormal defecation. Among them, diarrhea predominant IBS (IBS-D) is the most common, accounting for more than 45% of the total number of IBS cases [1]. The pathogenesis of IBS-D in western medicine has not been fully clarified, and it is believed that it is the result of the joint action of many factors, so the clinical treatment of IBS-D is mostly symptomatic treatment, lacking systematic and long-term effects, and the clinical efficacy of some patients is not ideal. The diagnosis and treatment of IBS-D with traditional Chinese medicine can significantly improve the clinical symptoms, improve the body immunity, and improve the quality of life of patients [2]. This paper summarizes the relevant literature on the diagnosis and treatment of IBS-D in traditional Chinese medicine in recent years, mainly from the etiology and pathogenesis of IBS-D, treatment methods and prescriptions, aiming to provide some ideas and references for the clinical diagnosis and treatment of IBS-D in traditional Chinese medicine.

2. Etiology and Pathogenesis

There is no name of "diarrhea type irritable bowel syndrome" in traditional Chinese medicine. According to its clinical symptoms, it can be classified into the categories of "abdominal pain", "diarrhea", etc. "Plain Question" discusses abdominal pain and diarrhea in detail, such as "the cold air stays in the small intestine, and the small intestine cannot form a cluster, so the abdominal pain will be released later" and "the meridians are popular, and the circulation is endless, the cold air enters the meridians and is delayed, crying but not working, the guest outside the pulse has less blood, the guest in the pulse has no air, so the stroke but pain" points out that the main

cause of abdominal pain is cold evil, and expounds its mechanism as "impassability leads to pain" and "dishonor leads to pain". According to the Inner Canon of Huangdi, "spring is hurt by the wind, and evil Qi lingers, which is due to the leakage of holes", "good disease in the long summer is due to the leakage of cold in the hole", "dampness is due to the leakage of cold", etc. "Jing Yue Book" mentions that "the kidney is the pass of the stomach, the fire of the gate of life declines, and the Yin cold is only prosperous, so it is after the fifth hour... That is, it makes the hole not stop leaking", pointing out that both external and internal injuries can lead to the occurrence of diarrhea.

The etiology of IBS-D is various, which is based on somatic weakness and can be induced by emotional, dietary, exogenous and other factors [3]. First of all, frailty of the body is the basis of the disease. If the body is frail, the Yang is insufficient, and the gastrointestinal tract cannot be warmed, the disease can occur. As the "Miraculous Pivot" said, "if Yang Qi is insufficient, Yin Qi is surplus, then the intestines in cold and abdominal pain". Secondly, emotional disorders can be mutually causal with IBS-D [4]. "Plain Question" said: "I know that all diseases are born of Qi. On the one hand, being too angry and worried can lead to the liver wood not being contained, riding on the spleen against the wind, further damaging the temper, and then being unable to transport the dregs to the large intestine under the influence of water and grain, which eventually manifests as diarrhea. At the same time, IBS-D has the characteristics of recurrent and intermittent attacks, which seriously affects the quality of life of patients and leads to psychological symptoms such as anxiety and depression [5]. Lin Yangjin et al. [6] classified patients with IBS-D according to the classification and determination of constitution in traditional Chinese medicine, and concluded that people with qi depression were prone to IBS-D. Moreover, improper diet is closely related to the pathogenesis of IBS-D. Excessive hunger and satiety, and partial appetite can lead to abnormal functions of the spleen and stomach, which can lead to abdominal pain, diarrhea and other symptoms. As the "Jing Yue Book" said: "if the diet is

not strict... Then the water will become wet, the grain will become stagnant, the essence of the gas can not be transfused, and even the combined pollution will fall and diarrhea will occur." Wei Wei et al [7] analyzed the correlation between serum diamine oxidase (DAO) and dietary habits, and the results showed that the decline of intestinal barrier function in IBS-D patients was closely related to dietary habits. Finally, external pathogens and six evils can induce this disease as the "Inner Canon of Huangdi" says, "patients with large bowel disease feel pain in their intestines and cry and wash. In winter, they feel cold, that is, discharge. When they feel pain in their umbilicus, they can't stand for a long time." "when they are wet, they will soak in the diarrhea." "when they are injured in the wind in spring, they will have diarrhea in summer".

By studying ancient medical books and combining with their own clinical experience, modern doctors pointed out that the occurrence of IBS-D was based on spleen deficiency, which was the syndrome of deficiency in origin but excess in excess. Taking qi stagnation as the sign, they believed that liver depression and spleen deficiency were the core pathogenesis of IBS-D [8]. Xu Jingfan, a master of traditional Chinese medicine, advocated that the onset of IBS-D was based on spleen deficiency and marked by liver depression. He believed that liver depression and spleen deficiency were the main pathogenesis of IBS-D [9], and pointed out that liver depression and spleen deficiency could affect each other. Patients with liver depression lasted for a long time, liver Qi was not sparse, and they were easy to turn into fire, resulting in irritability, anxiety and depression. Professor Tang Xudong discussed the pathogenesis of IBS-D based on the soil deficiency and wood depression, and the loss of intestinal organs [10], and believed that the liver and spleen are physiologically dependent on each other; Pathologically, it can also affect each other. Just like "deficiency of spleen and soil, liver and wood can take advantage of it", it will further damage the spleen and eventually lead to the loss of function in the intestine, which will lead to this disease. Professor Li Xuejun found in his clinical work that although there are many inducements for IBS-D, its root is still "centered on dampness". The pathogenesis is based on the imbalance of Qi, spleen deficiency and yang deficiency [11]. Professor Ge Huinan believes that the pathogenesis of IBS-D is due to spleen deficiency and excessive dampness. If the patient has a weak spleen and stomach, and the water and grain are not refined, resulting in dysregulation of qi movement and rising and falling, and gathering and generating dampness, the disease will occur [12]. Other scholars, based on the theory of "the spleen is bitter and wet, and the acute food is bitter and dry", believe that although the etiology and pathogenesis of IBS-D are complex, they are rooted in spleen deficiency and excessive dampness [13]. Clinically, although the liver stagnation and spleen deficiency syndrome IBS-D is more common, with the change of the disease, the Spleen Yang is insufficient and the kidney yang is involved over time, which can eventually develop into spleen kidney yang deficiency syndrome [14]. Professor Wang Chuijie believes that successive days can breed each other. Based on the medical prescription collection, he points out that the long diarrhea is caused by the deficiency of kidney yang, the fire failure of the life gate, and the inability to warm the Spleen Yang [15]. According to the consensus opinion of experts in TCM diagnosis and treatment of irritable bowel syndrome (2017)

[16], the pathogenesis of IBS-D is based on the deficiency of spleen and kidney yang, and the dysregulation of Qi mechanism is the target, and this disease will eventually lead to the loss of warmth of spleen and kidney, resulting in the deficiency of spleen and kidney yang syndrome.

To sum up, IBS-D disease is located in the intestine and is closely related to the heart, liver, spleen, kidney and other organs [15]. At the initial stage of onset, it is mainly qi stagnation; Then liver disease spreads to spleen, spleen deficiency and dampness accumulate; Long term illness and kidney lead to deficiency of kidney yang.

3. Treatment

3.1 Internal treatment of traditional Chinese Medicine

3.1.1 Dialectical treatment of IBS-D

The traditional dialectical treatment is mainly based on suppressing liver and strengthening spleen, strengthening spleen and eliminating dampness, warming and tonifying spleen and kidney, and the clinical efficacy is exact with Tongxie Yaofang, SLBZS, Sishen pill and other prescriptions. Shen Zhengyin et al. [17] based on the nine methods for treating diarrhea, on the basis of suppressing liver and strengthening spleen, they added Codonopsis pilosula, yam and other drugs for calming and soothing, and Agastache, Magnolia officinalis and other drugs for drying spleen to treat IBS-D. the research results proved that the modified Tongxie Yaofang had significant curative effect in improving abdominal pain, diarrhea and other symptoms. Qiao Nali concluded that Tongxie Yaofang combined with Chaihu Shugan San may be the best prescription for harmonizing liver and spleen in the treatment of IBS-D through mesh meta-analysis [18]. The research results of Zhang Quanwen et al [19] showed that SLBZS can regulate the brain gut peptide level of IBS-D patients, and has a significant effect in improving the body's immune function, anti-inflammatory and other aspects. Qiu Jiangwei [20] and others used SLBZS combined with conventional western medicine to treat IBS-D, and found that SLBZS can effectively regulate the immune function of patients and the level of human T lymphocytes. The study of Li Siqi et al [21] showed that Sishen pill can alleviate the abdominal pain symptoms of IBS-D rats with spleen kidney yang deficiency by reducing rpvl neuron activity and reduced visceral sensitivity. Based on the theory of yin-yang balance. Xu Xiaomei treated IBS-D with the principle of calming cold and heat, soothing the liver and regulating the spleen, which can balance the body's Yin and Yang, and the disease will go away by itself [22].

3.1.2 Classical prescriptions

Classical prescriptions, which are famous prescriptions from classic medical books, have been tested in clinical practice for thousands of years, and the clinical treatment of IBS-D can be described as "effective as a drum". Zhang Chunling, based on Professor Huang Huang's "prescription-disease-person" diagnosis and treatment idea, according to the "prescription person" theory, clinically divided IBS-D into six kinds, such as

Suitable for patients with Major Bupleurum Decoction, Suitable for patients with Xiao Chaihu Tang, Suitable for patients with Chaihu Jialong oyster soup, and "implement the classic prescription, carefully add and subtract" in the treatment of IBS-D, obtained good curative effect, and provided a new idea for the inheritance of the classic prescription [23]. Xu Fengqin attached great importance to the role of emotional pathogenic theory in the pathogenesis of IBS-D, advocated the treatment of liver and spleen together, leveled the cold and heat, and used Wumei Pill to treat, which not only alleviated the gastrointestinal symptoms of patients, but also adjusted the mental and psychological state of patients [24]. Huang Yulong et al [25] believed that modern diet has a thick taste of sorghum, and residents' physique is mostly damp and hot, so they used the method of clearing heat, removing dampness and stopping diarrhea to treat IBS-D, and found that Gegen Qinlian decoction can not only inhibit the gastrointestinal inflammatory response by regulating the expression of IL-10 and TNF- α , but also regulate the number of bifidobacteria and Lactobacillus acidophilus in the intestine, and regulate the intestinal microecological balance.

3.1.3 Chinese patent medicine

Chinese patent medicine is a traditional Chinese medicine product made with traditional Chinese medicine as raw material under the guidance of traditional Chinese medicine theory to prevent and treat diseases. It not only retains the curative effect of traditional Chinese medicine, but also is easy to carry and store, which improves the compliance of patients to a certain extent. An Chao et al [26] found that on the basis of the application of OTIUM bromide combined with SLBZS granules in the treatment of IBS-D can significantly improve the clinical curative effect, and make the serum levels of peroxidase reductase 1 (Prdx1), interleukin-13 (IL-13), and tumor necrosis factor - α (TNF- α) tend to be healthy. Liang Yuhua et al. [27] evaluated the efficacy and safety of traditional Chinese patent medicine combined with conventional Western Medicine (CWMT) in the treatment of IBS-D. the results showed that the total effective rate of Buzhong Yiqi pill (granule) + CWMT in the treatment of IBS-D was significantly better than that of CWMT. Wuling capsule + CWMT could significantly improve the abdominal pain, diarrhea and other discomfort of IBS-D patients, Qizhi Weitong granule + CWMT could significantly improve the symptoms of abdominal distension of patients, and Bupi Yichang pill, SLBZS granule (powder / pill) combined with western medicine in the treatment of IBS-D could reduce the incidence of adverse reactions. YELIYA Yeertai et al. [28] showed that Sishen pill, Tongxiening granule, Bupi Yichang pill, SLBZS granule have good efficacy and safety in the treatment of IBS-D with western medicine alone or in combination, and each has its own characteristics: SLBZS granule is suitable for the treatment of IBS-D caused by intestinal flora imbalance, Tongxiening granule can be used for IBS-D caused by visceral hypersensitivity, Sishen pill can be used for IBS-D caused by intestinal hyperfunction, and Tongxiening granule can be used for IBS-D patients with anxiety and depression. Lin Xiaoyuan et al [29] found that the effect of Sishen Pill on IBS-D rats was related to the regulation of the expression of tryptase (MCT), an indicator of mast cell activation in the colon, and the immediate early gene c-fos.

3.2 Acupuncture

Acupuncture and moxibustion can be used as the first choice of non drug therapy for the treatment of IBS-D, which has the advantages of easy operation and no side effects, and clinical research has confirmed that acupuncture and moxibustion can effectively improve the symptoms of IBS-D patients. Based on the academic thought of treating viscera with moxibustion meridian, Professor Chang Xiaorong achieved satisfactory curative effect in the treatment of IBS-D with acupuncture and moxibustion [30]. Zheng Jie et al used Tiao Shen Jian Pi acupuncture combined with moxibustion to treat IBS-D. the results showed that the total effective rate of the observation group (90.00%) was significantly higher than that of the control group (72.50%), and the D-lactic acid, diamine oxidase (DAO), endotoxin, and 5-HT levels of the observation group were lower than those of the control group [31]. The results suggested that Tiao Shen Jian Pi acupuncture combined with moxibustion could improve the intestinal barrier function and visceral sensitivity of IBS-D patients. Mao Jing et al [32] showed that acupuncture at Neiguan Acupoint could reduce the content of substance P (SP) in serum to improve the symptoms of mental and emotional abnormalities, visceral hypersensitivity, abdominal pain, diarrhea and other symptoms in IBS-D model rats.

3.3 External treatment of traditional Chinese Medicine

The principle of external treatment is the principle of internal treatment, and the medicine of external treatment is the medicine of internal treatment. The difference is the method of ear ". The external treatment of traditional Chinese medicine mainly focuses on acupoint application, ear acupoint embedding beans, moxibustion, etc., and it is often treated both inside and outside clinically. Shi Hao et al's clinical research showed that the application of Milli fire needle combined with acupoint application can significantly improve the clinical symptoms of IBS-D patients with spleen deficiency and dampness, such as abdominal pain, stool frequency, and can also adjust the level of 5-HT in patients [33]. "The ear is the place where blood is gathered", Zhang Yiqing and others selected the commonly used clinical empirical formula, combined with hepatobiliary points, spleen points, stomach points and other acupoints for bean embedding intervention in the treatment of IBS-D, and the total effective rate (88.46%) was significantly higher than that of the control group (63.46%), indicating that bean embedding at ear points can significantly improve the clinical efficacy of IBS-D patients [34]. Some research results showed that [35], moxibustion treatment of IBS-D model rats can reduce the intestinal inflammatory level and reduce visceral hypersensitivity, and its mechanism may be related to the expression levels of microrna-345-3p (miR-345-3p), microrna-216a-5p (miR-216a-5p) and nuclear factor kappa bp65 (NF- κ Bp65) in colon tissue. Among them, NF- κ Bp65 can promote the expression of cytokines, chemokines and adhesion molecules, thus promoting the occurrence and development of intestinal inflammation, and then the clinical symptoms of IBS-D; Both miR-345-3p and miR-216a-5p can inhibit the proliferation and activation of intestinal inflammatory cells by negatively regulating Cdk6 protein expression and BRCA2 protein expression, thereby inhibiting intestinal inflammation and improving IBS-D-related clinical

symptoms.

3.4 Prevention

Traditional Chinese medicine education attaches importance to the prevention of diseases. The Internal Classic clearly puts forward the idea of "treating diseases before they occur": "it is therefore not too late for saints to treat diseases before they occur, and to treat disorders before they occur... It is not too late for men to treat diseases after they have become drugs, and to treat disorders after they have become disorders, for example, it is still too late to go through wells and fight to cast a cone". In order to prevent the occurrence of IBS-D, we should take various preventive measures to improve the healthy qi and eliminate the inducements. For example, people with weak physique should strengthen physical exercise and eat less or avoid cold food; Patients with unhealthy eating habits should avoid spicy and irritating food, and limit the intake of alcohol, coffee, protein, etc. to reduce the burden of gastrointestinal tract; Those who are usually in a hurry should not forget to adjust their minds and emotions, and psychological intervention can be carried out when necessary; At the same time, they should adapt to natural changes and take care of themselves. They should live normally and work moderately to achieve the purpose of preventing IBS-D.

4. Summary

To sum up, on the basis of modern medicine, traditional Chinese medicine has made an in-depth analysis of the etiology and pathogenesis of IBS-D: IBS-D is based on physical weakness and can be induced by emotional, dietary, exogenous and other factors; In the early stage of the disease, qi stagnation is the main cause, followed by liver disease spreading to the spleen, spleen deficiency and dampness accumulation, and kidney yang deficiency due to long-term illness and kidney. Based on the in-depth understanding of IBS-D, the clinical treatment of IBS-D based on the thought of "syndrome differentiation and treatment" has exact curative effect: Traditional Chinese medicine can improve clinical symptoms, improve body immunity, and improve the quality of life of patients by regulating intestinal microecological balance, reducing visceral hypersensitivity, inhibiting gastrointestinal inflammatory reaction and other effects. The diagnosis and treatment of IBS-D with traditional Chinese medicine has the negative advantages of taking into account the individual differences of patients, low price, simple and easy to operate, rapid effect and so on, which is worthy of clinical promotion.

Traditional Chinese medicine shows unique advantages in the treatment of IBS-D through multi-target, multi-channel and multi-channel synergy. However, its complexity makes it difficult to carry out mechanism research and evidence-based medicine evaluation under the modern medical system: 1) most of the prescriptions for the clinical treatment of IBS-D are compound preparations, and the clinical treatment of IBS-D is often increased or decreased, and its prescription is not unchanged, so whether its efficacy varies from person to person needs further confirmation; 2) There are few studies on the mechanism of traditional Chinese medicine in the treatment of IBS-D and single traditional Chinese medicine in the treatment of IBS-D; 3) Some studies failed to fully

consider the long-term efficacy and recurrence of patients. Based on this, future research needs to further explore the effective ways of single traditional Chinese medicine in the treatment of IBS-D, expand the sample size, extend the research time, and further study the treatment of IBS-D by traditional Chinese medicine from the perspectives of molecular biology, genomics and so on.

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