

Research Progress of Banxia Xiexin Decoction in the Treatment of Chronic Gastritis

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Abstract: Banxia Xiexin decoction is a representative prescription of the acrid-opening and bitter-descending method, widely used for qi movement disorders and mixed cold-heat patterns. Chronic gastritis is a common digestive inflammatory disease with high incidence and recurrence, seriously affecting patients' quality of life. Banxia Xiexin decoction exerts favorable effects on chronic gastritis by inhibiting inflammatory factors, promoting gastric mucosal repair, and regulating intestinal flora. Clinically, it improves gastrointestinal hormone secretion and motility, alleviates inflammation, and reduces recurrence in HP-related gastritis. This paper reviews the basic and clinical research progress of Banxia Xiexin decoction for chronic gastritis to provide reference for clinical treatment.

Keywords: Banxia Xiexin decoction; chronic gastritis; research progress; mechanism of action

1. Introduction

Banxia Xiexin decoction is a classic TCM formula created by Zhang Zhongjing, recorded in *Treatise on Febrile Diseases and Synopsis of the Golden Chamber*. It regulates the spleen and stomach, normalizes qi movement, and exerts anti-inflammatory, antibacterial and immune-modulating effects, indicated for epigastric fullness, nausea, vomiting and borborygmus due to mixed cold and heat and spleen-stomach deficiency. Modern studies show that it also regulates intestinal flora, protects gastric mucosa and inhibits *Helicobacter pylori*, making it effective for chronic gastritis and peptic ulcer. Chronic gastritis is a common chronic gastric mucosal inflammation classified as atrophic and non-atrophic, with the highest prevalence among digestive diseases in China (up to 90% by endoscopy)[1]. Western medicine mainly uses symptomatic treatment with unsatisfactory outcomes and adverse reactions, while TCM emphasizes syndrome differentiation and individualized therapy. Corresponding to TCM "stomachache" and "epigastric fullness", chronic gastritis is mainly caused by exogenous pathogens, improper diet and emotional disorders leading to spleen-stomach weakness, mixed cold and heat, and disordered qi movement. This paper reviews the recent research progress of Banxia Xiexin decoction for chronic gastritis to provide references for clinical application.

2. A brief discussion on Banxia Xiexin decoction and TCM theory of chronic gastritis

In traditional Chinese medicine, chronic gastritis is categorized as epigastric distension and stomachache based on clinical manifestations. It mostly presents as a pattern of root deficiency with branch excess: root deficiency mainly refers to spleen-stomach qi deficiency or yin deficiency, while branch excess includes blood stasis, heat toxin, dampness retention, and qi stagnation, often occurring in combination[2]. Banxia Xiexin decoction was first recorded in *Qi Xiao Liang Fang* by Fang Xian in the Ming Dynasty and later included in *Shang Han Lun* and *Synopsis of the Golden Chamber*. It functions to descend stomach qi and relieve epigastric fullness, indicated for painless epigastric distension and dry vomiting. Its main ingredients are *Pinellia ternata*, *Scutellaria baicalensis*, *Coptis chinensis*, *Ginseng Radix*, *Zingiber officinale*, *Jujubae Fructus*, and roasted *Glycyrrhizae Radix*. *Pinellia* resolves masses and stops vomiting; *Scutellaria* and *Coptis* clear heat and dampness; dried ginger warms the middle and dissipates cold; ginseng and jujube tonify qi and spleen; roasted licorice harmonizes all herbs. The seven herbs work synergistically to regulate qi movement, balance cold and heat, and alleviate related syndromes[3].

Chronic gastritis refers to a variety of chronic gastric mucosal inflammatory lesions caused by different etiologies, and *Helicobacter pylori* infection (HP) is one of the important causes of this disease. HP eradication is an important method for the treatment of chronic gastritis and the prevention of gastric cancer. At present, quadruple therapy is mainly used in clinical western medicine, but it is difficult to achieve the ideal therapeutic effect[4]. In recent years, the advantages of traditional Chinese medicine in the treatment of various chronic diseases have been gradually highlighted. HP-related chronic gastritis belongs to the category of "stomach pipi" and "syndrome of pipi" in traditional Chinese medicine. The initial disease is in qi, qi stagnation and damp block, heat stagnation and phlegm condensation, long illness enters the

luo, dampness causes transformation of internal heat, spleen and stomach deficiency and cold, qi and Yin deficiency [5]. The development of the disease is closely related to the spleen and stomach. The initial disease is abundant, and after a long illness, it turns to deficiency, and the deficiency is accompanied by excess. The treatment is to soothe the liver and relieve depression, strengthen the spleen and stomach, deflate qi, warm and replenish the spleen and kidney, and repair the gastrointestinal mucosa[6]. Chen Qiuping et al. summarized the literature and found that when treating Hp infection with TCM, strengthening the body, clearing heat and removing dampness were the main herbs used[8]. Liu Binbin et al. found that among 244 cases of Hp infection in chronic gastritis, spleen-stomach damp-heat syndrome accounted for the highest proportion, up to 43%, followed by liver-stomach disharmony syndrome and spleen-stomach weakness syndrome [7]. Many doctors believe that the internal cause of HP-associated gastritis is the weakness of spleen and stomach, and the external cause is the feeling of pathogenic toxin, which leads to the obstruction of damp turbidity and the accumulation of toxin due to heat [9]. Zhang Shengsheng believes that diagnosis and treatment should be carried out in stages. In the early stage of Hp gastritis treatment, detoxication of toxic pathogens and unblocking of qi should be carried out, while in the later stage, the deficiency and excess of cold and heat should be adjusted smoothly [10]. According to the syndrome differentiation and treatment, Banxia Xiexin decoction is just in the pathogenesis, and can reconcile cold and heat, strengthen the health and dispel pathogenic factors[11].

3. Study on the mechanism of Banxia Xiexin decoction in the treatment of chronic gastritis

3.1 Inhibition of inflammatory factors

Banxia-xiexin decoction can reduce the damage of gastric mucosa and participate in the occurrence and development of many diseases by inhibiting the related inflammatory factors, such as cell proliferation, differentiation and apoptosis. Inflammation is one of the important factors in the occurrence of chronic gastritis, and blocking the damage of inflammation to mucosa is the key to the treatment of chronic gastritis. TNF signaling pathway, PI3K-Akt signaling pathway and NF- κ B signaling pathway are common inflammation-related pathways in the treatment of chronic gastritis. Banxia Xianxin Decoction can block the development of inflammation through multiple signaling pathways, thereby preventing and reversing atrophy [12]. Sun et al., through network pharmacology, analyzed 152 active components in Banxia Xiexin decoction, and enrichment analysis showed that Banxia Xiexin decoction was involved in the treatment of chronic gastritis, mainly by regulating TNF signaling pathway, PI3K-Akt signaling pathway, NF- κ B signaling pathway and affecting cell apoptosis[13]. Professor Liu Jie's team further verified it on an animal model, and the results suggest that: Banxia-xiexin Decoction can increase the expression of PI3K in the gastric mucosa of rats, decrease the expression of Akt and mTOR, thereby reduce the expression of HIF-1 α , thereby increase the level of P53 and reduce the expression of Bcl-2, and achieve the purpose of treating or even reversing PLGC[14]. However, animal studies on the core drug group "Rhizoma coptidis and Rhizoma pinellia" in Banxia Xiexin Decoction suggest that the main components of Rhizoma coptidis and Rhizoma pinellia can reduce serum inflammatory factor levels, inhibit JAK2/STAT3 pathway and angiogenesis, repair gastric mucosa morphology, thus preventing atrophic gastritis from developing into malignant tumors. And Coptis and Pinellia are commonly used in the treatment of chronic gastritis in clinical medicine. Xiang Yang et al. [15] found through molecular docking that the main active components of Rhizoma coptidis and Pinellia, such as berberine and methylcoptidine, could bind to the core targets of chronic atrophic gastritis, IL-1, IL-6, JAK2 and STAT3. In animal experiments, the active ingredients of Rhizoma coptidis and Pinellia rhizoma were used to interfere with CAG model mice, and the expression of inflammatory cytokines IL-1 and IL-6 in serum was inhibited, and the phosphorylation levels of JAK2 and STAT3 were reduced[16]. Notch signaling pathway is closely related to the occurrence of gastric cancer [17]. In mammals, Notch has four receptor subtypes, among which Notch 1 and Notch 2 subtypes are highly expressed in tumor tissues [19]. Studies have found that Banxia Xiexin decoction may play a therapeutic effect on chronic gastritis by down-regulating Notch1/2 [20]. Wnt/ β -catenin signaling pathway is involved in the occurrence and development of many diseases[18]. Studies have shown that Banxia-Xiexin decoction containing serum can inhibit the activity and clone formation of gastric cancer cells by inhibiting Wnt/ β -catenin signaling pathway, promote oxidative stress and induce cell apoptosis to participate in the treatment of gastric cancer[21]. Therefore, Banxia Xiexin decoction may inhibit the progression of inflammation by participating in multiple signaling pathways.

3.2 Promote the repair of gastric mucosa

Gastric mucosal injury is associated with increased gastric acid secretion, excessive proinflammatory cells, and decreased gastric mucosal blood flow. Vascular endothelial growth factor (VEGF) is a fundamental regulator of angiogenesis and is involved in maintaining mucosal blood flow[22]. Nitric oxide (NO) can affect the secretion of mucus, increase the

blood flow of the gastric mucosa, and protect the gastric mucosa by reducing oxidative stress [23]. Studies have shown that Banxia-Xiexin decoction can increase the expression of gastric mucosal protective factors NO and VEGF, increase t-NOS, reduce i-NOS, and increase the defense ability of gastric mucosa[24]. Banxia Xiexin decoction can protect the gastric mucosa and promote the repair of gastric mucosa by regulating the contents of NO and ET-1[25]. Huang Yanping et al. found that Banxia Xiexin decoction can regulate TGF- β /Smad signaling pathway, reduce HP-induced GES-1 cell damage, promote GES-1 cell proliferation, reduce mucosal damage, and promote mucosal repair [26]. The whole decoction and the drugs with different attributes of cold, warm and tonic in the decoction promote mucosal repair by affecting the expression of gastric mucosal repair factors EGF and VEGF [27].

3.3 Regulate intestinal flora

Banxia-xiexin Decoction has a positive effect on the intestinal microbial diversity of chronic gastritis model rats by changing the relative abundance of different bacteria in the gastrointestinal tract, which may be related to its therapeutic effect. According to the latest research, Banxia Xiexin decoction plays a role in chronic gastritis of spleen deficiency through a variety of mechanisms. Studies have found that Banxia Xiexin decoction can reduce the levels of inflammatory factors in serum, such as interleukin-1 α (IL-1 α), interleukin-10 (IL-10), interleukin-18 (IL-18), interferon- γ (IFN- γ) and tumor necrosis factor (TNF- α), indicating its anti-inflammatory effect [28]. In addition, the blood components of this recipe were identified by UPLC-Q-Orbitrap HRMS technology, and the mechanism of its action in the treatment of chronic gastritis of spleen deficiency was studied by combining network pharmacology. Studies have shown that Banxia Xiexin decoction may achieve the effect of treating chronic gastritis by inhibiting intestinal inflammation, regulating intestinal microorganisms and protecting intestinal barrier. Another study explored the regulation of Banxia Xiexin decoction on intestinal flora and its effect in alleviating DSS-induced diseases[29]. Studies have found that Banxia-Xiexin decoction treatment can improve a variety of symptoms associated with chronic gastritis, including weight change, disease activity index (DAI) score, and colon length. In addition, Banxia Xiexin decoction can reduce gastric mucosal injury and inflammatory response, and restore mucosal barrier function. The diversity of the GI microbiota was assessed by 16S rRNA sequencing, and its treatment was found to increase the balance and diversity of the GI microbiota. Metabolomics studies revealed that Banxia Xiexin decoction may play a role by regulating the metabolism of amino acids, purines and lipids. These findings suggest that Banxia-Xiexin decoction provides a potential therapeutic option for the treatment of chronic gastritis through its anti-inflammatory effects and regulation of intestinal flora. However, further studies are needed to fully understand the mechanism of action and to verify the effect of applying these findings in the clinic.

4. Pharmacological study of Banxia Xiexin decoction

According to modern pharmacological research, Pinellia hydrodecoction and alcohol precipitation can inhibit gastric acid secretion and protect gastric mucosa. At the same time, it has shown an inhibitory effect on Hp activity in vitro experiments [30]. Berberine, the active component of Coptis rhizoma, can inhibit gastric acid secretion and has a certain anti-inflammatory effect[31]. Scutellaria baicalensis decoction has a broad antibacterial spectrum and can treat diseases caused by a variety of pathogens [32]. Dried ginger can stop vomiting and strengthen the stomach. Its extract, dried ginger ether, can resist hydrochloric acid and inhibit stress ulcer[33]. Paeonol, one of the active ingredients of Mounan peel, has anti-inflammatory, analgesic and anti-ulcer effects[34]. Yujin decoction can inhibit gastric acid secretion by increasing plasma somatostatin level and play a protective role in gastric mucosa [35]. The combination of these ingredients repairs injured gastric mucosa, mitigates local inflammation, and exerts anti-Helicobacter pylori (Hp) activity. Integrated traditional Chinese and Western medicine yields synergistic effects: proton pump inhibitors (PPIs) and antibiotics rapidly improve the gastric microenvironment and eradicate Hp to relieve symptoms, while TCM regulates liver–stomach function to address the root cause based on zang-fu theory. As reported by Zhao Liang et al., Banxia Xiexin decoction attenuates mucosal injury from inflammatory mediators by reducing the virulence of CagA. It also inhibits VacA activity to preserve energy supply in gastric epithelial cells, promote mucosal self-repair, and reverse the suppression of B-cell differentiation, thereby restoring immune function and enhancing Hp elimination[36].

5. Clinical study of Banxia Xiexin decoction in the treatment of chronic gastritis

In the treatment of chronic gastritis, Ma Huimiao et al. found that Banxia-Xiexin decoction can improve gastrointestinal hormone secretion, reduce oxidative stress response and inflammatory response in patients with HP-related gastritis, increase the levels of GAS-17 and PGI, and reduce the levels of PGII, IL-6 and TNF- α [37]. Similar studies have found that after the intervention of Banxia Xiexin decoction, the secretion of IL-6 and CRP in patients decreased, and the levels of virulence factors CagA and VacA also decreased [38]. Bai Xuefong et al. found that after Banxia Xiexin decoction combined with

lansoprazole treatment, the levels of inflammatory factors and COX-2 in patients were low, CD3+, CD4+ content and serum PGE2 level were significantly increased, and the therapeutic effect was better than lansoprazole alone[39]. Peng Jing et al. found that Banxia Xiexin decoction could effectively relieve the symptoms of chronic gastritis by taking quadruple therapy as a reference, with a total effective rate of 96.7%[40]. Li Jingjing added and reduced medication based on Banxia Xiexin decoction, and found that it could better relieve symptoms, improve gastrointestinal motility, reduce inflammatory response and reduce recurrence rate[41]. On the basis of conventional western medicine, Sun Hongzhong et al combined with Pinellia-Xiexin decoction, and found that it was superior to the simple western medicine group in improving clinical symptoms, and was conducive to reducing the degree of congestion, edema and erosion on the surface of gastric mucosa and regulating the composition of gastric juice [42]. Xie Jingqiu and Liu Qian et al. found that compared with conventional western medicine, Banxia Xiexin decoction can more effectively improve the immune function of patients with chronic atrophic gastritis (CAG), relieve clinical symptoms, reduce inflammatory factor levels, improve Hp clearance rate, reduce gastric mucosal atrophy and improve gastric function [43]. In addition, a number of studies have shown that Banxia Xiexin decoction combined with Lianpu decoction, Chaihu Shugan powder, Xiangsha Pingwei powder, or combined with acupuncture, moxibustion, etc., has a good effect on chronic gastritis, and its clinical applicability is wide.

6. Summary and Prospect

Zhang Zhongjing Banxia-Xiexin decoction is used to treat the syndrome of constipation caused by deficiency of the central nervous system and the interaction of cold and heat. It works by regulating the qi mechanism of the spleen and stomach, and is suitable for digestive system diseases caused by the weakness of the spleen and stomach and the interaction of cold and heat. This method reflects the holistic thinking of traditional Chinese medicine and the harmony of Yin and Yang. It can be used for chronic gastritis and other gastrointestinal diseases by syndrome differentiation, and the dosage of Pinellia should be strictly controlled. Modern studies have shown that the mechanism of this recipe in the treatment of chronic gastritis involves inhibition of inflammation and repair of gastric mucosa, but there are obvious shortcomings: the quality of clinical research is low, the basic research is lack, the influencing factors of efficacy are unknown, and the pharmacological research on various mechanisms of action is not comprehensive.

In conclusion, Banxia Xiexin decoction has the potential for modern application, but high-quality research is needed to make up for the deficiency and clarify its mechanism of action and clinical value.

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