

Research Trends and Progress of Xiaobanxia Decoction in the Treatment of Chemotherapy - induced Nausea and Vomiting

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ABSTRACT

Xiaobanxia Decoction, derived from *Synopsis of the Golden Chamber* written by Zhang Zhongjing in the Eastern Han Dynasty, is a fundamental prescription in traditional Chinese medicine for warming and resolving phlegm-fluid retention, as well as harmonizing the stomach and descending adverse qi. Chemotherapy-induced nausea and vomiting (CINV) is one of the common and severe adverse reactions in cancer patients after chemotherapy, which can reduce patients' quality of life and adversely affect their compliance during treatment. As a classic prescription in traditional Chinese medicine, Xiaobanxia Decoction shows unique application advantages in the treatment of CINV. This article summarizes the research results from databases such as CNKI and PubMed, and reviews the clinical application, mechanism of action and research prospects of Xiaobanxia Decoction in the treatment of CINV.

KEYWORDS

Xiaobanxia decoction; Chemotherapy-induced nausea and vomiting; Cancer; Traditional Chinese medicine

1 Introduction

Globally, cancer has become a major disease that seriously endangers human health. Its incidence and mortality rates continue to rise, and the affected population is also showing a younger trend, which has imposed heavy economic pressure on the World Health Organization and the medical and health systems of various countries ^[1]. As a key treatment method for various malignant tumors, chemotherapy drugs, while inhibiting or killing cancer cells, their characteristic of "indiscriminate attack" can also cause a series of adverse reactions, which has become an unavoidable problem in clinical application. Notably, chemotherapy-induced nausea and vomiting seriously reduce patients' quality of life, leading to nutritional imbalance, dehydration, etc., and also increase patients' psychological burden and treatment compliance ^[2]. Western medicine mainly relies on 5-hydroxytryptamine receptor antagonists, dopamine receptor antagonists, etc. for the treatment of CINV, but there are problems such as limited efficacy and adverse reactions ^[3]. Traditional Chinese medicine (TCM), which has been passed down for more than 2,000 years, has a long history and rich experience in China. It is quite crucial to analyze the efficacy of traditional Chinese medicine in the prevention and treatment of CINV. As a classical prescription, Xiaobanxia Decoction has shown good therapeutic effects on CINV in both clinical practice and experimental research ^[4].

2 Basic overview of Xiaobanxia decoction

Xiaobanxia Decoction is a classic prescription from *Synopsis of the Golden Chamber* written by Zhang Zhongjing, a medical scientist in the Eastern Han Dynasty. Its composition is quite simple, containing only two core medicinal materials: Banxia (*Pinellia ternata*) and Shengjiang (ginger) ^[5]. Li Zhongzi, a physician in the Ming Dynasty, recorded in *Leigong Paozhi Yaoxing Jie* (Leigong's Explanation of Processed Medicinal Properties): "Banxia tastes pungent and mild, and can lower qi to stop vomiting..." ^[6]. Clinically, this medicine is a key drug for treating vomiting caused by phlegm-fluid retention. Shengjiang, with a pungent taste, can stop vomiting, relieve diarrhea, moderate Banxia, harmonize various medicines, and inhibit the toxicity of Banxia. It has always been renowned as the "supreme medicine for vomiting" ^[7]. The combination of these two medicines exerts the effects of resolving phlegm and dispersing fluid retention, harmonizing the stomach, and descending adverse qi together. It is a fundamental prescription for treating vomiting due to phlegm-fluid retention, and is mostly used in cases such as gastritis ^[8], inner ear vertigo ^[9], and gastrointestinal reactions after chemotherapy ^[10] that are attributed to phlegm-fluid retention vomiting. There are relevant records in *Beiji Qianjin Yaofang* (Essential Prescriptions for Emergencies) compiled by Sun Simiao, a famous medical scientist in the Tang Dynasty, stating that Xiaobanxia plus Fuling (*poria cocos*) Decoction can be used to treat various vomiting and hiccup symptoms, especially suitable for cases accompanied by symptoms such as stuffiness and hardness in epigastrium, retention of water-phlegm in the chest and diaphragm, dizziness, and palpitations. The *Taiping Huimin Heji Ju Fang* (Formulas of the Peaceful Benevolent Dispensary), an official medical book compiled in the Song Dynasty, also lists this prescription as a fundamental formula for treating vomiting, which is widely used in clinical modifications for various types of vomiting syndromes. It can be seen that there has been evidence for Xiaobanxia Decoction in treating vomiting from ancient times

to the present, providing a solid theoretical basis for the treatment of CINV in modern medicine.

3 Clinical application of Xiaobanxia decoction in the treatment of chemotherapy-induced nausea and vomiting

3.1 Observation on clinical efficacy

Xiaobanxia Decoction can be regarded as the ancestor prescription for treating various types of vomiting in clinical practice, including neurological vomiting, pregnancy vomiting, vomiting due to acute myocardial infarction, and post-chemotherapy vomiting ^[11]. In a clinical study ^[12], researchers selected 100 gastric cancer patients with nausea and vomiting after chemotherapy, and randomly divided them into a control group and an observation group, with 50 cases in each group. Both groups received intravenous drip of tropisetron hydrochloride to prevent vomiting before the start of chemotherapy. On the basis of this conventional intervention, the observation group was additionally given oral Xiaobanxia Decoction. The results showed that the effective rate of the observation group in controlling nausea and vomiting symptoms was higher than that of the control group. Moreover, studies have shown that using a rat pica model induced by cisplatin, Xiaobanxia Decoction can inhibit ferroptosis, such as iron deposition, mitochondrial abnormalities, and oxidative stress. The results of HE staining and ELISA experiments showed that after intervention with Xiaobanxia Decoction, the inflammatory damage in the gastric antrum and ileum tissues can be effectively reduced, and the levels of inflammatory factors such as HMGB1, IL-1 β and TNF- α can be decreased. The core mechanism of its action mainly relies on activating the Nrf2/SLC7A11/GPX4 signaling pathway, inhibiting the occurrence of ferroptosis, thereby alleviating CINV ^[13].

3.2 Modifications and variations in clinical application

In practical clinical application, Xiaobanxia Decoction is mainly used to treat various vomiting disorders. Vomiting, as a symptom, can be seen in the clinical manifestations of many different diseases, but its underlying pathological mechanism has commonalities, which are all caused by the dysfunction of the stomach, abnormal harmony and descending functions, leading to the disorder and upward rush of stomach qi. Based on this key pathogenesis, in clinical practice, by flexibly modifying and applying Xiaobanxia Decoction and taking "harmonizing the stomach to descend adverse qi, drying dampness and resolving phlegm" as the therapeutic principle to intervene in vomiting symptoms caused by various etiologies, good therapeutic effects can generally be achieved. In the process of clinical diagnosis and treatment, Xiaobanxia plus Fuling Decoction is widely used to treat symptoms such as dizziness and palpitations, stuffiness and fullness, and viral myocarditis caused by phlegm-fluid retention vomiting ^[14]. Qi Baoyin et al ^[15] selected 100 patients with hyperemesis gravidarum admitted from June 2013 to January 2015 as the research objects, divided them into a control group treated with western medicine and an observation group treated with Xiaobanxia Jupi Zhuru Decoction (decoction of Pinellia Tuber, Fresh Ginger, Tangerine Peel and Bamboo Shavings). The results showed that Xiaobanxia Jupi Zhuru Decoction had a good inhibitory effect on hyperemesis gravidarum, and the difference was statistically significant. Shengjiang Banxia Decoction uses one liter of fresh ginger juice ^[16], with the dosage of Banxia reduced by half. It is clinically used to treat patients with severe vomiting caused by cold fluid retention struggling and binding, and qi movement obstruction. This way of treating based on syndrome differentiation and modifying according to symptoms can make Xiaobanxia Decoction more effectively adapt to the conditions of different patients and improve the therapeutic effect.

4 Mechanism of action of Xiaobanxia decoction in the treatment of chemotherapy-induced nausea and vomiting

4.1 Regulation of neurotransmitters

Chemotherapy-induced vomiting is closely related to a variety of neurotransmitters, among which 5-hydroxytryptamine (5-HT) is one of the key factors. Relevant studies have shown that Xiaobanxia Decoction can inhibit the overexpression of tryptophan hydroxylase 1 (TPH1) in the ileum, thereby reducing the synthesis of 5-HT, and alleviating cisplatin-induced vomiting through anti-inflammatory pathways ^[17]. The experimental results of researchers such as Yu Gongchang ^[18] also showed that Xiaobanxia Decoction can significantly reduce the levels of 5-HT in the serum, ileum and medulla oblongata tissues of rats receiving chemotherapy. It can inhibit the activity of TPH1 in the ileum tissue and tryptophan hydroxylase 2 in the medulla oblongata, and at the same time promote the metabolism of 5-HT, thus playing a role in the prevention and treatment of acute chemotherapy-induced nausea and vomiting. Xiaobanxia Decoction may affect the vomiting reflex arc by regulating other neurotransmitter systems such as dopamine, exerting a

synergistic antiemetic effect, but its specific mechanism remains to be studied.

4.2 Protection of gastrointestinal mucosa and regulation of gastrointestinal motility

Chemotherapeutic drugs can cause damage to the gastrointestinal mucosa, leading to gastrointestinal dysfunction and ultimately resulting in nausea and vomiting ^[19]. Studies by Zhang Qilong and others ^[20] have shown that Xiaobanxia Decoction can promote the secretion of mucin by mucosal goblet cells, facilitate the repair of gastrointestinal mucosa, enhance the mucosal barrier function, and reduce the stimulation of harmful substances to the gastrointestinal tract. Researchers such as Liu Wanqing ^[21] found through experiments that Xiaobanxia Decoction can inhibit the spontaneous contraction of isolated ileum in normal rats, reducing the tension and amplitude during contraction, which has a positive effect on the prevention and treatment of CINV. In terms of regulating gastrointestinal motility, Xiaobanxia Decoction can excite the smooth muscles of the isolated gastric fundus and antrum in rabbits ^[22], inhibit the contraction of duodenal smooth muscles, and has an antagonistic effect on the forced spasm of gastrointestinal smooth muscles caused by acetylcholine chloride. It can alleviate chemotherapy-induced vomiting by regulating the rhythm of gastrointestinal peristalsis and relieving gastrointestinal spasm.

4.3 Anti-inflammatory effects

During the course of chemotherapy, inflammatory reactions can be induced in the body. The release of inflammatory mediators can stimulate the gastrointestinal tract and the vomiting center. Inflammatory responses in the gastrointestinal tract are one of the main causes of chemotherapy-induced nausea and vomiting ^[23]. Chemotherapeutic drugs are cytotoxic; while effectively killing tumor cells, they often cause collateral damage to normal tissue cells of the body. Such damage may trigger an inflammatory cascade reaction in the body ^[24]. These inflammatory mediators can act on the gastrointestinal tract through the blood circulation, stimulate the nerve endings under the gastrointestinal mucosa, cause spasm and peristalsis disorders of gastrointestinal smooth muscles, damage the integrity of the gastrointestinal mucosal structure, and lead to gastrointestinal dysfunction and imbalance. As a classic formula in traditional Chinese medicine, modern pharmacological studies have shown that both ginger and pinellia, the two herbs in Xiaobanxia Decoction, have antioxidant effects and exhibit unique anti-inflammatory properties ^[25]. Multiple experimental studies have confirmed that after intervention with Xiaobanxia Decoction, RNA-seq results indicated that it can reduce the mRNA level of F4/80, a major marker of macrophages. By inhibiting the body's inflammatory response, it alleviates chemotherapy-induced nausea and vomiting ^[26]. Meanwhile, animal experiment results showed that Xiaobanxia Decoction may inhibit the activation of the nuclear factor- κ B signaling pathway in the gastric antrum and ileum tissues ^[27], reduce the gene transcription and protein synthesis of inflammatory factors, alleviate the damage of inflammatory reactions to the gastrointestinal tract, protect the integrity of the gastrointestinal mucosa, maintain the normal peristaltic rhythm of the gastrointestinal tract, and relieve CINV symptoms.

5 Conclusion

As a classic traditional Chinese medicine prescription, Xiaobanxia Decoction has shown good clinical efficacy and potential mechanism of action in the treatment of chemotherapy-induced nausea and vomiting, demonstrating the unique value of traditional Chinese medicine in cancer supportive care and providing a paradigm for the integration of traditional Chinese medicine into the modern comprehensive cancer treatment system. The core of cancer supportive care is to improve the quality of life and prolong the survival time, and the advantage of traditional Chinese medicine lies in achieving the effect of eliminating pathogenic factors without damaging healthy qi through overall regulation. The combined application of traditional Chinese medicine and Western medicine, with their respective unique advantages, has achieved a synergistic effect in the clinical treatment of many diseases. Although there are certain limitations in the current research on Xiaobanxia Decoction, with the continuous deepening of research and the development of technology, Xiaobanxia Decoction is expected to play a greater role in the field of CINV prevention and treatment, bringing more benefits to the majority of cancer patients.

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