

Research Status of Traditional Chinese Medicine in the Treatment of Gastric Precancerous Lesions

Yuxin Jing¹ & Jianping Hui²

¹ Shaanxi University of Chinese Medicine, China

² Affiliated Hospital of Shaanxi University of Chinese Medicine, China

Correspondence: Jianping Hui, Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, 712000, China. E-mail: jbtm369at163.com

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Abstract

Gastric cancer is an extremely common malignant tumour in China, with high morbidity and mortality rates, posing a serious threat to the life and health of the people. Pre-cancerous gastric lesions are considered to be an important stage in the development of gastric cancer, so timely monitoring of pre-cancerous gastric lesions and effective treatment are the key links in the prevention and control of gastric cancer. Traditional Chinese medicine has been widely used in the treatment of gastric precancerous lesions and has shown its unique advantages. This article systematically describes the etiology and mechanism of this disease and the current status of clinical treatment research, with the aim of providing valuable references for the formulation of clinical treatment plans and the development of related medicines.

Keywords: gastric precancerous lesions, traditional chinese medicine treatment, current status of research

1. Introduction

Gastric cancer (GC) is the fifth most common malignant tumour in the world and the fourth most common cause of cancer death[1]. It is particularly alarming that the incidence rate of GC in China, as the hardest hit area, accounts for 40% of the global total. In China, the incidence rate of gastric cancer is the fourth highest among malignant tumours, and the mortality rate is even the third highest[2], posing an extremely serious threat to human life and health. Current studies mostly suggest that the pathogenesis of gastric cancer follows the Correa model[3]: Normal gastric mucosa→chronic non-atrophic gastritis→chronic atrophic gastritis (CAG)→intestinal epithelial hyperplasia (IM) and/or dysplasia→gastric cancer. Currently, gastric precancerous lesions in a broad sense include chronic atrophic gastritis (CAG), intestinal epithelial hyperplasia (IM), and heterotopic hyperplasia (Dys). PLGC is an extremely critical and high-risk stage in the development of gastric cancer. Therefore, early intervention and active treatment is the key to preventing the development of gastric cancer. The development of PLGC is closely related to a variety of factors, such as an unbalanced diet, H. pylori infection, and genetic factors. In clinical treatment, the main strategies are to eliminate the causes of the disease, reduce the symptoms and improve the inflammatory response of the gastric mucosa. However, it is often difficult to achieve the desired therapeutic effect by relying only on western medicine, and a unified treatment protocol for PLGC has not yet been developed. Numerous studies have shown[4] that TCM can effectively intervene in PLGC through various mechanisms, including regulation of cell proliferation and apoptosis, modulation of inflammation, inhibition of angiogenesis, inhibition of epithelial-mesenchymal transition, inhibition of glycolysis, anti-oxidative stress, anti-Helicobacter pylori infection, adjustment of autophagy levels, and regulation of the balance of the intestinal bacterial flora, and so on.

2. Chinese Medicine Etiology and Pathogenesis

Pre-cancerous gastric lesion is a modern medical term, but there is no clear record of it in the traditional medical literature of China. According to its clinical manifestations, such as distension and discomfort, pain, loss of appetite (nausea) and noisy symptoms in the stomach and epigastric region under the heart, traditional medicine classifies it into the categories of ‘plumpness’, ‘pain in the stomach and epigastric region’, and ‘vomiting acid’ and so on. Traditional Chinese medicine classifies it as ‘plumpness’, ‘stomach and epigastric pain’, ‘acid vomiting’ and other TCM symptoms.

Most scholars believe that the etiology of PLGC is closely related to dietary disorders, emotional disorders, internal injuries due to fatigue, feeling of foreign poisonous evils, or improper use of medication, which lead to a series of changes in the accumulation of food, stagnation of qi, blood stasis, dampness-heat, phlegm, and evil poisons in the internal congestion of phlegm, etc. The pathology of PLGC is blamed on the stomach, and it has a close relationship with the liver and spleen organs[5], and is manifested as a syndrome of deficiency of this standard, and a syndrome of mixed deficiencies and realities. At present, this disease is divided into five types: liver and stomach disharmony, spleen and stomach dampness and heat, spleen and stomach weakness, stomach and yin insufficiency, and gastric stasis and obstruction[6], and the key to its treatment is to regulate the spleen and stomach in the middle jiao and to combine with the application of the method of transforming dampness, dispelling phlegm, activating blood, and detoxifying poison.

3. Clinical Treatment

3.1 Traditional Chinese Medicine (TCM) Decoction

3.1.1 Treatment with the addition and subtraction of meridian formulae

Liu Minghe[7] et al. believed that this disease is an evidence of the symptoms of the underlying deficiency, with the weakness of the spleen and stomach as the main symptom, and the depression of liver qi as the symptom, therefore, it is appropriate to treat patients with CAG with liver-depression and spleen-deficiency type by dredging the liver and resolving the depression and strengthening the spleen and the stomach, and the formula is Xiao Chaihu Decoction Combined with Xiangsha Six Junzi Decoction. The control group received conventional Western medical treatment, while the observation group took Xiao Chaihu Decoction with Xiangsha Liu Junzi Decoction (Chaihu, Fabanxia, Muxiang, Scutellaria baicalensis, Sha Ren (later), Codonopsis pilosulae, Chen Pi, Poria, Ginger, Atractylodes macrocephala, Radix et Rhizoma Glycyrrhizae, and Jujubae) on top of the treatment in the control group. After 1 month of treatment, the TCM symptom scores such as nausea, acid reflux, fatigue and gastric mucosal pathological scores of the observation group were better than those of the control group ($P < 0.05$). The therapeutic effect of the observation group was remarkable, and its total effective rate was as high as 93.59%, which was significantly different from that of the control group of 82.05% ($P < 0.05$).

Zhou Jingyi[8] believes that the weakness of spleen and stomach is an important influencing factor that leads to gastric mucosal atrophy and ultimately causes intestinalisation, which is also related to heterotrophic hyperplasia to a certain extent, and Shengyang Yi Gastric Decoction is closely related to the symptoms of spleen and gastric weakness, so this formula was chosen for treatment. Comparing the main symptoms and pathological scores of PLGC between the two groups, the observation group was treated with Shengyang Yiqi Decoction (Banxia, Paeonia lactiflora, Radix et Rhizoma Glycyrrhizae, Rhizoma Atractylodis Macrocephalae, Poria cocos, Fenghuang, Qianghou, Ginger, Atractylodis Macrocephalae, Bupleurum officinale, Tangerine Pippi, Red Ginseng, Jujubae, Copper Cordyceps sinensis), and the control group was treated with western medicines. At the end of the two-week treatment, the overall effective rate of the observation group was as high as 95%, which was significantly higher than that of the control group (72.5%), and the difference between the two groups was statistically significant ($P < 0.05$).

Lv Anding[9] et al. included 160 PLGC patients, of which 80 cases in the control group were treated with quadruple therapy (colloidal bismuth pectin, omeprazole, amoxicillin, metronidazole), and 80 cases in the observation group were treated with the combination of quadruple therapy by using the Banxia Xiexin Decoction with Flavouring Decoction (Banxia, Baicalcium Scutellariae, Dried Ginger, Radix Panax Ginseng, Rhizoma Ziziphiella, Fructus Jujubae, Glycyrrhiza glabrae, Baicalcium Scutellariae and Radix Panax Ginseng for heat more than cold and less than cold; and Radix Panax Ginseng for cold more than heat). After a two-week treatment, the overall effective rate of the observation group reached 95%, while that of the control group was 85%, and the difference in efficacy between the two groups was statistically significant ($P < 0.05$). The study showed that the combination of Banxia Xiexin Decoction and the four-combination therapy can significantly improve the clinical symptoms of PLGC patients, effectively regulate the secretion of gastrin and pepsin, promote the repair process of the damaged gastric mucosa, help to reverse the pathological changes of gastritis, and accelerate the process of *Helicobacter pylori* (Hp) conversion.

Hong Wuhan[10] et al. included 118 patients with chronic atrophic gastritis with intestinal epithelial hyperplasia, in which the observation group was treated with oral astragalus Jianzhong Decoction (astragalus, caramel, peony, cinnamon sticks, ginger, jujube, and roasted licorice), and gastric fuchun tablets were treated as the control group. The study showed that compared with the control group, the clinical therapeutic effect of the observation group was significantly better, and the levels of tumour necrosis factor and serum inflammatory factor were significantly reduced, and the degree of improvement of these factors was even more significant after treatment. At the same

time, the TCM symptom score of the observation group was significantly lower. Comparison between the two groups showed that the difference was statistically significant ($P < 0.05$).

3.1.2 Treatment by Adding and Subtracting Experimental Prescriptions

Professor Wei Muxin[11] believes that the pathogenesis of this disease is weakness of the spleen and stomach, phlegm stasis and blood obstruction, and in the clinical treatment of this disease, resolving phlegm-dampness and eliminating blood stasis are taken as the core strategy, supplemented by strengthening the spleen and stomach and tonifying the positive deficiencies, therefore, a formula of resolving phlegm and eliminating blood stasis was proposed to treat this disease. In the control group, conventional western medicine was used for oral treatment, while the treatment group was given the formula of adding and subtracting formula for resolving phlegm and eliminating blood stasis (Chen Pi, Faganxia, fried Jin Jin, Curcuma longa, Poria, Salviae Miltiorrhizae, Xianhe Cao, Bai Hua Snake Tongue Cao, Semen Aromaticus, fried Semen Coicis Seed, and Vine Pear Root). After 6 months of treatment, the improvement of clinical symptoms and the reduction of pathological grading of the treatment group were better than that of the control group, and the total clinical effective rate of the treatment group was as high as 92.68%, which was significantly higher than that of the control group (73.17%), and the difference between the two groups was statistically significant ($P < 0.05$).

Professor Chen Weijian[12] summarised clinical experience and believed that PLGC patients had more spleen deficiency and phlegm-dampness evidence, so he created his own empirical formula of Three Herbs Stomach Regulating Decoction, with the basic formula: tai zi ginseng, gluten-fried *Atractylodes macrocephala*, Poria cocos, *Xianhe cuspidata*, dandelion, white-flower snakeweed, dan shen, roasted liquorice, curcuma longa. After 6 months of treatment, the clinical symptoms of the patients were significantly improved, the number of patients with pathology suggesting severe CAG and the number of patients with moderate and severe IM decreased, and the number of patients with Dys cleared, and the differences were all statistically significant ($P < 0.05$).

Dai Minglong[13] believed that gastrointestinal stasis and toxicity is the basic pathogenesis of PLGC, and clinically it should be balanced between deficiency and reality, with the use of both ventilation and tonicity, and the treatment should be based on the principles of strengthening the spleen, opening the channels, and detoxification, and he formulated a formula to remove stasis, detoxify and clear toxins and clear the channels, with the addition of subtractions, for the treatment of PLGC. Addition and subtraction: for blood stasis, add Yanhuisuo, Wu Lingyi, Pu Huang; for Qi stagnation, add Citrus aurantium, Fructus Fructus; for Yin deficiency, add Fructus schisandrae chinensis, *Ophiopogon flexuosus*, Lily of the Valley; for blood deficiency, add Radix Rehmanniae Praeparata, Cornu Cervi Pantotrichum, Fructus Lycii. The control group was treated with Gastric Fuchun tablets, and the observation group was treated with the formula of removing blood stasis, detoxifying and clearing collaterals on the basis of Gastric Fuchun tablets. After 12 weeks of treatment, the total effective rate of the observation group reached 92.98%, while the total effective rate of the control group was 73.68%. Comparing the data of these two groups, the difference was statistically significant ($P < 0.05$).

Professor Wang Ruiping[14] believed that spleen deficiency is the root of the disease, and phlegm, blood stasis and toxicity are the key links in the pathogenesis of the disease, so the treatment should be to support the positive energy, and eliminate phlegm by removing blood stasis, and formulated a formula to strengthen the spleen and remove blood stasis for the treatment of PLGC, which consisted of the following ingredients: tai zi ginseng, fried *atractylodes macrocephala*, astragalus, poria, Job's tear grains, Chonglou, white-flowered snakeroot, curcuma longa, and salvia miltiorrhiza. The control group was treated with conventional Western medicine, and the treatment group added the formula of strengthening the spleen and eliminating blood stasis on the basis of the control group. After 12 weeks of treatment, the total effective rate of the treatment group (93.34%) was higher than that of the control group (73.34%) ($P < 0.05$).

According to Professor Ma Guitong[15], CAG is an evidence of deficiency, and the key to its pathogenesis lies in the weakness of the spleen and stomach, and the interconnection of stasis and heat, so the treatment should be based on strengthening the spleen and benefiting the qi, combined with the methods of activating blood circulation and removing blood stasis, and clearing heat and removing toxins, and the self-proposed Gastric Kei Drink was used to treat the evidence of spleen and stomach weakness in CAG. The treatment group was given Stomach Kei Drink (Radix Astragali, Radix et Rhizoma Ginseng, Rhizoma Curcuma longa, Radix Angelicae Sinensis, Radix et Rhizoma Dandelionis, Citrus aurantium dulcis, Rhizoma Augustus), and the control group was given Mosapride Tablets + Selenium Yeast Capsules for oral intake. After 6 months of treatment, the treatment group was superior to the control group in terms of improvement of clinical symptoms and reduction of the degree of pathological atrophy of gastric mucosa.

3.2 Proprietary Chinese Medicine Treatment

Proprietary Chinese medicines (pCms) and Chinese herbal tonics (CHTs) are both important forms of treatment in the field of traditional Chinese medicine (TCM), each of which has its own characteristics and demonstrates its respective advantages in different aspects. Proprietary Chinese medicines (pCms) are pills, tablets, capsules, oral liquids, granules, etc. made from Chinese herbal medicines under the guidance of Chinese medicine theories and processed in accordance with prescribed prescriptions and preparation techniques. Proprietary Chinese medicine formulations used in the treatment of PLGC usually have the efficacy of strengthening the spleen and benefiting qi, promoting qi and blood circulation, and expelling phlegm and detoxifying toxins, and have the advantages of being convenient to store, safe and effective, and conducive to prolonged consumption by patients with chronic diseases, and are widely used in the treatment of PLGC.

Zhang Hongxing[16] et al. observed that Gastro Fuchun tablets had a significant improvement on the general state and macroscopic manifestations of rats, and partially reversed their pathological state, which in turn reduced the incidence of PLGC, through the control experiments of 30 rats with gastric precancerous lesion model respectively. This further verified the mechanism of action of Gastric Fuchun Tablets, which regulates the apoptotic process of gastric epithelial cells and exerts anti-tumour proliferation effects by inhibiting the abnormal activation of PI3K/Akt signalling pathway, thus effectively blocking the disease progression of PLGC.

Zhu Xiaojing[17] et al. used morodan to treat 104 patients with chronic atrophic gastritis with intestinal metaplasia, and the rates of gastric mucosal atrophy and IM reversal were 47.1% and 51.0%, respectively, with an overall effective rate of 65.4%; the rates of reversal of OLGA and OLGIM staging from a high staging (Stage III~IV) to a low staging (Stage 0~II) were 49.3% and 52.4%, respectively; and the rates of OLGA, OLGIM Stage III~IV patients had a significantly higher reversal rate than Stage I~II patients (both $P < 0.01$).

A study involving a multicentre, randomised controlled study revealed[18] that the combination of Yujin granules and folic acid can more effectively improve gastric mucosal atrophy in patients with chronic atrophic gastritis (CAG) and chronic atrophic gastritis with intestinal epithelial chemosis or heterotelic hyperplasia (PLGC) and to some extent reverse their heterotelic proliferation, as compared to treatment with folic acid only.

Ye Chunrong[19] and others used the combination of Yigongning capsule and Rebapatide tablets in the treatment of chronic atrophic gastritis (CAG), which was able to effectively improve the clinical symptoms and endoscopic gastric mucosal manifestations of the patients, and further slow down or even reverse the pathological development of the gastric mucosal tissues, so as to block the transformation of CAG from inflammation to cancer to a certain extent. This will somehow block the transformation of CAG from 'inflammation' to 'cancer'.

3.3 Traditional Chinese Medicine External Treatment

In addition to oral administration of Chinese medicines, acupuncture, acupoints paste, auricular pressure beans and other Chinese medicine external treatment characteristics of the therapy, through the stimulation of specific points in the body, regulating the operation of qi and blood, to achieve the dredging of meridians and collaterals, support the positive and eliminate the evil, and play a total of harmonisation of the spleen and the stomach. These external Chinese medicine treatments not only have significant therapeutic effects, but also have small adverse reactions and good long-term effects, which greatly improves patients' compliance and quality of life.

Jin Jiayan[20] and others revealed that the combined use of acupuncture and moxibustion techniques to stimulate the foot-sanli acupoint region in CAG rats significantly elevated the expression levels of CK18, CK19, and calcitonin gene-related peptide (CGRP) in this region, and increased the number of mast cells. In addition, this combination therapy can effectively promote the functional recovery of Merkel cells and regulate neuropeptides to normal levels.

In a study by Wang Fang[21] et al, 98 patients with chronic atrophic gastritis (CAG) of the spleen and stomach deficiency and cold type were selected as a sample, and a control group was established. In the control group, the patients received a 4-week course of treatment with millifire acupuncture combined with the Yuanluo Tongjing method, with specific acupuncture points being Gongsun and Chongyang. After this course of treatment, the inflammatory condition of the gastric mucosa of the patients was significantly improved. Meanwhile, the serum test results showed that the levels of gastric actin and gastrin were significantly reduced, while the levels of growth inhibitor increased.

Guo Yi[22] et al. treated 120 CAG patients with acupoint submergence at the acupoints of the foot-sanli, the middle epigastric region, and the stomach yu. By comparing the main symptoms and gastroscopic gastric mucosal pathology scores of the patients before and after treatment, it was concluded that acupoint burrowing therapy has

a positive effect on improving the symptoms and gastric mucosal pathology of patients with chronic atrophic gastritis and is safe.

Sun Xiliang[23] and others used stomach pain relief particles combined with auricular pressure beans to treat 90 patients with Hp-infected chronic atrophic gastritis, after treatment, the patients' points of clinical symptoms such as gastrointestinal and epigastric pain, coeliac distension, nausea and vomiting, belching and other clinical symptoms were significantly reduced, and gastric mucosa of gastric mucous membrane under gastroscopy were improved, which was a very significant clinical effect.

Ma Gang[24] et al. used Astragalus Jianzhong Tang combined with acupoints paste to treat 45 patients with CAG, after treatment, the patients' points of gastric pain, nausea, malaise and other symptoms were significantly reduced, and at the same time, the level of PGI was higher than the control group, and the level of PGII was lower than that of the control group, suggesting that the combined treatment has the effect of regulating the secretion of pepsinogen.

4. Summary and Outlook

In long-term medical practice, TCM has demonstrated unique advantages in the treatment of gastric precancerous lesions with its unique theoretical system, rich therapeutic experience and remarkable efficacy. Through the summary of extensive clinical practice and animal studies, we found that TCM in the treatment of PLGC can not only effectively relieve the symptoms of patients and significantly improve their quality of life, but also, more importantly, it can reverse the pathological process of gastric precancerous lesions to a certain extent, thus effectively reducing the incidence of gastric cancer. Chinese medicine treats precancerous gastric lesions in various ways, covering herbal tonics, acupuncture therapy, acupoint plasters and other means. Each of these methods has its own characteristics and is capable of identifying and treating patients according to their different conditions and physique. Evidence-based treatment greatly improves the accuracy and effectiveness of treatment, bringing better treatment results to patients. Looking into the future, TCM still has a broad development prospect and great potential in the field of treatment of gastric precancerous lesions. At the same time, there are some limitations and shortcomings of TCM in the treatment of PLGC. In particular, there is a lack of high-quality, large-sample, multicentre clinical trials to further verify its efficacy and safety in relevant clinical observations and animal experiments. In addition, the long treatment period of gastric precancerous lesions has led to a certain degree of impact on the continuity and reliability of follow-up studies. To compensate for these shortcomings, we need to further increase the sample size, extend the follow-up period, and standardise the efficacy assessment criteria. At the same time, we also need to strengthen interdisciplinary co-operation and introduce modern scientific and technological means, such as bioinformatics and molecular diagnostic techniques, in order to reveal in greater depth the mechanism of action of TCM in the treatment of gastric precancerous lesions. The implementation of these measures will help to further improve the efficacy of TCM in the treatment of gastric precancerous lesions, and provide valuable references for the formulation of clinical treatment protocols and the research and development of related medicines.

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