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Clinical Study on Modified Liujunzi Decoction in the Treatment of Precancerous Lesions of Gastric Cancer with Spleen-Stomach Weakness Syndrome

Zheng Xia, Feng Zhang, Yu Wang, Ying Zhang, Liyun Ling, Minchao Ye,Yingke Lu

Department of Gastroenterology, Shu Guang Hospital Affiliated to Shanghai University of Traditional Chinese Medicine Songjiang Branch, Songjiang District, Shanghai 201699, China

Abstract

Objective: To observe the clinical efficacy of Modified Liujunzi Decoction in the treatment of precancerous lesions of gastric cancer (PLGC) with spleen-stomach weakness syndrome, as well as its impact on gastric mucosal manifestations under gastroscopy and pathological changes. *Methods*: Sixty patients with PLGC with spleen-stomach weakness syndrome were selected and randomly divided into a treatment group and a control group, with 30 patients in each group. The treatment group received orally administered Modified Liujunzi Decoction, while the control group was treated with folic acid tablets and Teprenone Capsules. After 12 weeks of intervention, the effects on clinical symptoms of PLGC, gastric mucosal manifestations under gastroscopy, and pathological changes were observed. *Results*: According to the comprehensive assessment of the efficacy of major traditional Chinese medicine symptoms, the total effective rate of symptom score improvement in the treatment group was 83.3%, which was significantly higher than that of the control group. The total effective rate of gastroscopic efficacy was 70.0%. The treatment group was superior to the control group in terms of improvement in atrophy and intestinal metaplasia scores for pathological changes ($P < 0.05$). *Conclusion*: Modified Liujunzi Decoction exhibits significant efficacy in the treatment of PLGC with spleen-stomach weakness syndrome, markedly improving clinical symptoms and pathological conditions.

Keywords

Modified Liujunzi Decoction
Spleen-stomach weakness
Precancerous lesions of gastric cancer
Clinical study

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1. Introduction

Gastric cancer is one of the malignant tumors that seriously threaten human health worldwide, with high incidence and mortality rates. As a critical stage in the development and progression of gastric cancer, precancerous lesions of gastric cancer (PLGC) have received widespread attention. PLGC mainly includes pathological changes such as intestinal metaplasia and dysplasia. Effective intervention at this stage is significant for reducing the incidence of gastric cancer. Currently, Western medicine has certain limitations in treating PLGC, while traditional Chinese medicine has demonstrated unique advantages and potential in preventing and treating PLGC [1]. Liu Junzi Tang, as a classic prescription, has the effect of strengthening the spleen and benefiting qi. This study aims to explore the therapeutic effect of modified Liu Junzi Tang on spleen and stomach deficiency type PLGC, providing a reference for clinical treatment.

2. Clinical data

2.1. General information

This study included 60 patients with PLGC, all from the outpatient and inpatient departments of Fangta Traditional Chinese Medicine Hospital in Songjiang District, Shanghai, from July 2023 to October 2024. The patients were divided into a treatment group and a control group using a random number table method, with 30 patients in each group. In the treatment group, there were 18 males and 12 females, with an age range of 32–68 years and an average age of (48.5±7.2) years. The disease duration ranged from 2–10 years, with an average duration of (6.5±2.1) years. In the control group, there were 16 males and 14 females, with an age range of 35–65 years and an average age of (49.2±6.8) years. The disease duration ranged from 3–9 years, with an average duration of (6.2±2.3) years. There were no statistically significant differences in gender, age, and disease duration between the two groups ($P > 0.05$), indicating comparability.

2.2. Diagnostic criteria

2.2.1. Western medicine diagnostic criteria: Gastroscope diagnostic criteria

Gastroscope diagnostic criteria are formulated with reference to the "Chinese Consensus on Chronic Gastritis" and the "Digestive System Tumors" classified by WHO's tumor pathology and genetics. Endoscopically, the mucosa appears red and white, mainly white, with flattened or even disappeared mucosal folds, partial mucosal blood vessels exposed, and may be accompanied by mucosal granules or nodules [2].

2.2.2. Western medicine diagnostic criteria: Pathological diagnostic criteria

Atrophy: Diagnosis is based on the atrophy of the inherent glands in the pathological biopsy of chronic gastritis. Mild atrophy refers to a decrease in the number of inherent glands by less than 1/3 of the original number; moderate atrophy refers to a decrease in the number of inherent glands between 1/3 and 2/3 of the original number; severe atrophy refers to a decrease in the number of inherent glands by more than 2/3 of the original number, or even complete disappearance.

Intestinal metaplasia: The mild intestinal metaplasia area is less than 1/3 of the total area of glands and surface epithelium; the moderate intestinal metaplasia area is between 1/3 and 2/3 of the total area of glands and surface epithelium; the severe intestinal metaplasia area is greater than 2/3 of the total area of glands and surface epithelium.

Intraepithelial neoplasia: It is judged based on abnormalities in both structure and cell morphology. Structural abnormalities manifest as disordered epithelial arrangement and loss of normal cell polarity; cell morphological abnormalities include nuclear irregularity, deep staining, increased nuclear-cytoplasmic ratio, and increased mitotic activity. Low-grade intraepithelial neoplasia typically exhibits structural and cytological abnormalities limited to the lower half of the epithelium, equivalent to mild or moderate dysplasia; whereas high-grade intraepithelial neoplasia may extend these abnormalities to the upper half or even the full thickness of the epithelium, corresponding to severe dysplasia or carcinoma in situ.

2.2.3. Diagnostic criteria in traditional Chinese medicine (TCM)

Referring to the "Consensus Opinions on the Diagnosis and Treatment of Chronic Atrophic Gastritis in Traditional Chinese Medicine", the diagnosis is made

as a spleen and stomach weakness syndrome. The main symptoms include fullness or dull pain in the stomach, preference for pressure or warmth on the stomach, pale tongue, and weak pulse. Secondary symptoms include poor appetite, loose stools, fatigue, shortness of breath, and laziness to speak, and postprandial fullness in the stomach. The diagnosis requires the presence of both main symptoms and tongue manifestations, as well as at least two secondary symptoms, with reference to the pulse condition.

2.3. Inclusion criteria

(1) Age between 20 and 80 years old.

(2) Meeting the diagnostic criteria for precancerous lesions of gastric cancer (chronic atrophic gastritis with moderate to severe intestinal metaplasia and/or low-grade intraepithelial neoplasia) confirmed by gastroscopy and pathological examination in Western medicine.

(3) The syndrome differentiation in TCM is compatible with the spleen and stomach weakness syndrome.

(4) Patients are willing to participate in this study and have signed the informed consent form.

2.4. Exclusion criteria

(1) Patients with peptic ulcer, or those suspected of having malignant changes based on gastroscopy and pathological diagnosis.

(2) Patients with severe diseases affecting major organs such as the heart, lungs, brain, liver, and kidneys, or those with mental disorders.

(3) Female patients who are pregnant or breastfeeding.

2.5. Elimination criteria

(1) Patients who take other medications to treat this disease during the treatment period.

(2) Patients who fail to complete the treatment cycle due to adverse reactions or other reasons.

3. Treatment methods

3.1. Treatment group

Patients will be given orally modified Liu Junzi Decoction. The prescription consists of: Ginseng 9 g, Atractylodes 9 g, Poria 9 g, Prepared Glycyrrhiza Root 9 g, Pinellia 6 g, Dried Tangerine Peel 6 g, *Salviae Miltiorrhizae* 9 g, *Curcuma Zedoary* 9 g, Chuanxiong 10 g, Agrimony Herb 15 g, *Hedyotis Diffusa* 30 g, *Scutellaria Barbata* 15 g. The above herbs will be boiled in water, one dose per day, taken twice.

3.2. Control group

Patients will take folic acid tablets orally, three times a day, 10mg each time, and also teprenone capsules, three times a day, 50 mg each time.

3.3. Treatment course and precautions

Both groups of patients will receive treatment for a period of 12 weeks. During the treatment process, it is prohibited to use any other Chinese or Western medications for the treatment of chronic gastritis. Patients need to stop taking medications related to disease treatment 1 month before being included in the study, avoid spicy, greasy, and stimulating foods, maintain good lifestyle habits, and maintain a stable mental state. At the same time, strengthen communication with patients, conduct regular telephone follow-ups, provide reminders for follow-up visits, ensure convenient conditions for medical visits, and timely understand patients' responses after taking medication.

4. Observation indices and methods

4.1. TCM symptom score

Patients' clinical symptoms were scored according to the grading and quantification criteria for chronic atrophic gastritis symptoms. The symptoms were classified into four levels: none, mild, moderate, and severe. The primary symptoms were scored as 0, 2, 4, and 6, respectively, while the secondary symptoms were scored as 0, 1, 2, and 3, respectively. The total scores of the two groups of patients before and after treatment were calculated, and the disease severity was classified into mild (0–12 points), moderate (13–24 points), and severe (25–36 points) based on the total scores. Changes in TCM symptom scores were observed to evaluate the treatment effect.

4.2. Gastroscopy and pathological efficacy

4.2.1. Gastroscopy

Electronic gastroscopy was performed by a gastroenterologist from the hospital to observe indicators such as gastric mucosal color, vascular transparency, granular hyperplasia, bleeding points and their sizes, lesion scope, severity, etc., under endoscopy. The indicators were graded and scored as normal, mild, moderate, and severe, with scores of 0, 1, 2, and 3, respectively. Changes in scores before and after treatment were compared to evaluate the efficacy of gastroscopy.

4.2.2. Pathological examination

During gastroscopy, 2–3 tissue samples were taken from areas of the gastric mucosa with obvious lesions under endoscopy, ensuring that the two samples were close to each other. The biopsy tissues were fixed with 10% formaldehyde, and then routinely processed by a pathologist for paraffin embedding, sectioning, and HE staining. Pathological changes were observed and recorded, with atrophy and intestinal metaplasia scored as "0, 3, 6, 9" according to the four levels of "none, mild, moderate, and severe". Low-grade intraepithelial neoplasia was scored as "9", and chronic inflammation was scored as "0, 1, 2, 3". The changes in scores before and after treatment were compared to evaluate the pathological efficacy. The main symptoms and signs were observed and recorded on the first day of the initial diagnosis (Day 0), Week 6, and Week 12. Gastroscopy and pathological examination were performed once before treatment and once 12 months after treatment.

4.3. Statistical methods

The collected data were entered and organized using an Excel database and analyzed using SPSS 23.0 statistical software. Counting data were tested using the chi-square test, measurement data were tested using the *t*-test, and ordinal data were tested using the rank sum test. When $P > 0.05$, it indicated that there was no statistically significant difference; when $P < 0.05$, it indicated that there was a statistically significant difference; and when $P < 0.01$, it indicated that there was a highly statistically significant difference.

5. Treatment results

5.1. Improvement of TCM symptom scores

(1) The average total score of TCM symptoms in the treatment group before treatment was (22.5±4.2) points, and the average total score after treatment was (10.2±3.1) points. There was a statistically significant difference between before and after treatment ($P < 0.05$).

(2) The average total score of TCM symptoms in the control group before treatment was (21.8±3.8) points, and the average total score after treatment was (14.5±3.5) points. There was a statistically significant difference between before and after treatment ($P < 0.05$).

(3) The total effective rate of improvement in TCM symptom scores was 83.3% in the treatment group and 60.0% in the control group. There was a statistically significant difference between the two groups ($P < 0.05$). The details are shown in **Table 1**.

5.2. Gastroscope efficacy

(1) The total effective rate of gastroscope efficacy in the treatment group was 70.0%, including 0 cases of complete recovery, 6 cases (20.0%) of marked effectiveness, 15 cases (50.0%) of effectiveness, and 9 cases (30.0%) of ineffectiveness.

(2) The total effective rate of gastroscope efficacy in the control group was 40.0%, including 0 cases of complete recovery, 3 cases (10.0%) of marked effectiveness, 9 cases (30.0%) of effectiveness, and 18 cases (60.0%) of ineffectiveness.

(3) There was a statistically significant difference in the total effective rate of gastroscope efficacy between the two groups ($P < 0.05$). The details are shown in **Table 2**.

5.3. Pathological effect

5.3.1. Improvement of atrophy

The treatment group had an average atrophy score of (4.2±1.2) before treatment and (2.1±0.8) after treatment. The difference was statistically significant ($P < 0.05$).

The control group had an average atrophy score of (4.0±1.0) before treatment and (3.0±0.9) after treatment.

Table 1. Improvement of TCM symptom scores

Group	Sample size (*n*)	Total score before treatment	Total score after treatment	Total effectiveness rate (%)
Treatment group	30	22.5 ± 4.2	10.2 ± 3.1	83.3
Control group	30	21.8 ± 3.8	14.5 ± 3.5	60.0

Table 2. Comparison of the gastroscope efficacy

Group	Sample size (n)	Cured (cases)	Markedly effective (cases)	Effective (cases)	Ineffective (cases)	Total effective rate (%)
Treatment group	30	0	6 (20.0)	15 (50.0)	9 (30.0)	70.0
Control group	30	0	3 (10.0)	9 (30.0)	18 (60.0)	40.0

Table 3. Comparison of atrophy scores

Group	Sample size (n)	Atrophy score before treatment	Atrophy score after treatment
Treatment group	30	4.2 ± 1.2	2.1 ± 0.8
Control group	30	4.0 ± 1.0	3.0 ± 0.9

Table 4. Comparison of intestinal metaplasia scores

Group	Sample size (n)	Intestinal metaplasia score (Pre-treatment)	Intestinal metaplasia score (Post-treatment)
Treatment group	30	3.8 ± 1.0	1.8 ± 0.6
Control group	30	3.6 ± 0.8	2.5 ± 0.7

The difference was also statistically significant ($P < 0.05$).

There was a statistically significant difference in atrophy scores between the treatment and control groups after treatment ($P < 0.05$). The details are shown in **Table 3**.

5.3.2. Improvement of intestinal metaplasia

The treatment group had an average intestinal metaplasia score of (3.8±1.0) before treatment and (1.8±0.6) after treatment. The difference was statistically significant ($P < 0.05$).

The control group had an average intestinal metaplasia score of (3.6±0.8) before treatment and (2.5±0.7) after treatment. The difference was statistically significant ($P < 0.05$).

There was a statistically significant difference in intestinal metaplasia scores between the treatment and control groups after treatment ($P < 0.05$). The details are shown in **Table 4**.

5.3.3. Improvement of intraepithelial neoplasia

In the treatment group, 2 patients with low-grade intraepithelial neoplasia showed improvement.

In the control group, 1 patient with low-grade intraepithelial neoplasia showed improvement.

6. Discussion

6.1. Exploration of etiology and pathogenesis

According to traditional Chinese medicine, the spleen and stomach are the foundation of postnatal life and the source of qi and blood biochemistry. Weakness of the spleen and stomach plays a key role in the occurrence and development of precancerous lesions of gastric cancer. Weakness of the spleen and stomach can lead

to insufficient biochemical generation of qi and blood, resulting in the loss of nourishment for the gastric mucosa and deficiency of healthy qi, making it susceptible to invasion by external pathogens. After invasion by external pathogens, pathological products such as qi stagnation, blood stasis, and dampness-heat can arise internally, further aggravating damage to the gastric mucosa and promoting disease progression. In the modified formula of Liu Junzi Decoction, ginseng serves as the monarch herb, with the effect of strengthening the spleen and nourishing qi, which can enhance spleen and stomach function and promote qi and blood biochemistry. *Atractylodes macrocephala*, *Poria cocos*, and dried tangerine peel are minister herbs that assist ginseng in strengthening the spleen and regulating qi. *Hedyotis diffusa* and *Scutellaria barbata* clear heat and detoxify, *Agrimonia pilosa* has the dual effect of astringing to stop bleeding and tonifying deficiencies, *Curcuma zedoaria* promotes qi circulation and breaks blood stasis, *Salvia miltiorrhiza* promotes blood circulation and removes blood stasis, and Chuanxiong promotes blood circulation and qi movement. These herbs, when combined, can achieve the effects of promoting qi circulation to relieve pain, clearing heat and resolving dampness, removing stasis to generate new tissue, thus improving the pathological state of patients with spleen and stomach deficiency type PLGC [3].

6.2. Analysis of treatment results

6.2.1. Improvement of TCM symptom scores

The treatment group showed significant superiority over the control group in terms of improvement in TCM symptom scores. This may be because the modified Liu Junzi Decoction regulates spleen and stomach function and promotes qi and blood biochemistry, thereby improving the overall physical condition of patients and relieving a series of symptoms such as gastric distension, dull pain, poor appetite, and loose stools. Its regulatory effect on the spleen and stomach may involve multiple links, such as enhancing gastrointestinal motility, promoting the secretion of digestive juices, and improving the body's immune system [4].

6.2.2. Gastroscopy and pathological effects

Gastroscopy effect: The total effective rate of gastroscopy in the treatment group was higher than that in the control group, indicating that Modified Liu Jun Zi Tang has a certain repair effect on gastric mucosal lesions. It may improve the blood circulation of the gastric mucosa, promote the proliferation and repair of gastric mucosal cells, reduce mucosal inflammation, bleeding, and other lesions, thereby improving the gastric mucosal appearance observed under endoscopy.

Pathological effect: In terms of pathology, the treatment group showed better improvement in atrophy and intestinal metaplasia scores than the control group. This suggests that Modified Liu Jun Zi Tang can inhibit the atrophy of gastric mucosal glands and reduce the degree of intestinal metaplasia. It may achieve this by regulating signaling pathways related to cell proliferation and differentiation, inhibiting the growth and differentiation of abnormal cells, and promoting the repair and regeneration of normal cells, thereby improving the pathological state [5].

6.3. Innovations and limitations of this study

6.3.1. Innovations

This study adopted a randomized and controlled research method to conduct a systematic clinical observation on the treatment of spleen and stomach deficiency type PLGC with modified Liu Jun Zi Tang. It included a comprehensive evaluation of clinical symptoms, endoscopic mucosal manifestations, and pathological results, providing relatively comprehensive clinical evidence for the treatment of PLGC with traditional Chinese medicine.

Through the analysis of the modified formula of Liu Jun Zi Tang and observation of its curative effect, the mechanism of action of traditional Chinese medicine in the treatment of PLGC was further revealed. That is, by regulating the function of the spleen and stomach, balancing qi, blood, yin, and yang, and eliminating pathological products, the goal of treating the disease can be achieved.

6.3.2. Limitations

The sample size was relatively small, which may have some impact on the accuracy and reliability of the research results. In subsequent studies, the sample size should be appropriately expanded to more accurately evaluate the therapeutic effect of the modified Liu Jun Zi Tang.

The observation time was relatively short, only 12 weeks, and the long-term efficacy and safety of the modified Liu Jun Zi Tang have not been fully understood. Future studies can extend the observation time to further explore its long-term efficacy and safety issues.

7. Conclusion

This study aimed to explore the clinical efficacy of modified Liu Jun Zi Tang in the treatment of precancerous lesions of gastric cancer (PLGC) with spleen and stomach deficiency, as well as its impact on endoscopic mucosal manifestations and pathological changes. Through a randomized controlled trial of 60 patients with PLGC and spleen and stomach deficiency, it was found that modified Liu Jun Zi Tang has significant efficacy in the treatment of PLGC.

Firstly, in terms of comprehensive efficacy evaluation of traditional Chinese medicine (TCM) symptoms, the total effective rate of symptom score improvement in the treatment group was 83.3%, which was significantly higher than that in the control group. This result indicates that the modified Liu Jun Zi Tang has significant advantages in improving TCM symptoms of patients with precancerous lesions of gastric cancer (PLGC) with spleen and stomach deficiency. After treatment, symptoms such as loss of appetite, abdominal distension, and loose stools were significantly relieved, which may be attributed to the function of Liu Jun Zi Tang in strengthening the spleen, nourishing qi, harmonizing the stomach, and promoting digestion.

Secondly, the evaluation results of gastroscopy efficacy showed that the total effective rate of gastroscopy efficacy in the treatment group was 70.0%, which was better than that in the control group. Gastroscopic observation revealed that symptoms such as gastric mucosal inflammation and erosion were significantly reduced in the treatment group, and the mucosal repair status was ideal. This suggests that the modified Liu Jun Zi Tang can not only effectively improve TCM symptoms but also promote gastric mucosal repair, thereby improving mucosal appearance under gastroscopy.

Furthermore, in terms of pathological changes, the treatment group was significantly better than the control group in improving atrophy and intestinal metaplasia scores. Pathological section examination showed that the degree of pathological changes, such as gastric mucosal atrophy and intestinal metaplasia, was significantly reduced in the treatment group, and some patients even showed reversal of pathological changes. This result further verifies the efficacy of modified Liu Jun Zi Tang in the treatment of PLGC, indicating that it can effectively improve the pathological state of patients and delay or prevent the progression of precancerous lesions of gastric cancer.

In summary, modified Liu Junzi Decoction has significant efficacy in treating spleen and stomach deficiency type PLGC, which can significantly improve the clinical symptoms and pathological conditions of patients. This may be related to the multiple mechanisms of modified Liu Junzi Decoction, such as strengthening the spleen and nourishing qi, harmonizing the stomach and promoting digestion, and promoting the repair of gastric mucosa. Therefore, modified Liu Junzi Decoction can be used as an effective treatment for spleen and stomach deficiency type PLGC, and it is worthy of further promotion and application in clinical practice.

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Disclosure statement

The authors declare no conflict of interest.

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