

## Treatment of gastric precancerous lesions with Weiansan

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**CONCLUSION:** WAS improves clinical symptoms by suppressing GA, IM and dysplasia and eliminating *H pylori*.

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**Key words:** Weiansan; Gastric precancerous lesions; Clinical observation; *H pylori* elimination

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### Abstract

**AIM:** To observe the curative effect of Weiansan (WAS) on gastric precancerous lesions (GPL) and *H pylori* elimination.

**METHODS:** Seventy-six patients with GPL were randomly divided into two groups: WAS group ( $n = 42$ ) and Weifuchun (WFC) group ( $n = 34$ ). The patients in the WAS group were administered 5 g WAS 3 times a day, and the patients in the WFC group took WFC (4 tablets) 3 times a day. To monitor inflammation of gastric mucosa, degree of glandular atrophy (GA), intestinal metaplasia (IM) and dysplasia, and *H pylori* infection, all patients underwent gastroscopy and biopsy with pathological examination before and after treatment. Fifty male Sprague-Dawley (SD) rats were used in animal experiments. Of these, 10 served as the control group ( $n = 10$ ), 40 were given ranitidine combined with *N*-methyl-*N*<sup>1</sup>-nitro-*N*-nitrosoguanidine (MNNG) for 12 wk and divided into 4 groups randomly: model group ( $n = 10$ ), high-dose WAS group ( $n = 10$ ), low-dose WAS group ( $n = 10$ ) and WFC group ( $n = 10$ ). Twelve weeks later, all rats were killed and a 2 cm × 1 cm tissue was taken from the lesser curvature of the gastric antrum. *H pylori* infection was determined by the fast urease method.

**RESULTS:** The curative effect in WAS groups was similar to that in WFC groups. There was no statistical difference in degree of GA, IM and dysplasia between WAS and WFC groups. The rate of *H pylori* infection in the model group (positive/negative: 9/1) was significantly higher than that in the control group (positive/negative: 1/9) ( $P < 0.01$ ). *H pylori* elimination in the high-dose WAS group (positive/negative: 4/6) and low-dose WAS group (positive/negative: 6/4) was similar to that in the WFC group (positive/negative: 4/6) ( $P > 0.05$ ).

### INTRODUCTION

Gastric precancerous lesion (GPL) is one of the diseases of the digestive system, easily occurring in gastric mucosa with changes such as gastric epithelial dysplasia (GED) and intestinal metaplasia (IM) resulting in chronic atrophic gastritis (CAG)<sup>[1]</sup>. Traditional Chinese medicine (TCM) can prevent and cure GPL, and has become one of the hotspots in research<sup>[2]</sup>. In order to find its accurate and effective therapy, GPL was treated with Weiansan (WAS) and its effect on eliminating *H pylori* was evaluated.

### MATERIALS AND METHODS

#### Patients

Seventy-eight patients were diagnosed as insufficiency of the spleen- and stomach-qi or stagnation of qi and stasis of blood. CAG was confirmed by gastroscopy. The patients were randomly divided into two groups: WAS group ( $n = 42$ ) and Weifuchun (WFC) group ( $n = 34$ ).

The WAS group included 32 males and 10 females aged 24-69 years with a mean age of  $40 \pm 2.1$  years. Of the 42 patients in this group, 20 had mild CAG and 22 had moderate to severe CAG.

The WFC group included 24 males and 10 females aged 25-68 years with a mean age of  $41 \pm 2.3$  years. Of the 34 patients in this group, 14 had mild CAG and 20 had moderate to severe CAG. There was no significant difference between the two groups.

#### Experimental animals

Fifty 15-d old male Sprague-Dawley rats weighing

**Table 1** Changes of GA in WAS and WFC groups after treatment

Group	Cases (n)	Atrophy improvement			No change	Severe
		0	+	++<-		
WAS	42	2	22	6	10	2
WFC	34	2	16	8	8	0

0: Have changes but not achieve a state (less than a +); +: Effective; ++<-: Obviously effective.

100-150 g were bought from Experimental Animal Centre, Chinese Academy of Medical Sciences. The feed was purchased from Keao Xieli Feed Limited Company.

The evaluation standard of clinical curative effects was drawn up according to the 2<sup>nd</sup> version of "Clinical Research Guiding Principle of New Medicine of TCM" and other corresponding reports<sup>[3]</sup>.

Disappearance of clinical symptoms and active inflammation, improvement of chronic inflammation, reduction of GA, IM and gastric epithelial dysplasia (GED) were judged as curative. Disappearance of main clinical symptoms, improvement of acute and chronic inflammation, two-degree reduction of GA, IM and GED were judged as obviously effective. Improvement of clinical symptoms, one-degree reduction of GA, IM and GED were judged as effective. No improvement of clinical symptoms and pathological change was judged as ineffective.

#### Clinical research method

To observe the mucous membrane inflammation, degree of GA, IM and GED, all the patients underwent gastroscopy and pathological examination before and after 24 wk of treatment. The rate of *H pylori* infection was also determined. The patients in WAS group received 5 g WAS 3 times a day, while the patients in WFC group were given 4 tablets of WFC 3 times a day for 12 wk as a course of treatment. The two groups received two courses of the treatment.

#### Experimental method

One week after increasing compatibility, the rats drank MNNG (50 µg/L) and were fed standard powder feed containing 0.03% ranitidine for 12 wk as previously described<sup>[4]</sup>. Ten rats in the control group were fed normally. After administration of MNNG for 12 wk, the other 40 rats were divided into 4 groups, 10 rats in each group. The rats in the model group were given physiological saline *via* gavages (1 mL/100 g) once a day; the rats in the high-dose WAS group were physiological saline *via* gavages (5 g\*20/65 g body weight); the rats in the low-dose WAS group and WFC group were fed by gavages individually (1 mL/100 g) once a day. After administration of WAS and WFC for 12 wk, all the rats in the 5 groups were killed and their stomachs removed. The gastric cavity was cut open along the greater curvature, cleaned and fixed in buffered formalin solution. A 2 cm × 1 cm tissue was removed from the lesser curvature of the gastric antrum. *H pylori* situation was determined by the

**Table 2** Changes of GED and IM in WAS and WFC groups after treatment

Group	Cases (n)	GED and IM improvement			No change	Severe
		0	+	++<-		
WAS	20	2	8	2	4	2
WFC	16	0	4	6	4	2

0: Have changes but not achieve a state (less than a +); +: Effective; ++<-: Obviously effective.

fast urease method. The *H pylori*-eliminating effect in the 5 groups was compared.

#### Statistical analysis

The pairs-*t* test was applied to the data before and after the treatment, the ratio was examined with chi-square test, and the rank material was examined with Ridit. All analyses were performed with SPSS 10.0.  $P < 0.05$  was considered statistically significant.

## RESULTS

#### Effect of WAS and WFC on glandular atrophy

The degree of GA, IM and GED was classified into mild, moderate and severe grades according to gastroscopy findings. The patients received gastroscopy and pathological examination respectively before and after 24 wk of treatment. Improvement of clinical symptoms was analyzed. According to the evaluation standard, clinical curative effects were judged as curative, obviously effective, effective and ineffective, respectively.

The results suggested that the above-mentioned indexes had no significant difference between the WAS and WFC groups before and after treatment ( $P > 0.05$ ). After treatment, such indexes were improved both in the WAS group and in the WFC group ( $P < 0.05$ ), suggesting that both WAS and WFC could improve GA, IM and dysplasia. The total effective rate for alleviating the GA degree was 71.43% in the WAS group and 76.47% in the WFC group, respectively (total effective rate for alleviating the GA degree = the alleviated GA degree/total cases × 100%)

The total effective rate for alleviating the GED and IM degree was 60.00% in the WAS group and 62.50% in the WFC group, respectively (total effective rate of alleviating the GED and IM degree = the alleviated GED and IM degree/total cases × 100%). The histological changes in GED and IM were not obvious in both groups after treatment. It might be due to a too short period of treatment, concentration of medicine, and combined herbal medicine treatment.

#### Elimination of *H pylori* in patients after treatment with WAS and WFC

Before treatment, *H pylori*-infected patients were examined in both groups. After treatment, the eradication rate of *H pylori* in the WAS group was higher than that in the WFC group ( $P < 0.05$ ), indicating that the *H pylori*-eliminating effect in WAS group was better than that in the WFC group (Table 1, Table 2, Table 3, Table 4).

Table 3 Curative effect in WAS and WFC groups

Group	Cases (n)	cure	Obviously effective	Effective	Ineffective	Effective rate (%)
WAS	42	4	20	12	6	85.71
WFC	34	4	12	12	6	82.35

Table 4 *H pylori* elimination in WAS and WFC groups

Group	Cases (n)	Positive	Negative	Negative rate (%)
WAS	42	6	36	85.74 <sup>a</sup>
WFC	34	13	21	61.71

<sup>a</sup>*P* < 0.05 vs WFC group.

### *H pylori* situation in animal experiment and eliminating effects of WAS and WFC

Compared with the control group (positive/negative: 1/9), the *H pylori* situation in the model group (positive/negative: 9/1) was noticeably better (*P* < 0.01). The *H pylori*-eliminating effect in the high-dose WAS group (positive/negative: 4/6) and low-dose WAS group (positive/negative: 6/4) was similar to that in the WFC group (positive/negative: 4/6) (*P* > 0.05). The eradication rate of *H pylori* in the three groups was obviously higher than that in the model group (*P* < 0.05, Tables 5 and 6).

## DISCUSSION

GPL belongs to the “stomach distension” and “epigastralgia” category in traditional Chinese medicine. It results from spleen and stomach injury, blood stasis due to impeding circulation of qi and blood caused by improper diet, the 6 abnormal climatic factors and the 7 abnormal emotions. The keys are spleen deficiency, qi stagnation and blood stasis. The main local symptoms are distension and fullness of the stomach, belches and poor appetite, constipation or diarrhoea. The general symptoms are lassitude and weakness, dizziness and emaciation, sallow complexion, pale and dark tongue. The basic factor and pathogenesis are deficiency in origin and excess in superficiality, and complicated syndromes of deficiency and excess. Therefore it should be treated both causally and symptomatically. The corresponding principle of WAS is to strengthen the spleen, replenish and regulate qi, invigorate blood. Our clinical study demonstrated that the total effective rate for GPL was about 85.70%, indicating that WAS plays a certain role in blocking GPL. WAS is composed of astragalus root, pilose asiabell root, bighead atractylodes rhizome, cinnamon bark, red sage root, scorpion, rhizome corydalis, fructus anrantii, processed grain and wheat, *etc.*

In the decoction, astragalus root, pilose asiabell root, bighead atractylodes rhizome, and cinnamon bark increase the gastric mucosa barrier, enhance the immunity, strengthen the phagocytic function of the reticuloendothelial system, elevate the lymphocyte transformation rate and promote anti-body formation.

Table 5 *H pylori* situation in GPL of model and control groups after 12 wk of treatment

Group	Cases (n)	Positive	Negative	Infective rate (%)
Model group	10	9	1	90 <sup>a</sup>
Control group	5	0	5	0

<sup>a</sup>*P* < 0.01 vs control group.

Table 6 *H pylori* eliminating situation after 12 wk of treatment

Group	Cases (n)	Positive	Negative	Eliminating rate (%)
High-dose WAS group	10	4	6	60
Low-dose WAS group	10	6	4	40
WFC group	10	4	6	60
Model group	10	9	1	10

Red sage root, scorpion, and rhizome corydalis containing a broad spectrum of anti-neoplastic components, may invigorate the blood to remove blood stasis, relieve spasm and pain, inhibit tumour occurrence, improve the gastric mucosa blood circulation, accelerate topical inflammation absorption, help atrophic glands to restore and remove the deleterious substance in epithelial cells. Fructus anrantii, processed grain and wheat can relieve depression of liver-qi, activate qi and promote digestion<sup>[5]</sup>. These herbal medicines cooperate in harmony and exert a major effect on GPL.

A total of 7496 cases related to CAG have been reported, and the insufficiency type of the spleen and stomach ranks first<sup>[6]</sup>, indicating that insufficiency of the spleen correlates positively with the severity of gastric diseases. The *H pylori* infection rate and the degree of infection in patients with qi-stagnation and middle-warmer deficiency are remarkably different from those in patients with other types of CAG, suggesting that the *H pylori* infection rate is closely related to insufficiency of the spleen which has become the most important factor for stomach cancer development. Therefore insufficiency of the spleen and qi stagnation should be closely monitored because of their high carcinogenic tendency. Our study has confirmed that strengthening the spleen can improve GPL, reduce gastric mucosa inflammation, help atrophic glands to regenerate and restore, reverse and restore gastric mucosa dysplasia and IM, promote differentiation and maturation of atypical cells to normal cells. Drugs strengthening the spleen increase the gastric mucosa barrier effect and protect carcinogens from attacking by enhancing immunity, strengthening the phagocytic function of the reticuloendothelial system and promoting the lymphocyte transformation rate. All these indicate that the method of strengthening the spleen can prevent GPL, and this method has become one of the therapies for preventing and treating gastric mucosa precancerous lesions<sup>[7,8]</sup>.

In addition, studies also indicate<sup>[9-11]</sup> that microcirculation dysfunction is generally followed by CAG. The

common clinical symptoms include fixed stomach pain and purple dark or dark red or pale dark or ecchymosed tongue. In our study, gastroscopy demonstrated that the degree of GA, IM and GED in blood stasis type of GPL was more severe than that in other types, suggesting that the mechanism underlying blood stasis exists in GPL. Gastric mucosa dysplasia and IM highly correlate with microcirculation. Blood-invigorating herbal medicines can remove blood stasis and protect gastric mucosa by improving GPL, gastric mucosa microcirculation, establishing collateral circulation, improving local ischemia and hypoxia, increasing gastric mucosa blood flow, reducing inflammation and helping atrophic glands to regenerate. Therefore invigorating the blood to remove blood stasis has also become the key to preventing and treating gastric mucosa precancerous lesions.

In conclusion, according to the pathogenesis of insufficiency of the spleen and blood stasis, the therapy for GPL can be established. Treatment of PGL with WAS is to strengthen the spleen, replenish and invigorate qi and blood. Furthermore, WAS can improve the clinical symptoms of GPL by suppressing GA, IM and dysplasia and eliminating *H pylori*.

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