

• *Helicobacter pylori* •

Effect of Hewei-Decoction on chronic atrophic gastritis and eradication of *Helicobacter pylori*

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for alleviation of symptoms and signs. Also, the decoction is efficacious in *H pylori*-negative cases.

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Abstract

AIM: To demonstrate the effect of Hewei-Decoction (Decoction for regulating the stomach) on chronic atrophic gastritis (CAG) and eradication of *Helicobacter pylori*.

METHODS: Ninety patients with CAG entering the investigation were divided into six differentiation syndromes, based on their major symptoms and signs. Hewei-Decoction was taken by all the patients orally for 4 or 8 wk. The efficacy was assessed by both the composite accumulation of reduced scores of major symptoms and the eradication of *H pylori*. χ^2 test was used to compare the efficacy between *H pylori*-positive and negative cases, and to disclose the relationship between efficacy and eradication of *H pylori*.

RESULTS: In patients with six different syndrome types, the efficacy of Hewei-Decoction was 91.67% (11/12), 92.86% (13/14), 97.22% (35/36), 87.50% (14/16), 75.00% (6/8), 75.00% (3/4) respectively. The rate of highly efficacious was 58.33% (7/12), 50.00% (7/14), 77.78% (28/36), 62.50% (10/16), 12.50% (1/8) and 25.00% (1/4), respectively. The total efficacy was 91.11% (82/90), and the rate of highly efficacious was 60.00% (54/90). The eradication rate of *H pylori* was 67.86% (38/56). The therapeutic effect of Hewei-Decoction was better in *H pylori* positive cases than that in *H pylori*-negative cases with the total effect of 96.43% vs 82.35% ($P < 0.05$). In 56 *H pylori* positive cases, the therapeutic effect was better in *H pylori* eradicated cases than that in *H pylori*-existent cases with the total effect of 97.37% vs 72.22% ($P < 0.01$).

CONCLUSION: Hewei-Decoction is effective in most cases of all the syndrome types. The results indicate that eradication of *H pylori* is one of the important mechanisms

INTRODUCTION

Chronic atrophic gastritis (CAG) has a high incidence in adult population and the incidence increases with age. It is one of the most important pre-cancerous lesions and few therapeutic drugs have been proved to be effective in current Western medical system. In traditional Chinese medicine (TCM), CAG belongs to the categories of "weitong" (gastric pain), "piman" (feeling of fullness), "outu" (vomiting), "caoza" (gastric discomfort), and "tunsuan" (acid regurgitation). Based on the major symptoms and signs, cases of CAG are differentiated into several syndrome types including pathogenic cold attacking the stomach, damp heat in the spleen and stomach, disharmony between the liver and stomach, qi deficiency of the spleen and stomach, yang deficiency of the spleen and stomach, yin deficiency of the stomach and blood stasis blocking collaterals, and then the corresponding recipes are made to treat different syndromes. However, the exploitation of so many drugs and recipes is really perplexing, which might limit the standardization of TCM investigations. Therefore, it is essential to explore a common recipe that has good compliance on most cases of different syndrome types, and at the same time the efficacy of this recipe could be evaluated objectively and quantitatively. In this investigation, the efficacy of Hewei-Decoction was evaluated by the combination of accumulation of reduced scores of major symptoms and eradication of *Helicobacter pylori* (*H pylori*).

MATERIALS AND METHODS

Case selection

One hundred and twenty two cases of CAG were confirmed by gastroscopic and histological examinations from September 2001 to December 2003. Cases with any one

of the following were excluded from this investigation: peptic ulcer, severe systemic diseases, severe metaplasia or dysplasia or pre-cancerous lesions, women in pregnancy or lactation period, hypersensitive constitution and allergic to many drugs, dropping out of the investigation before the end of treatment, the follow-up period shorter than 4 wk after treatment. Ninety patients (55 males, 35 females, aged from 32 to 72 years) entered this investigation.

Syndrome differentiation of CAG

All cases were differentiated into the following six types on the basis of their chief manifestations^[1]: (1) 12 cases of pathogenic cold attacking the stomach; (2) 14 cases of damp heat in the spleen and stomach; (3) 36 cases of disharmony between the liver and spleen; (4) 16 cases of qi deficiency in the spleen and stomach; (5) 8 cases of yang deficiency in the spleen and stomach; (6) 4 cases of yin deficiency in the stomach (Table 1).

Prescriptions of Hewei-Decoction

Taizhishen (*Radix Pseudostellaria Heterophylla*) 20 g, shanyao (*Rhizoma Dioscoreae*) 25 g, baizhu (*Rhizoma Atractylodis Macrocephalae*) 12 g, chaihu (*Radix Bupleuri*) 10 g, zhishi (*Fructus Aurantii Immaturus*) 10 g, xiangfu (*Rhizoma Cyperi*) 12 g, baishaoyao (*Radix Paeoniae Alba*) 12 g, huanglian (*Rhizoma Coptidis*) 5 g, wuzhuyu (*Fructus Evodiae*) 3 g, jinei jin (*Endothelium Corneum Gigeriae Galli*) 6 g, shanzha (*Fructus Crataegi*) 15 g, maiya (*Fructus Hordei Germinatus*) 15 g, shenqu (*Massa Fermentata Medicinalis*) 12 g, shenggancao (*Radix Glycyrrhizae*) 6 g, houpu (*Cortex Magnoliae Officinalis*) 12 g, fabanxia (*Rhizoma Pinelliae Praeparatae*) 12 g were ground into fine powders, 20 g was boiled and taken orally twice daily for 4 wk, and in some cases for an additional period of 4 wk if necessary.

Elucidation of Hewei-Decoction

Ingredients of taizhishen and shanyao were used to nourish the spleen and stomach. Ingredients of baizhu, chaihu, zhishi, xiangfu and baishaoyao were modified from the recipe of Sinisan (powder for treating cold limbs), which was used to soothe the liver and regulate the spleen, thus relieving the disharmony between the liver and spleen. Ingredients of

huanglian and wuzhuyu were used to regulate the coldness and warmth in the stomach and the middle energizer. Ingredients of jinei jin, shanzha, maiya and shenqu were all peptic drugs, which were used to promote digestion, remove stagnation and regulate the spleen and stomach. Ingredients of houpu and fabanxia were used to dry dampness and eradicate fullness in the middle energizer. Shenggancao served as guiding drug with the function of mediating properties of other drugs.

Effect assessment

Two experienced professional TCM doctors performed effect assessment cross-blindly 1 wk and 4 wk after Hewei-Decoction treatment, according to the standards established in 1989 by the Subcommittee of Digestive Diseases of Chinese Integrative Medicine^[2,3].

Effect assessment of composite reduced-score accumulation

The therapeutic effect was demonstrated by the composite accumulation of reduced scores (CARS) of all major symptoms in this method. To quantify the grade of major symptoms or signs, every symptom was scaled into three levels according to its severity (Table 2). The results were evaluated as follows: (1) highly efficacious: completely clear of all the major symptoms, CARS ≥ 95%; (2) obviously efficacious: great improvement of the major symptoms, CARS ≥ 70%; (3) efficacious: the major symptoms were improved, CARS ≥ 30%; (4) no effect: no improvement of the major symptoms, CARS ≤ 30%.

CARS were calculated using the following formula:

$$CARS (\%) = [(accumulated\ scores\ before\ treatment - accumulated\ scores\ after\ treatment) \div accumulated\ scores\ before\ treatment] \times 100\%$$

Assessment of *H pylori* eradication *H pylori* infection was detected by the combination of C¹⁴-urease breath test, Gram stain and rapid urease test of biopsy samples before treatment, and reassessed 4 wk after treatment. χ^2 test was used to compare the efficacy between *H pylori*-positive and negative cases, and to disclose the relationship between efficacy and eradication of *H pylori*.

RESULTS

In cases of pathogenic cold attacking the stomach, the

Table 1 Syndrome differentiation of CAG patients

Syndrome types	Chief manifestations	n
PCAS	Sudden onset of gastric pain aggravated by pressure and alleviated by hot compression, preference for warmth and aversion to cold, absence of thirst, preference for hot drinks, white tongue coating, wiry and tense pulse	12
DHSS	Fullness or distending pain in the gastric area, bitter taste and stickiness in the mouth, heavy sensation in head and body, dyschesia, feverish sensation in the anus, red tip of the tongue with yellow and greasy coating, wiry and smooth pulse	14
DLS	Distending pain in gastric area radiating to hypochondriac area, fullness in chest, belching, sighing, vomiting, restlessness, irritability, insomnia, dyschesia, or diarrhea or constipation, pale tongue with thin and yellow coating, wiry pulse	36
QDSS	Fullness in gastric area, worse after meals; anorexia, lassitude, loose stools, pale and swollen tongue with thin and white coating, deep and weak pulse	16
YDSS	Continuous dull pain in gastric area relieved by warmth, pressure and intake of food; vomiting of clear fluid, anorexia, lassitude, cold limbs, loose stool, pale and swollen tongue with thin and white coating, thready and weak pulse	8
YDS	Dull burning pain in gastric area, restlessness and thirsty, dry mouth and throat, dry stools, dizziness, insomnia, poor appetite, feverish sensation in palms and soles, red tongue with little coating or peeling cracks on the tongue, thready and rapid pulse	4

PCAS: pathogenic cold attacking the stomach; DHSS: damp heat in the spleen and stomach; DLS: disharmony between the liver and spleen; QDSS: qi deficiency in the spleen and stomach; YDSS: yang deficiency in the spleen and stomach; YDS: yin deficiency in the stomach.

Table 2 Grade quantifications of chief symptoms and signs

Symptoms	1	2	3
Gastric fullness	Slight	Endurable	Unendurable
Dull gastric pain	Slight	Endurable	Unendurable
Pricking gastric pain	Slight or none	Endurable	Severe and fixed
Dryness in mouth	Occasionally	In morning	On whole day
Bitter taste	Occasionally	In morning	On whole day
Tastelessness	Occasionally	From time to time	Frequently
Nausea	Occasionally	From time to time	Frequently
Stickiness in mouth	Occasionally	From time to time	Frequently
Acid regurgitation	Occasionally	From time to time	Frequently
Loose stools	Occasionally	Frequently	Severe
Dyschesia	Slight	Moderate	Severe
Dry stools	Occasionally	Frequently	Severe
Black stools	Occasionally	Moderate	Severe
Anorexia	Reduction of food $\leq 1/4$	Reduction of food $\leq 1/3$	Reduction of food $\leq 1/2$
Fullness in chest	Slight	Sometimes	Severe
Lassitude	Slight	Hard to deal with daily tasks	Unable to deal with daily tasks
Short breath	After physical exercises	After mild physical exercises	Even in calm status
Yellow urine	Occasionally	Frequently, with scanty urine	Dark yellow severe and scanty urine

Table 3 Effect assessment of composite accumulation of reduced scores

Syndrome types	HE	OE	E	NE	Total efficacy (%)
CAS	7	2	2	1	91.67
DHSS	7	3	3	1	92.86
DLS	28	6	1	1	97.22
QDSS	10	2	2	2	87.50
YDSS	1	2	3	2	75.00
YDS	1	2	0	1	75.00

HE: highly efficacious, OE: obviously efficacious, E: efficacious, NE: no effect.

Table 4 Relationship between efficacy and *H pylori* infection

	Results of treatment		Total
	Effective	Ineffective	
<i>H pylori</i> positive before treatment	54	2	56
<i>H pylori</i> negative before treatment	28	6	34
Total	82	8	90

$g = 1$, $\chi^2 = 5.175$, $^aP < 0.05$ vs *H pylori* negative.

Table 5 Relationship between efficacy and *H pylori* eradication

	Results of treatment		Total
	Effective	Ineffective	
<i>H pylori</i> eradicated after treatment	37	1	38
<i>H pylori</i> non-eradicated after treatment	13	5	18
Total	50	6	56

$g = 1$, $\chi^2 = 8.074$, $^bP < 0.01$ vs *H pylori* non-eradicated.

overall efficacy of Hewei-Decoction (including highly efficacious, obviously efficacious and efficacious) was 91.67% (11/12), and the rate of highly efficacious was 58.33% (7/12). In cases of damp heat in the spleen and stomach, the overall efficacy of the decoction and the rate of highly efficacious were 92.86% (13/14) and 50.00% (7/14) respectively. In cases of disharmony between the liver and stomach, the overall efficacy of the decoction and the rate of highly efficacious were 97.22% (35/36) and 77.78%

(28/36) respectively. In cases of qi deficiency of the spleen and stomach, the overall efficacy of the decoction and the rate of highly efficacious were 87.50% (14/16) and 62.50% (10/16) respectively. In cases of yang deficiency of the spleen and stomach, the overall efficacy of the decoction and the rate of highly efficacious were 75.00% (6/8) and 12.50% (1/8) respectively. In cases of yin deficiency of the stomach, the overall efficacy of the decoction and the rate of highly efficacious were 75.00% (3/4) and 25.00% (1/4), respectively (Table 3). On the whole, the total efficacy was 91.11% (82/90), and the rate of highly efficacious was 60.00% (54/90).

The eradication rate of *H pylori* was 62.50% (5/8), 60.00% (6/10), 72.73% (16/22), 70.00% (7/10), and 60% (3/5), respectively, in cases of pathogenic cold attacking the stomach, damp heat in the spleen and stomach, disharmony between the liver and stomach, qi deficiency of the spleen and stomach, and Yang deficiency of the spleen and stomach. In cases of Yin deficiency of the stomach, only one case was *H pylori* positive, and *H pylori* infection was eradicated after treatment. The total eradication rate was 67.86% (38/56). The therapeutic effect of Hewei-Decoction was better in *H pylori*-positive cases than that in *H pylori* negative cases, the total effect was 96.43% vs 82.35% ($P < 0.05$, Table 4). In 56 *H pylori*-positive cases, the therapeutic effect was better in *H pylori*-eradicated cases than that in *H pylori*-non-eradicated cases, the total effect was 97.37% vs 72.22% ($P < 0.01$, Table 5).

DISCUSSION

As a pre-cancerous lesion with a high incidence in middle-aged and old population, CAG is one of the critical gastric diseases, to which researchers in both clinical and basic fields have paid great attention^[4,5]. However, few therapeutic drugs have been proved to be effective. The focus is shifted to traditional medicines. According to the previous work, CAG could be differentiated into several syndrome types^[6-10]. It is no doubt that the precise differentiation is the basis for reasonable treatment, which means that different syndrome types require different prescriptions. Indeed, many drugs

and recipes in TCM have been proved to be effective on CAG^[11-15]. However, too many prescriptions for one disease though manifesting different symptoms and signs are really perplexing, especially for basic and clinical medical researchers. This situation would bring obstacles to establish a uniform, concise and precise standard that is easier to be understood and accepted. One way to solve this problem is to form a prescription that is effective on most cases of different syndromes. The other way is to select drugs that have been proved to have effect on objective and measurable signs or examinations, which is also the requirement of evidence-based medicine^[16-20].

The composition of Hwei-Decoction followed the basic therapeutic principles in TCM of keeping the balance, which means that this prescription took the balance into first consideration. The selection of drugs took special care of the balance between yin and yang, heat and cold, dryness and moistness on the whole, which was purposed to adapt to most cases of different syndromes. It is believed that *H pylori* infection may be an important pathogenic factor in CAG^[21,22]. So it is reasonable to take the eradication of *H pylori* as an objective measurement to evaluate the therapeutic effect on CAG.

In this investigation, Hwei-Decoction was shown to be effective in most cases of different syndrome types. The total efficacy was 91.11% (75.00-97.22% in different syndrome types), which was a little higher than that reported by Zhang *et al.* The rate of highly efficacious was 60.00% (25.00-77.78% in different syndrome types). It was noticeable that there were differences in efficacy among syndrome types. The best effect was achieved in cases of disharmony between the liver and stomach, next in cases of damp heat in the spleen and stomach, followed by pathogenic cold attacking the stomach, qi deficiency of the spleen and stomach, yang deficiency of the spleen and stomach, and yin deficiency of the stomach.

On the whole, the eradication rate of *H pylori* was 67.86%, which was roughly accordant with the rate of highly efficacious. This is comparable to the result (with *H pylori* eradication of 66.04%) reported by Wang. It is interesting that the therapeutic effect of Hwei-Decoction was paralleled with *H pylori* eradication, and better in *H pylori*-positive cases than that in *H pylori*-negative cases. It was strongly indicated that the alleviation of major symptoms was relevant to *H pylori* eradication.

In summary, Hwei-Decoction is effective in most cases of all the syndrome types. The eradication of *H pylori* is one of the important mechanisms for alleviation of symptoms and signs. Also, the decoction is efficacious in *H pylori*-negative cases. Further research is necessary to disclose the underlying mechanisms involved in the symptomatic improvement.

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