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

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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 cases 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. \( \chi^2 \) 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 for alleviation of symptoms and signs. Also, the decoction is efficacious in H pylori-negative cases.

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Key words: Chronic atrophic gastritis; Helicobacter pylori infection; Hewei-Decoction

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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, 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 symptoms were included in the study, (1) duration of CAG duration of more than 1 year, (2) CAG with atrophy and intestinal metaplasia, (3) CAG with Gastric cancer precursors (intestinal metaplasia to dysplasia, to cancer), (4) positive CAG biopsy report, (5) CAG with gastric cancer family history, and (6) alcohol and tobacco abuse. Exclusion criteria were (a) patients who had undergone chemotherapy or radiation therapy, (b) patients on gastric acid inhibitors, (c) patients with any severe disease of the heart, liver, kidney or other organs, (d) patients with diabetes, hypertension, etc. and (e) patients who were pregnant or lactating.
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**

Taizishen (*Radix Pseudostellariae Heterophylla*) 20 g, shanyao (*Rhizoma Dioscoreae*) 25 g, baizhu (*Rhizoma Atractyloidis Macrocophala*) 12 g, chaihu (*Radix Bupleuri*) 10 g, zhishi (*Fructus Aurantii Immaturus*) 10 g, xiangfu (*Rhizoma Cyperi*) 12 g, baishaoyao (*Radix Paronyiae Alba*) 12 g, huanglian (*Rhizoma Coptidis*) 5 g, wuzhuyu (*Fructus Evodiae*) 3 g, jineijin (*Matsa Fermentatae Medicinalis*) 12 g, shenggancao (*Radix Glycyrrhizae*) 12 g, maiya (*Rhizoma Pseudostellariae Heterophylla*) 20 g, shanyao (*Rhizoma Dioscoreae*) 12 g, huanglian (*Rhizoma Coptidis*) 12 g, wuzhuyu (*Fructus Evodiae*) 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 taizishen 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 jineijin, 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 $\geq 95\%$; (2) obviously efficacious: great improvement of the major symptoms, CARS $\geq 70\%$ (3) efficacious: the major symptoms were improved, CARS $\geq 30\%$; (4) no effect: no improvement of the major symptoms, CARS $\leq 30\%$. CARS were calculated using the following formula:

$$CARS(\%) = \left(\frac{\text{accumulated scores before treatment} - \text{accumulated scores after treatment}}{\text{accumulated scores before treatment}}\right) \times 100\%.$$  

**Assessment of *H pylori* eradication**

*H pylori* infection was detected by the combination of C$^{13}$-urease breath test, Gram stain and rapid urease test of biopsy samples before treatment, and reassessed 4 wk after treatment. $\chi^2$ 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 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 |
| Dyscheia                  | Slight| Moderate | Severe |
| Dry stools                | Occasionally| Frequently| Severe |
| Black stools              | Occasionally| Moderate | Severe |
| Anorexia                  | Reduction of food ≤ 1/4| Reduction of food ≤ 1/3| Reduction of food ≤ 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               |

Table 4 Relationship between efficacy and H pylori infection

| Results of treatment | Effective | Ineffective | Total |
|----------------------|-----------|-------------|-------|
| **H pylori positive** before treatment | 54        | 2           | 56    |
| **H pylori negative** before treatment | 28        | 6           | 34    |
| Total                | 82        | 8           | 90    |

Table 5 Relationship between efficacy and H pylori eradication

| Results of treatment | Effective | Ineffective | Total |
|----------------------|-----------|-------------|-------|
| **H pylori eradicated** after treatment | 37        | 1           | 38    |
| **H pylori non-eradicated** after treatment | 13        | 5           | 18    |
| Total                | 50        | 6           | 56    |

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. 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. 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\cite{11-20}. 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\cite{16-20}.

The composition of Hewei-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 \textit{H pylori} infection may be an important pathogenic factor in CAG\cite{11-20}. So it is reasonable to take the eradication of \textit{H pylori} as an objective measurement to evaluate the therapeutic effect on CAG.

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

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

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