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Efficacy and safety of Huangqi Jianzhong decoction in the treatment of chronic atrophic gastritis: A meta-analysis

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Abstract

BACKGROUND

Chronic atrophic gastritis is a persistent disorder of the digestive system where the gastric mucosa epithelium and glands undergo atrophy, leading to a decrease in their number and thinning of the gastric mucosa. It is worth noting that the prevalence of chronic atrophic gastritis is higher in China compared to the global average, and it is also considered a precancerous condition for gastric cancer.

AIM

Chronic atrophic gastritis is a persistent illness characterized by the progressive disappearance of healthy gastric glands due to repeated injury. Huangqi Jianzhong decoctions are widely used in China to treat chronic atrophic gastritis. However, there is limited scientific evidence regarding their efficacy in treating this illness. This study aimed to evaluate the efficacy of Huangqi Jianzhong decoction in treating chronic atrophic gastritis.

METHODS

The present meta-analysis adhered to the PRISMA guidelines and used the Cochrane Collaboration methodology. We performed a comprehensive search for clinical trials investigating the use of Huangqi Jianzhong decoction in treating chronic

atrophic gastritis published until January 2023. The risk of bias and the quality of the included studies were evaluated using the Cochrane Handbook guidelines. Finally, a meta-analysis was conducted using the RevMan 5.4 software.

RESULTS

INTRODUCTION

Chronic atrophic gastritis is characterized by the loss of gastric glandular structures caused by inflammation. [1] The prevalence rate of chronic atrophic gastritis in China is higher than the global incidence of 0%–10.9%.[2] This illness is currently classified as a precancerous stomach lesion.[3] Gastric cancer is the fifth most common cancer worldwide and the third leading cause of cancer-related deaths.[4] Given these facts, appropriate management of chronic atrophic gastritis is critical.[5] The majority of chronic atrophic gastritis cases are associated with *Helicobacter pylori* (HP) infection, which should be treated in most cases.[6] However, recent studies have indicated that the eradication rate of HP has decreased below 80% owing to increased antibiotic resistance, lack of compliance, and adverse effects.[7] Therefore, alternative treatments that can effectively and safely reduce the symptoms of chronic atrophic gastritis and improve patients' quality of life must be investigated.

Traditional Chinese medicine (TCM) is currently a viable treatment option.[8] TCM doctors assess a patient's condition by examining tongue manifestations, pulse palpation, and specific symptoms before prescribing a medicine. [9] In TCM, a syndrome refers to a group of symptoms experienced by a patient. [10] Patients with chronic atrophic gastritis may present with the cold–heat complex syndrome, which is characterized by symptoms including distending stomach pain, belching, and a yellow tongue coating.

Huangqi Jianzhong decoction is a traditional Chinese herbal formula comprising seven herbs, including Fructus Jujube (Dazao), Radix Astragali (Huangqi), Rhizoma Zingiberis Recens (Shengjiang), Ramulus Cinnamomi (Guizhi), Radix Glycyrrhizae

(Gancao), Paeoniae Radix Alba (Baishao), and Saccharum Granorum (Yitang).[11] This decoction is used to treat gastrointestinal diseases, including chronic gastritis, atrophic gastritis, peptic ulcers, and HP-related gastritis, and was first mentioned in Zhongjing Zhang's *Synopsis of Prescriptions of the Golden Chamber*.[11] A previous study found that Huangqi Jianzhong decoction can reduce TNF, IL-1, and IFN levels.[12] However, the safety and efficacy of this herbal formula remain debatable.

Herein, a systematic review of relevant literature was conducted to assess the efficacy and safety of Huangqi Jianzhong decoction in treating chronic atrophic gastritis. The study analyzed the total effective rate, HP clearance rate, pepsinogen I (PG-I) levels, TCM syndrome scores (including stomachache and acid reflux), recurrence rates, and any adverse effects associated with the use of Huangqi Jianzhong decoction.

MATERIALS AND METHODS

2.1. Study selection and search strategy

This meta-analysis adhered to the PRISMA guidelines and the Cochrane Collaboration methodology.[13] A comprehensive search was conducted across nine electronic databases, including PubMed, Web of Science, Cochrane Library, Embase, Medline, CNKI, Wanfang, Cqvip, and SinoMed. The search was performed from the inception of the databases until January 2023. The following keywords were used in the search strategy: (atrophic gastritis OR gastritis, atrophic OR CAG OR chronic gastritis OR gastric atrophy OR gastric mucosal atrophy) AND ("huangqi jianzhong decoction" OR "huangqi jianzhong tablets" OR "huangqi jianzhong formula" OR "huangqi jianzhong pills" OR "huangqi jianzhong capsules" OR "huangqi jianzhong tang"). This strategy aimed to identify relevant studies on the use of Huangqi Jianzhong decoction for treating chronic atrophic gastritis.

2.2. Inclusion and exclusion criteria

The meta-analysis included studies that met the following inclusion criteria: (1) patients diagnosed with chronic atrophic gastritis based on endoscopy and pathology; (2) participants aged ≥18 years; and (3) the primary outcomes of interest were the total effective rate, HP clearance rate, PG-I levels, TCM syndrome scores, recurrence rates, and adverse effects. Studies were excluded based on the following criteria: (1) non-clinical trials; (2) studies without full-text availability; and (3) studies lacking comprehensive data. A total of 13 studies that met the inclusion criteria were included in the meta-analysis.

2.3. Data extraction and quality evaluation

The literature reviews were conducted independently by two researchers. They reviewed the titles and abstracts of the identified studies based on the established exclusion and inclusion criteria. Studies that did not meet the criteria were excluded. The researchers then reviewed the full text of the selected studies for final inclusion. Disagreements between the two researchers were assessed by a third-party researcher during the screening process and resolved through negotiation. Data including authors, publication details, participant age and sex, intervention, study duration, and results were extracted from the selected studies. The risk of bias of all included studies was independently assessed by the two researchers, and any disagreements were resolved by a third-party researcher. The included studies' risk of bias was assessed following the Cochrane Handbook guidelines, evaluating seven key domains: random sequence generation, allocation concealment, caregiver blinding, patients, outcome assessors, incomplete outcome data collection, and selective reporting. Each domain was assigned a score, with 2, 1, and 0 indicating a high risk, unclear risk, and low risk of bias, respectively. The overall risk of bias was classified as follows: a score of 0–2 indicated a low risk of bias (high quality), that of 3–5 indicated a moderate risk of bias (moderate quality), and that of 6–8 indicated a high risk of bias (low quality).

2.4. Data analysis and outcomes

In this study, several outcome indicators were used, including the total effective rate, HP clearance rate, PG-I levels, TCM syndrome scores, recurrence rates, and adverse effects. The total effective rate was calculated using the following formula: (number of clinical recoveries + number of effective cases + number of markedly effective cases) divided by the total number of cases and the resulting value multiplied by 100%. Additionally, statistical analysis was conducted using RevMan 5.4. Categorical variables were expressed as relative risks (RRs) with 95% confidence intervals (CIs), whereas continuous variables were expressed as mean differences (MDs) with 95%CIs. A p-value of <0.05 was considered statistically significant. The I^2 statistic was used to examine heterogeneity among the included studies. A fixed-effects model was used if I^2 was <50% (low heterogeneity), whereas a random-effects model was used if I^2 was >50% (significant heterogeneity). A sensitivity analysis was performed to evaluate the reliability and stability of the results by removing the study with the greatest weight from the analysis. Funnel plots were used to assess publication bias in randomized controlled trials (RCTs) involving ≥10 participants. Funnel plots can help identify potential bias or asymmetry in data. These statistical analyses were performed to assess the robustness and validity of the findings of our meta-analysis.

RESULTS

3.1. Study search and selection

The sequential steps in the literature search process are shown in Figure 1. A total of 13 studies involving 1,269 participants were included in the meta-analysis. Initially, the database searches yielded 474 studies. Of these, 104 duplicates were removed, and the remaining 370 studies were further evaluated. From these, 13 studies were selected for the meta-analysis (Figure 1). Table 1 provides a comprehensive overview of the study characteristics, including age, sex, number of cases, interventions, and outcomes assessed.

Figure 1. Flow diagram illustrating the study selection process.

Table 1. Descriptions of the studies included in the review.
HQJZD: Huangqi Jianzhong decoction.

3.2. Evaluation of risk of bias in the included studies

Among the included studies, eight had a high risk of bias, while five had a moderate risk of bias. The most prevalent biases among the studies were related to random sequence generation and allocation concealment. Figure 2 depicts a graphical representation of the risk-of-bias assessment.

Figure 2. Overview of the risk of bias associated with the reviewed studies.

3.3. Assessment of the primary outcome

3.3.1. Total effective rate

Thirteen studies were included in the total effective rate analysis. As shown in Figure 3, the experimental group showed a significant decrease in the total effective rate (RR = 1.24; 95%CI [1.18, 1.30], $p < 0.001$), with a low heterogeneity ($I^2 = 0\%$; $p = 0.6$), compared with the control group. Furthermore, evaluation of the funnel plot asymmetry revealed little evidence of publication bias. Moreover, the data did not change significantly after excluding the study with the highest weight from the analysis.

Figure 3. Forest plots representing the effect of chronic atrophic gastritis on the total effective rate in the experimental group *vs* the control group.

3.3.2. HP clearance rate

This meta-analysis included two studies that reported improvements in HP clearance rates. Figure 4 shows the effect of chronic atrophic gastritis on the total HP clearance rate, demonstrating a significant effect (RR = 1.20; 95%CI [1.05, 1.38],

$p = 0.009$). Low heterogeneity was observed ($I^2 = 0\%$; $p = 0.36$), indicating a consistent outcome across the studies. Furthermore, the data remained unchanged after excluding the study with the highest weight from the analysis.

Figure 4. Forest plots representing the effect of chronic atrophic gastritis on the HP clearance rate in the experimental group *vs* the control group.

3.3.3 PG-I levels

Four studies that analyzed PG-I levels were included in this meta-analysis, and the effect of Huangqi Jianzhong decoction on these levels is shown in Figure 5. No significant difference in PG-I levels was observed between the two groups (MD = 4.99; 95%CI [−1.59, 11.58], $p = 0.14$). However, there was no significant heterogeneity ($I^2 = 99\%$; $p < 0.001$), indicating variability among the studies. Furthermore, the data did not exhibit significant changes after excluding the study with the highest weight from the analysis.

Figure 5. Forest plots representing the effect of chronic atrophic gastritis on PG-I levels in the experimental group *vs* the control group.

3.3.4 TCM syndrome scores

This meta-analysis included seven studies focusing on stomachache improvement. Figure 6 shows the role of Huangqi Jianzhong decoction in alleviating stomachache. The Huangqi Jianzhong decoction group exhibited a significant improvement in stomachache compared with the control group (MD = −0.63; 95%CI [−0.68, −0.58], $p < 0.001$; Figure 6A). However, substantial heterogeneity ($I^2 = 54\%$; $p = 0.04$) was observed, indicating variability among the studies. The analysis also revealed a significant difference in acid reflux between the two groups (MD = −0.48; 95%CI [−0.63, −0.33], $p < 0.001$), despite marked heterogeneity ($I^2 = 82\%$; $p < 0.001$;

Figure 6B). The results showed no significant changes after excluding the study with the highest weights from the analysis.

Figure 6. Forest plots representing the effect of chronic atrophic gastritis on stomachache and acid reflux in the experimental group *vs* the control group.

3.3.5. Recurrence rates and adverse effects

Two studies comparing Huangqi Jianzhong decoction with a control group were included in the pooling data for the recurrence rates of patients with chronic atrophic gastritis. A significant difference in recurrence rates was observed between the Huangqi Jianzhong decoction and control groups (RR = 0.15; 95%CI [0.04, 0.66], $p = 0.01$]. Low heterogeneity was observed ($I^2 = 0$%; $p = 0.92$), indicating a consistent outcome across the studies. Furthermore, five studies were pooled to compare the adverse effects in the Huangqi Jianzhong decoction and control groups. However, no significant difference in adverse effects was observed between the two groups (RR = 1.07; 95%CI [0.53, 2.17], $p = 0.86$; Figure 7). Moreover, the data did not exhibit significant changes after excluding the study with the highest weight from the analysis.

Figure 7. Forest plots representing the effect of chronic atrophic gastritis on recurrence rates and adverse effects in the experimental group *vs* the control group.

DISCUSSION

This study aimed to conduct a comprehensive review of the scientific literature on the efficacy and safety of Huangqi Jianzhong decoction in patients with chronic atrophic gastritis. The results suggest that Huangqi Jianzhong decoction is an effective treatment for this illness. The study demonstrated that the Huangqi Jianzhong decoction group exhibited significant improvements in the total effective rate, HP clearance rates, and TCM syndrome scores (associated with stomach pain and acid reflux), as well as decreased recurrence rates compared with the control group.

Huangqi Jianzhong decoction has been used to treat various symptoms, including abdominal upset or pain, belching, abdominal bloating, nausea, vomiting, loose stools, sensations of fullness, upper abdominal burning, and lower extremity coldness or weakness. Existing data support its use in the treatment of chronic gastritis,[8] suggesting that Huangqi Jianzhong decoction has many therapeutic targets in treating chronic gastritis.[8] The results of our meta-analysis support previously reported findings. [12-15] Furthermore, using Huangqi Jianzhong decoction, the total effective rate and HP clearance rate significantly improved, whereas the scores for stomachache and acid reflux and the recurrence rates of patients significantly decreased. These findings are statistically significant and consistent with earlier findings. [12-15]

We also assessed the safety of Huangqi Jianzhong decoction by examining its adverse effects. There were no significant differences in adverse effects between the Huangqi Jianzhong decoction and control groups. However, it is essential to note that only one study reported adverse effects in both groups. In the control group, adverse effects including nausea, mild gastrointestinal reactions, and bloating were reported, while in the Huangqi Jianzhong decoction group, adverse effects included headache, rash, nausea, and mild gastrointestinal reactions [16].

This study had several limitations. First, among the included trials, only three provided information on how participants were randomly assigned to experimental groups, and none provided follow-up data. This could introduce potential biases in the results. Second, while HP infection is the most prevalent cause of chronic atrophic gastritis, other factors can also contribute to this illness. The specific causes in the included studies may not have been fully investigated. Third, all the clinical trials included in this meta-analysis were conducted and published in China, which could limit the generalizability of the findings to other populations. Notably, the overall effect rate was used as the primary outcome measure in all trials to assess the efficacy of Huangqi Jianzhong decoction in treating chronic atrophic gastritis.

CONCLUSION

This review emphasizes the efficacy of Huangqi Jianzhong decoction in improving the total effective rate, HP clearance rate, TCM syndrome scores, and recurrence rates in adults with chronic atrophic gastritis. Furthermore, we recommend conducting additional high-quality RCTs to further evaluate this treatment strategy.

ARTICLE HIGHLIGHTS

Research background

Chronic atrophic gastritis is a persistent disorder of the digestive system where the gastric mucosa epithelium and glands undergo atrophy, leading to a decrease in their number and thinning of the gastric mucosa. It is worth noting that the prevalence of chronic atrophic gastritis is higher in China compared to the global average, and it is also considered a precancerous condition for gastric cancer.

Research motivation

Currently, Western medicine treatments for chronic atrophic gastritis can only slow down the progression of the disease and are not capable of providing an effective cure. Therefore, we aim to investigate the therapeutic effects of Huangqi Jianzhong Decoction on chronic atrophic gastritis from the perspective of traditional Chinese medicine, aiming to enhance patients' quality of life.

Research objectives

To assess the therapeutic efficacy of Huangqi Jianzhong Decoction for chronic atrophic gastritis.

Research methods

We conducted a literature review on the treatment of chronic atrophic gastritis with Huangqi Jianzhong Decoction, focusing on publications up until January 2023. The

collected literature was analyzed for heterogeneity, and a meta-analysis was performed using Revman 5.4 and the Cochrane Handbook.

Research results

We included a total of 13 articles, comprising 1269 patients. The findings of our analysis revealed that the use of Huangqi Jianzhong Decoction in the treatment of chronic atrophic gastritis led to significant improvements in various aspects. These improvements included an increased clearance rate of Helicobacter pylori, alleviation of symptoms such as stomach pain, and a reduction in the recurrence rate of patients. However, there was no significant change observed in the levels of Pepsin I.

Research conclusions

Huangqi Jianzhong Decoction has a significant therapeutic effect on patients with chronic atrophic gastritis, including improvements in the clearance rate of Helicobacter pylori, reduction of stomachache, alleviation of gastric acid reflux, and decreased disease recurrence rate.

Research perspectives

Traditional Chinese medicine represents a longstanding treatment approach in China. When approaching the treatment of chronic atrophic gastritis from a traditional Chinese medicine perspective, our focus lies not only on symptom relief but also on studying treatment methods that effectively address the condition. By doing so, we aim to improve the overall quality of life for patients, going beyond mere alleviation of the disease process.

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