

Traditional Chinese Medicine as add-on treatment of triple/quadruple therapy for *Helicobacter pylori* infection: an overview of systematic reviews and meta-analyses (Protocol)

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Abstract:

Background: In recent years, many studies reported the anti-Hp effects of Traditional Chinese Medicine. Based on these studies, there had been many relevant systemic reviews and meta analyses with variable results

Aim: This overview aims to investigate the general characteristics and assess the methodological quality of these systemic reviews/meta analyses (SR/MAs).

Method: In this overview, we intend to include systemic reviews/meta analyses with comparison of Chinese medicine and western medicine on *Helicobacter pylori* infection by searching databases of Medline, Embase, Web of Science, China National Knowledge Infrastructure Database (CNKI), Chinese VIP Information (VIP), Chinese Medical Databases (CMB) and Wan-Fang Database until January 6st, 2026. AMSTAR 2 and GRADE system tools will be adopted to assess the methodological quality and evidence quality characteristics.

Conclusion: The methodological quality of these SR/MAs will be assessed as clinical evidence and our result may help further use of them.

Key Words: traditional Chinese medicine; *Helicobacter pylori*; systemic review;

Introduction

HELICOBACTER PYLORI (Hp) is a gram-positive and microaerophilic bacterium that colonizes the gastric mucosa.^{1,2} Globally, >50% of people are infected, and the overall prevalence is higher in developing countries.² Hp is one of the major factors inducing pathological changes such as gastritis and digestive ulcer, as well as atrophy, intestinal metaplasia, intraepithelial neoplasia, and mucosa-associated lymphoid tissue lymphoma (MALT).² Diagnostic tests for Hp infection include rapid urease test, urease breath test, culture, microscopic demonstration of the organism, stool antigen, antibody response as well as endoscopy.³

Proton pump inhibitors (PPIs) in combination with antibiotics have been used for eradicating Hp. PPI based triple therapy, a 14-day treatment with PPI and two antibiotics (e.g. clarithromycin and amoxicillin) was recommended previously and adopted worldwide with a reported eradication rate of 70%–85%.² However, in recent decades, reports from different areas showed that the eradication rate of

clarithromycin triple therapy declined.² Resistance of antibiotic was thought to be the main cause of the decline.⁴ What's more, antibiotic resistance rates are increasing throughout world.^{4,5} Triple therapy was not recommended to be utilized in areas with high rates of clarithromycin resistance.^{1,2}

In recent years, many studies reported the anti-Hp effects of Traditional Chinese Medicine (TCM) which included Chinese proprietary medicine (e.g. Jing Hua Wei Kang Capsule⁶), Chinese medicine extractives (e.g. berberine⁷) and Chinese herbs (e.g. Ban Xia Xie Xin Soap⁸). Many randomized controlled trials were complemented to evaluate the efficacy and safety of TCM combined with PPI-based triple therapy (PTT, i.e. PPI plus two antibiotics) or bismuth containing quadruple therapy (BCQT, i.e. PPI, bismuth and two antibiotics). Based on these studies, there had been many relevant systemic reviews and meta-analyses with variable results.⁶⁻⁸ This overview aimed to investigate the general characteristics and assess the quality of these systemic reviews/meta analyses (SR/MAs).

Methods

Source of literature and search strategy

We intend to perform a systemic literature search in the databases of MEDLINE, EMBASE, Web of Science, China National Knowledge Infrastructure Database (CNKI), Chinese VIP Information (VIP), Chinese Medical Databases (CMB) and Wan-Fang Database until January 6st, 2026. The articles of academic journals, dissertation and conference proceedings will also be included as well irrespective of gray literature status. The search strategies for electronic databases are listed in Appendix 1 (taking PubMed as an example). What's more, the reference lists of studies will also be searched for potentially relevant titles.

Inclusion and Exclusion criteria

The following criteria will used for literature selection, and the studies that meet the criteria are eligible for further overview. (1) Patients: The subjects enrolled were Hp infectors with/without Hp related diseases such as gastritis, ulcer, etc. The diagnosis of Hp infection accord with guidelines of "Fifth Chinese National Consensus Report on the management of Helicobacter pylori infection". (2) Interventions: The subjects in Treatment group underwent interventions of Traditional Chinese Medicine combined with PTT or BCQT. The Chinese medicine included Chinese herb medicine, Chinese proprietary medicine but not Chinese herbal medicine extractives. (3) Control: The subjects in control group underwent therapies of PTT or BCQT only. (4) Outcomes: The main outcome was eradication rate. The secondary outcome could be side effect rate, relief of digestive symptoms (remission rate), and healing of ulcer (healing rate and total effectiveness rate). (5) Study type: The study design consisted of a systemic review and/or meta analyses (SR/MA).

The studies that meet these criteria will be excluded: (1) The articles of redundant publications; (2) The studies that did not complement calculation of meta-synthesis although titled "meta-analysis" or "systemic review". (3) Systemic reviews of studies in vitro; (4) Articles published as abstracts or protocols no matter their publication types.

Study selection

All retrieved trials will be screened by 2 reviewers independently in steps. Step 1, a potential screening of titles and abstracts will be implemented for relevant articles. Step 2, full text screening will be retrieved than for further assessment according to the inclusion and exclusion criteria. The plan for solving disagreement is discussing or consulting of another specialist.

Data collection

Two reviewers independently extract the data from including SR/MAs with the items of authors, publication year, sample size, intervention in groups, main outcome of eradication rate and secondary outcomes (remission of digestive symptoms, healing of digestive ulcers and side effects). Piloted forms will be built for data extraction.

Appendix 1 Searching Strategy for Medline

- #1. "Helicobacter pylori"[Mesh] OR Helicobacter pylori[Title/Abstract]
- #2. "Medicine, Chinese Traditional"[Mesh] OR herbal medicine OR herb* OR Chinese medicine OR traditional Chinese Medicine OR Chinese Traditional Medicine OR TCM[Title/Abstract] OR herbal formula decoction OR proprietary medicine OR patent medicine
- #3. "meta-analysis"[Publication Type] OR meta analysis[Title/Abstract] OR meta-analysis[Title/Abstract] OR systemic review[Title/Abstract]
- #4. #1 AND #2 AND #3

Eradication rate was defined as negative rate after eradication therapy.³ Healing of ulcers was divided into 3 grades, i.e. curing, effectiveness and non-effectiveness, according to endoscopy examinations before and after eradication therapy. Curing was defined as disappear of ulcer lesion and inflammatory manifestation around. Effectiveness meant ulcer lesion narrowed to be less than 50%. Non-effectiveness meant ulcer narrowed but still more than 50%. Healing rate was defined to be ratio of curing numbers and total numbers (Healing rate=curing number/total number × 100%). Total effectiveness rate of ulcer was defined as percentage of patients with curing, effectiveness (Total effectiveness rate = [(total number – non-effectiveness number)/total number × 100%].⁹ Total remission rate of digestive symptoms was defined as the percentage of patients with relief of any digestive symptoms.⁷ Side effect rate was defined to be the percentage of patients with at least one side effect.⁹

Assessment of methodological quality

Two reviewers assess the quality of each included review independently. Assessment of Multiple Systematic Review 2 (AMSTAR 2) scale⁹ will be adopted for assessment of methodological quality. A piloted form will also be built for data extraction and further assessment.

Assessment of quality of clinical evidences

The Grades of Recommendations, Assessment, Development and Evaluation (GRADE) approach was used to assess the level of evidence and summarize each outcome by two reviewers independently.¹⁰

Conclusion

Our study will generate evidence for TCM in the treatment of Hp infection and help to reduce the uncertainty about the effectiveness of Hp infection, which will encourage further suggestions for TCM clinical practice or guideline.

Conflict of Interest

The authors declare no conflicts of interest.

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