Efficacy of traditional Chinese medicine for chronic gastritis
A meta-analysis of randomized controlled trials

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Abstract
Background: To systematically evaluate efficacy of traditional Chinese medicine (TCM) in treating chronic gastritis (CG).

Methods: Data sources from PubMed, Embase, Springer Link, China National Knowledge Infrastructure, Chinese Scientific Journals Database, Chinese Biomedicine Database, and Wan-fang database were searched up to July 5, 2018. Review Manager software version 5.3, the Cochrane Collaboration’s risk of bias tool, and the Grading of Recommendations Assessment, Development, and Evaluation profiler software were conducted for this meta-analysis.

Results: Sixteen studies involving 1673 participants (906 vs 767) were included in this study. Pooled data showed significant statistical differences between TCM groups and current routine pharmacotherapy (RP) groups in overall clinical efficacy (odds ratio [OR] 4.65; 95% confidence interval [CI] 3.29, 6.56; P < .00001), efficacy under endoscopy (OR 2.46; 95% CI 1.12, 5.43; P = .03), stomach distension (mean difference [MD] −0.37; 95% CI −0.56, −0.19; P < .0001), stomachache (standardized MD [SMD] −0.80; 95% CI −1.45, −0.14; P = .02), and belching (SMD −2.00; 95% CI −3.80, −0.20; P = .03). However, acid regurgitation (SMD −0.71; 95% CI −1.69, 0.28; P = .16) and anorexia (SMD −0.75; 95% CI −2.30, 0.80; P = .38) showed no significant statistical differences between 2 groups. In addition, incidence of adverse reactions of TCM groups was lower than that of RP groups.

Conclusion: Evidence from this meta-analysis suggests that TCM could be more efficacious than current RP in treating CG. But further standardized research of rigorous design should be needed to further validate its efficacy.

Abbreviations: CAG = chronic atrophic gastritis, CG = chronic gastritis, CIs = confidence intervals, CSG = chronic superficial gastritis, EGFRs = epidermal growth factor receptors, GC = gastric cancer, GRADE = the Grading of Recommendations Assessment, Development, and Evaluation, Hp = Helicobacter pylori, MD = mean difference, NF-κB = nuclear transcription factor kappa B, OR = odds ratio, PGE2 = prostaglandin E2, RCTs = randomized clinical trials, RP = routine pharmacotherapies, SMD = standardized mean difference, TCM = traditional Chinese medicine.

Keywords: chronic gastritis, meta-analysis, traditional Chinese medicine

1. Introduction

Chronic gastritis (CG) is defined as an inflammation even atrophy on the gastric mucosa, usually accompanied with gastric mucosal lesions including structural alterations of glandular compartment. Based on its different elementary lesions, this condition is classified into 2 different levels: a basic level and a hierarchically higher level. Helicobacter pylori (Hp), as a class I carcinogen, is the most common cause of CG around the world. Furthermore, CG is biologically and epidemiologically connected with the development of gastric cancer (GC) in a population. With an increasing incidence of CG in China, risk of GC has been growing, thereby seriously affecting people’s daily life.

Numerous efforts including histopathologic examination of gastric biopsy specimens have been made to look into pathogenesis of CG, but we lack a straightforward analysis of cancer risk, as well as its treatment. As current routine pharmacotherapies (RPs), Hp eradication agents, antiacid, spasmylocytic, and gastric mucosa protectant have been put into clinical practice. However, efficacy of these RP is less than satisfactory. Therefore, many sufferers have turned to traditional Chinese medicine (TCM) for help. So far, 4 relevant studies have been published. However, 2 conducted meta-analyses of chronic atrophic gastritis (CAG) not
One reported a systematic review of Huangqi Jianzhong Tang for CG. The remaining 1 reported a PRISMA-compliant systematic review and meta-analysis of common mechanism of pathogenesis in gastrointestinal diseases treating in single Chinese medicine formula. Nevertheless, the current state of evidence of TCM for CG remains inadequately explained. Therefore, a meta-analysis of randomized controlled trials was conducted to evaluate its efficacy.

2. Materials and methods

2.1. Searching strategy

The following seven electronic databases were searched up to July 5, 2018: PubMed, Embase, Springer Link, China National Knowledge Infrastructure, Chinese Scientific Journals Database, Chinese Biomedicine Database, and Wan-fang database. No limitation was conducted for language in literature search. Ambiguous or missing information was obtained through combining electronic searches with manual searches. The following medical terms used individually or in combination in literature retrieval were as follows: “traditional Chinese medicine,” “TCM,” “Chinese medicine,” “herbs,” “chronic gastritis,” “gastritis,” and “randomized controlled trial.”

2.2. Inclusion and exclusion criteria

Literatures meeting all of the following criteria were included: randomized controlled trials; patients with CG; more than 4 weeks in treatment course; and RP including Hp eradication agents, antacid, spasmylytic, or gastric mucosa protectant. Literatures meeting the following criteria were excluded: literature reviews; no control group; not TCM but RP in experiment groups; and incomplete or error data in included literatures.

2.3. Literature screening

Literature search, study selection, and data extraction were independently conducted by 2 reviewers. Information of data extraction was as follows: authors, study design (baseline), characteristics of patients, sample size, details of intervention, and outcome measurements (primary outcome, secondary outcomes, follow-up, withdrawals or dropouts, and side effects). One reviewer extracted the initial data, and the other subsequently reexamined each trial and verified their results.

2.4. Quality assessment

The evaluation of methodologic quality was conducted by 2 independent researchers on the basis of the Cochrane Collaboration’s risk of bias tool. The specific details were as follows: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; and selective reporting. Disagreements were resolved after discussing with a 3rd investigator.

2.5. Data synthesis and analysis

Review Manager 5.3 software was used for statistical analysis from more than 2 separate studies to generate forest plots, 95% confidence intervals (CIs), and odds ratio (OR) or standardized mean difference (SMD) or mean difference (MD). Statistical heterogeneity was statistically computed by using the Chi-squared ($\chi^2$) test and inconsistency index statistic ($I^2$). A model of fixed effect could be appropriate where statistical heterogeneity exists ($I^2 < 50\%$ or $P > .05$). Otherwise, random effect model was used ($I^2 > 50\%$ or $P < .05$). In addition, potential sources of substantial heterogeneity were evaluated by sensitivity analysis. And publication bias was estimated by funnel plots. Meanwhile, to understand current situation of evidence rating and analyze possible problems, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was performed to grade the evidence quality of published systematic reviews/meta-analyses of CG. GRADE profiler version 3.6 was used for calculating overall quality of grading evaluation for the review of evidence.

3. Results

3.1. Study description

Based on the retrieval strategy and screened records, a total of 1260 full-text articles were initially identified. In accordance with our inclusion and exclusion criteria, 16 randomized clinical trials involving 1673 participants (906 in experiment groups and 767 in control groups) were included in this study. All trials were published on Chinese literatures in China mainland. Experiment groups used TCM while control groups used RP. Flow chart of literature search process is shown in Figure 1. Clinical characteristics of included studies are described in Table 1. Meanwhile, to present discrepancies among different TCMs, constituents of herbal formulae are listed in Table 2.

3.2. Risk of bias evaluation

Two researchers independently evaluated methodologic quality of included trials using the Cochrane Collaboration’s risk of bias tool. And results of this quality summarized in Table 3 showed that all included studies were biased with high risks and the quality was generally poor. But all of them accounted for baseline comparability. As for generation of random sequence, 4 studies used specific methods including random number table, coin flipping, and picking method. However, the remaining eleven only mentioned “randomization” with no explanation of random-allocation process. Besides, no studies mentioned or allocation concealment. Meanwhile, considering the integrity of outcome data, follow-up visit, and intention-to-treat analysis should have been conducted for all included studies. And only 3 trials reported no withdrawals or dropouts in treatment course. In a word, inadequate reporting may result in possible bias and risk validity of the results (Fig. 2).

3.3. Effects of the interventions: primary outcome

3.3.1. Comparison of overall clinical efficacy

Based on the TCM Illness Diagnosis Affect Standard and Guiding Principles for Clinical Research of New TCM, efficacy assessment is divided into 4 grades: cure, clinical symptoms disappeared; markedly effective, clinical symptoms markedly improved; effective, clinical symptoms improved; ineffective, clinical symptoms did not improve even deteriorate. Specifically, improvement of clinical symptoms is not only evaluated by clinical manifestation, but judged from pathologic changes on
gastric mucosa by endoscopy. Therefore, both of the 2 items are used for overall clinical efficacy. In addition, symptom scores are analyzed by mean ± standard deviation. Meanwhile, according to the nimodipine method,[40] efficacy index is calculated with a formula \[ \frac{\text{pretreatment symptom scores} - \text{posttreatment symptom scores}}{\text{pretreatment symptom scores}} \times 100\% \]. In addition, we did not conduct a sensitivity analysis because of no substantial heterogeneity in primary outcome.

3.3.2. TCM vs RP. Fifteen studies[23–36,38] with a total of 1547 patients reported overall clinical efficacy. Because of discrepancy in treatment courses, subgroup analysis of durations of 4, 6, and 8 weeks was performed. Meanwhile, with a good homogeneity \( \chi^2 = 5.05, P = .99, I^2 = 0\% \) for this analysis, a fixed effect model was conducted to estimate pooled effect size. Results of subgroup analysis showed that higher clinical efficacy rate was attributed to TCM groups than RP groups for 4 weeks (OR 4.47; 95% CI 2.71, 7.37; \( P < .00001 \)),[23,24,26,28,32,34,36,38] 6 weeks (OR 9.15; 95% CI 1.91, 43.90; \( P = .006 \))[30] and 8 weeks (OR 4.45; 95% CI 2.68, 7.37; \( P < .00001 \)).[25,27,29,31,33,35] Meanwhile, the combined OR was 4.65 (95% CI 3.29, 6.56) with significant overall effect (\( Z = 8.71, P < .00001 \)) between TCM groups and RP groups (Fig. 3). However, potential publication bias was observed by asymmetrical funnel plot in Figure 4.

3.4. Secondary outcomes
3.4.1. Efficacy under endoscopy. In the period of treatment, 3 trials including 282 participants reported efficacy under endoscopy.[26,33,37] Because of no significant heterogeneity \( \chi^2 = 0.85, P = .65, I^2 = 0\% \), a fixed effect model was performed (Fig. 5). Meanwhile, higher efficacy under endoscopy was attributed to TCM groups than RP groups on the improvement

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**Figure 1.** Flow chart of the process for literature retrieval. CG = chronic gastritis, TCM = traditional Chinese medicine.
of pathologic changes of gastric mucosa (OR 2.46; 95% CI 1.12, 5.43; P = .03) (Fig. 5).

3.4.2. Stomach distension. In the included trials, TCM-treated 221 patients and RP-treated 218 patients were included in 4 trials of stomach distension improvement. As shown in Figure 6, pooled estimates were conducted by using a model of random effect for significant heterogeneity ($\chi^2 = 12.96, P = 0.005, I^2 = 77\%$). The combined MD was −0.37 (95% CI −0.56, −0.19) with significant overall effect ($Z = 3.92, P < .0001$), indicating that TCM groups had potentially superior to RP groups on the improvement of stomach distension.

3.4.3. Stomachache. Four trials of 221 patients in TCM group and 218 in RP group were qualified with description of stomachache alleviation. Considering significant heterogeneity ($\chi^2 = 29.53, P < .00001, I^2 = 90\%$) between 2 groups in Figure 7, random-effects model was used for statistical analysis. Meanwhile, results of this analysis favored TCM group by pooled data (SMD = −0.80; 95% CI −1.45, −0.14) and test for overall effect ($Z = 2.39, P = .02$).

3.4.4. Acid regurgitation and belching. Four studies of acid regurgitation and belching involving 439 patients were identified for the comparison between TCM groups and RP groups. As shown in Figures 8 and 9, significant heterogeneity can be perceived both acid regurgitation ($\chi^2 = 66.02, P < .00001, I^2 = 95\%$) and belching ($\chi^2 = 150.29, P < .00001, I^2 = 98\%$) (Fig. 9). Therefore, random effect models were conducted. However, compared with RP groups, TCM

### Table 1

| Study ID (author, year) | No. of participants (E/C) | Age (E/C) | Duration | Experiment group | Control group (RP) | Outcome measures |
|-------------------------|---------------------------|-----------|----------|------------------|-------------------|-----------------|
| Zhao et al, 2018[24]    | 30/30                     | E: 26–79  | C: 24–80 | 4 wks            | TCM               | 1               |
| Guo et al, 2017[26]     | 40/38                     | E: 21–70  | C: 21–68 | 4 wks            | TCM               | 1               |
| Xue, 2017[25]           | 43/43                     | E: 46–76  | C: 47–75 | 8 wks            | TCM               | 1               |
| Zeng et al, 2015[27]    | 48/48                     | E: 21–70  | C: 23–68 | 4 wks            | TCM               | 1               |
| Jin, 2015[27]           | 43/43                     | E: 25–78  | C: 26–77 | 8 wks            | TCM               | 1               |
| Yu et al, 2015[28]      | 40/40                     | E: 22–76  | C: 22–76 | 4 wks            | TCM               | 1               |
| Yang et al, 2014[29]    | 100/100                   | E: 18–85  | C: 20–63 | 8 wks            | TCM               | 1               |
| Ye, 2014[29]            | 40/40                     | E: 27–78  | C: 28–76 | 6 wks            | TCM               | 1               |
| Yu, 2013[30]            | 40/40                     | E: 38.5 ± 2.3 | 8 wks | TCM               | 1               |
| Li, 2013[31]            | 64/64                     | E: 29–68  | C: 27–70 | 4 wks            | TCM               | 1               |
| Han, 2013[32]           | 30/30                     | E: 32–66  | C: 34–67 | 8 wks            | TCM               | 1               |
| Zhang et al, 2010[34]   | 33/32                     | E: 38.60 ± 8.48 | C: 39.95 ± 7.62 | 4 weeks | TCM               | 1               |
| Chen et al, 2009[35]    | 61/59                     | E: 18–77  | C: 19–81 | 8 wks            | TCM               | 1               |
| Lin, 2008[36]           | 90/58                     | E: 30–67  | C: 28–68 | 4 wks            | TCM               | 1               |
| Gong et al, 2006[37]    | 84/42                     | E: 19–65  | C: 20–61 | 17 wks           | TCM               | 1               |
| Guo, 2006[38]           | 120/60                    | E: 19–70  | C: 18–67 | 4 wks            | TCM               | 1               |

1 = overall clinical efficacy, 2 = gastroscopic cure rate, 3 = gastroscopic scores, 4 = clinical symptom scores, 5 = clinical symptom efficacy, 6 = clinical symptom improvement rate, 7 = the ratio of clinical symptom scores, 8 = Hp negative rate, 9 = pathologic scores, 10 = the rate of side effects, 11 = recurrence rate, 12 = the serum gastrin levels, E = experiment group, C = control group, Hp = Helicobacter pylori, TCM = traditional Chinese medicine, RP = routine pharmacotherapies.
Table 2
The ingredients of each formula.

| Author          | Ingredients of each formula                                                                 |
|-----------------|---------------------------------------------------------------------------------------------|
| Zhou et al., 2019[23] | Bupleurum chinense DC (Chai Hu) 10 g                                                        |
| Guo et al., 2019[24]  | Atractylodes macrocephala Koidz. (Ban Zhi) 15 g                                               |
| Jin, 2015[25]     | L. (Pu Gung Ying) 30 g                                                                       |
| Guo et al., 2017[26] | Atractylodes macrocephala DC (Chai Hu) 9 g                                                  |
| Li, 2013[27]      | Atractylodes macrocephala Koidz. (Ban Zhi) 15 g                                              |
| Zeng et al., 2015[28] | Poria cocos (Schw.) Wolf (Fu Ling) 14 g                                                      |
| Yu et al., 2015[29] | Poria cocos (Schw.) Wolf (Fu Ling) 14 g                                                      |
| Yang et al., 2015[30] | Poria cocos (Schw.) Wolf (Fu Ling) 14 g                                                      |
| Ye, 2015[31]      | Poria cocos (Schw.) Wolf (Fu Ling) 14 g                                                      |
| Yu, 2013[32]      | Poria cocos (Schw.) Wolf (Fu Ling) 14 g                                                      |
| Yan et al., 2018[33] | L. (Pu Gung Ying) 30 g                                                                       |

(continued)
groups had significant statistical difference in belching (SMD = −2.00; 95% CI = −3.80, −0.20; P = .03) (Fig. 9), while no significant statistical difference in acid regurgitation (SMD = −0.71; 95% CI = −1.69, 0.28; P = .16) (Fig. 8).

**3.4.5. Anorexia.** Three trials with description of anorexia improvement were included involving 239 participants (121 in TCM groups and 118 in RP groups). As shown in Figure 10, results implied that TCM groups were more positive effects than RP groups.

**3.4.6. Other secondary outcomes.** As for other secondary outcomes, Han study reported endoscopy scores and clinical symptom efficacy. Gong et al study reported clinical symptom improvement rate and Hp negative rate. Zhang et al study reported the ratio of clinical symptom scores. Yang et al study reported pathologic scores and the serum gastrin levels. Jin study and Yang et al study reported the rate of side effects. Gong and Gong study and Guo study reported recurrence rate. Because these outcomes were reported by only 1 or 2 studies, they were only qualitatively analyzed. However, with the evaluation of efficacy in treating CG, results implied that TCM groups were more positive effects than RP groups.

**3.5. Safety evaluation**

Meta-analysis of 6 trials evaluated safety of TCM in the course of treatment. Two had no adverse reactions during TCM treatment. Four reported adverse reactions, which included nausea, vomiting, abdominal pain, dizziness, diarrhea, constipation, anorexia, rash, waist and leg pain, sexual dysfunction, weak, abnormal weight loss. However, these adverse events did not have impact on experimental process.

**3.6. GRADE evidence of quality**

To grade evidence quality of this meta-analysis of CG and RP, GRADE system, which classifed the strength of recommenda-
Table 3
Evaluation of methodologic quality of the included studies based on the Cochrane Handbook.

| Study ID        | Baseline     | Randomization            | Blinding | Allocation concealment | Follow-up | Withdrawals or dropouts | Jadad score |
|-----------------|--------------|--------------------------|----------|------------------------|-----------|-------------------------|-------------|
| Zhao et al, 2018 [23] | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | NR          |
| Guo et al, 2017 [24] | Comparability | Random number table      | NR       | NR                     | NR        | NR                      | NR          |
| Xue, 2017 [25]    | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | NR          |
| Zeng et al, 2015 [26] | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | NR          |
| Jin, 2015 [27]    | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | NR          |
| Yu et al, 2015 [28] | Comparability | Coin flipping            | NR       | NR                     | NR        | No                      | 3           |
| Yang et al, 2014 [29] | Comparability | Mention not described    | NR       | NR                     | NR        | No                      | 3           |
| Ye, 2014 [30]     | Comparability | Picking method           | NR       | NR                     | NR        | No                      | 3           |
| Yu, 2013 [31]     | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | 1           |
| Li, 2013 [32]     | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | 1           |
| Han, 2013 [33]    | Comparability | Mention not described    | NR       | NR                     | NR        | No                      | 2           |
| Zhang et al, 2010 [34] | Comparability | Random number table      | NR       | NR                     | NR        | NR                      | 2           |
| Chen et al, 2009 [35] | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | 1           |
| Lin, 2008 [36]    | Comparability | Random sampling          | NR       | NR                     | NR        | NR                      | 1           |
| Gong et al, 2006 [37] | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | 1           |
| Guo, 2006 [38]    | Comparability | Mention not described    | NR       | NR                     | NR        | NR                      | 1           |

NR = not reported.

Figure 2. Risk of bias graph and summary.
tions as strong or weak, evaluates the quality of a body of evidence as high, moderate, low, and very low.\(^{41,42}\) Moreover, these levels were based on 5 downgrade factors: limitations, inconsistency, indirectness, imprecision, and publication bias.\(^{43-47}\) As shown in Figure 11, results of GRADE for this meta-analysis suggested that evidence quality was “very low.”

4. Discussion

Results of this meta-analysis show that TCM is superior to RP in the treatment of CG. Meanwhile, adverse events (namely safety evaluation) in TCM groups were significantly lower than that in RP groups, indicating that TCM can improve CG to a certain degree. Based on these, it possibly suggests that TCM is a promising therapy in treating CG and provides practitioners with important reference value on clinical syndrome differentiations. However, high risk of bias was identified in all included studies using the Cochrane Collaboration’s risk of bias tool. Moreover, results of GRADE evidence classification for the quality level indicated “very low,” which could imply that this meta-analysis did not include complete original data and some included trials contained a few methodologic defects.

It is well-established that Hp infection is the most common etiology associated with CG.\(^{48}\) This pathogenesis is related to inflammation cells (mononuclear cells, plasma cells, predominantly lymphocytes, and macrophages) infiltration,\(^{49-51}\) thereby resulting in gastric mucosal injury. Another pathogenesis of CG is associated with immune dysfunction that a complex interaction of autoantibodies against the parietal cell proton pump and sensitized T cells progressively destroy the parietal cells.\(^{52}\) So far, numerous modern pharmacologic researches have verified efficacy of TCM for CG. On one hand, an experimental datum has suggested that Wei-Wei-Kang-Granule could treat CAG in rats by regulating the expression of epiderminal growth factor receptors (EGFRs) and nuclear transcription factor kappa B (NF-\(\kappa\)B), whose mechanisms are possibly related with reduction in expression of EGFR and NF-\(\kappa\)B in gastric mucosa.\(^{53}\) Other animal experiment has showed that licoflavone could significantly ameliorate gastric pathology and increase serum prostaglandin E\(_2\) (PGE\(_2\)) level, enhance acidic mucin secretion by epithelial cells, and improve gastric microcirculation in rat with chronic superficial gastritis (CSG). These effects were associated with the up-regulation of serum PGE\(_2\) level.\(^{54}\) On the other hand, a clinical research have also indicated that Yiweikang capsule have the effects of activating the flow of qi to check pain and removing blood stasis for gastritis patients, possibly by inhibiting secretion of gastric acid, decreasing activity of pepsase, and regulating the serum gastrin.\(^{55}\) Meanwhile, other clinical research has
suggested that Weikangfu Granule can reverse intestinal metaplasia and atypical hyperplasia in patients of CG with Pi-deficiency syndrome, and the effect may be way of increasing the level of Zn, Cu, cyclic adenosine monophosphate, and superoxide dismutase in gastric mucosa, promoting cell differentiation, enhancing cellular immunity, and reducing oxygen free radicals and lipid peroxidation.\(^{[56]}\)

Nevertheless, a fact that potential limitations preclude us from drawing definite conclusions should be recognized. First, low methodologic quality of this meta-analysis must be acknowledged. Without the implementation of blinding and allocation concealment, this study may potentially exist in some subjective bias including selection bias, detection bias, and performance bias. Moreover, only 2 trials used a method of
random number table. 1 used coin flipping method, 1 used a picking method. The remaining 11 trials reported no detailed randomization method. Therefore, little or no description in the generation of random sequences could potentially result in high risk of selection bias. Furthermore, no trial reported follow-up visit, which possibly led to attrition bias. In addition, evaluation of overall clinical efficacy was mainly based on compound outcomes. Besides, degrees of clinical efficacy improvement were divided into 4 levels (namely cure, markedly effective, effective, and ineffective) was based on multiple clinical manifestation and pathologic changes on gastric mucosa by endoscopy. These inconsistent judging criteria could lead to misclassification bias. In addition, no calculation method of sample size was mentioned in included trials. To acquire additional methodologic information or statistical data, we had tried our best to contact the original authors by telephone or e-mail. But unfortunately, either their receive responses did not meet our requirements or no response had been returned.

Second, existence of potential publication bias may influence quality of this meta-analysis. In this study, all of included trials were conducted in China and published in Chinese. This geographically limited distribution, to some extent, was identified...
as low quality of reporting. Besides, studies with negative efficacy could be ignored, which may further lead to publication bias. In addition, some efforts to acquire additional unpublished data or documents were made through contacting corresponding authors. But no useful data or documents were obtained. Furthermore, although a rigorous and comprehensive searching strategy was performed by 2 independent investigators who strictly followed the selection criteria, the possibility of some potential missing literatures cannot be ruled out.

Third, discrepancies in interventions should be taken into consideration. For TCM groups, although TCM were orally administered for patients, different dose and frequency of taking medication existed. As for RP groups, although RP belongs to conventional western medicine in the treatment of CG, treatments of dual or triple therapy were not separately analyzed, as well as discrepancies in administration. Taken together, these limitations could contribute to the heterogeneity in this meta-analysis.

Finally, quality of evidence in this paper should be noticeable. There were small sample sizes of the included studies (shown in Table 1) and a high risk of bias within RCTs (shown in Table 3). Meanwhile, this meta-analysis of GRADE indicated that evidence quality was “very low” (shown in Fig. 11). Therefore, rigorously designed, large-scale, multi-center RCTs are warranted to evaluate efficacy of TCM for CG and draw more reliable conclusions. Despite above limitations in this study, this meta-analysis demonstrated that TCM could be a promising alternative therapy in treating CG compared with RP.

5. Conclusion

Results of this meta-analysis indicate that TCM could offer certain advantages in the treatment of CG. However, because of weakness in sample sizes and evidence of this methodologic quality, further standardized researches including well-designed and strictly implemented trials should be required.

Author contributions

Conceived and designed the experiments: ZWL. Performed the article search: ZXY, YKD, TM. Analyzed the data: ZXY, YKD, TM, XYL, WHC, YML. Contributed reagents/materials/analysis tools: RZZ, XBZ, PJ, JHY, SL. Wrote the paper: ZXY. Read and approved the final manuscript: ZXY, YKD, TM, XYL, WHC, YML, RZZ, XBZ, PJ, JHY, SL, LSZ, ZWL. Study supervision: ZWL, LSZ. Conceptualization: Zi-xing Yan, Li-sheng Zheng, Zhen-wen Lin. Data curation: You-mei Liu, Li-sheng Zheng. Formal analysis: Teng Ma, Xiao-ying Lin, Wen-hui Chen, You-mei Liu, Ruo-zhen Zu, Xiao-bin Zhang, Peng Jiang, Jian-hua Yang, Sheng Li. Funding acquisition: Zhen-wen Lin. Methodology: Zi-xing Yan, Yun-kai Dai, Teng Ma, Xiao-ying Lin, Wen-hui Chen, You-mei Liu, Ruo-zhen Zu, Xiao-bin Zhang, Peng Jiang. Project administration: Li-sheng Zheng, Zhen-wen Lin. Resources: Zi-xing Yan, Xiao-ying Lin, Wen-hui Chen, Jian-hua Yang. Software: Yun-kai Dai, Xiao-ying Lin, Wen-hui Chen, You-mei Liu, Xiao-bin Zhang, Peng Jiang, Jian-hua Yang, Sheng Li. Supervision: Li-sheng Zheng. Validation: Xiao-ying Lin, Ruo-zhen Zu, Sheng Li, Zhen-wen Lin. Visualization: Yun-kai Dai, Teng Ma, Li-sheng Zheng, Zhen-wen Lin. Writing – original draft: Zi-xing Yan. Writing – review & editing: Yun-kai Dai, Teng Ma. Zhen-wen Lin orcid: 0000-0003-2895-8491.
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