Review

Chaihu-Shugan-San, an oriental herbal preparation, for the treatment of chronic gastritis: A meta-analysis of randomized controlled trials

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Abstract

Ethnopharmacological relevance: Chronic gastritis is a very common disease of the digestive tract. Although herbal preparation Chaihu-Shugan-San (CSS) has been widely used as an alternative treatment for chronic gastritis in East Asia, its effectiveness is not verified. The purpose of this meta-analysis is to evaluate the effectiveness of CSS in treating various types of chronic gastritis.

Materials and methods: Retrospective review of pertinent literature via Embase, China National Knowledge Infrastructure database, Wanfang Data, Vip Information and the Cochrane Library search using the keywords “Chaihushugan” or “Chaihu Shugan” or “Chai Hu Shu Gan” or “Chaihu Shu Gan”.

Twenty-one trials were identified including 2572 patients (1384 in CSS group and 1188 in chemotherapy group). Each trial was independently reviewed by two assessors.

Results: The risk ratios of bile reflux gastritis, chronic superficial gastritis, chronic atrophic gastritis, and chronic erosive gastritis in the CSS-treated and chemotherapy groups were 1.30, 1.20, 1.24, and 1.48, respectively. CSS had more therapeutic effect in various types of chronic gastritis patients for improving clinical response compared with the chemotherapy group. Of the 21 trials administrating CSS to patients, no adverse event was reported.

Conclusions: CSS was more effective compared to chemotherapy in the treatment of chronic gastritis and no serious side-effects were identified. However, the evidence is insufficient because of the low methodological quality of the included trials. More full-scale, randomized, double-blind, placebo-controlled clinical trials are recommended to further evaluate the therapeutic benefit of CSS.

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1. Introduction

Chronic gastritis is a very common disease of the digestive tract, which affects many people of all ages (Siurala et al., 1968; Sipponen et al., 1994; Weck and Brenner, 2006). It can be caused by a range of factors, such as alcohol, stress, long-term use of non-steroidal anti-inflammatory drugs (e.g., aspirin, ibuprofen, and naproxen), infection with Helicobacter pylori, resulting in an imbalance between offensive acid–pepsin secretion and defensive mucosal factors like mucin secretion and cell shedding. To date, chronic gastritis remains a poorly understood entity, with no current effective pharmacological strategies for the management of chronic gastritis and related dyspeptic symptoms (Chen et al., 2010; Qasim and O’Morain, 2002).

Chaihu-Shugan-San (CSS), a famous Chinese prescription, composed of Radix Bupleuri (Bupleurum chinense DC.), Pericarpium Citri Reticulatae (Citrus reticulate Blanco), Radix Paeoniae Alba (Paeonia lactiflora Pall.), Radix Glycyrrhizae (Glycyrrhiza uralensis Fisch.), Fructus Aurantii (Citrus aurantium L.), Rhizoma Chuanxiong (Ligusticum chuanxiong Hort.), and Rhizoma Cyperi (Cyperus rotundus L.), has been widely used in the clinic for treating various types of chronic gastritis (Zhong and Gong, 2007; Zhang et al., 2010). Albiflorin, ferulic acid, glycyrrhetic acid, glycyrrhizic acid, hesperidin, isoliquiritigenin, liquiritin, merazin hydrate, naringin, neohesperidin, and paeoniflorin were the major active compounds of the prescription (Hu et al., 2010; Su et al., 2010). Some studies also showed that CSS could treat various gastrointestinal disorders, such as gastric ulcers and inflammation related to helicobacter pylori infection, gastrointestinal infections or antibiotic-associated diarrhea, chronic erosive gastritis, by modulating the host immune functions, e.g. systemic cytokine production (Ao et al., 2007; Qiu et al., 2011; Zhong and Gong, 2007; Zhang et al., 2010).

In recent years, many studies have indicated that oriental herbal preparation and their extracts have the favorable effects in the treatment of chronic gastritis (Khayyal et al., 2001; Qin et al., 2009a; Zhang et al., 2010; Zhong and Gong, 2007). The greatest hindrance for the acceptance of traditional Chinese medicine in the Western world is the scientific evaluation. Despite the extensive use of CSS in contemporary China, most of the evidence about CSS is anecdotal and has not been properly studied with scientifically rigorous trials, especially on human subjects. Therefore, this article reviewed available evidence on CSS and evaluated research data to offer guidance for both doctors and patients with chronic gastritis. The information would be helpful to assess the overall effectiveness and safety of CSS on chronic gastritis.

2. Materials and methods

2.1. Literature search

Relevant randomized controlled trials (RCTs) were identified from the Cochrane Central Register of Controlled Trials (The Cochrane Library 2012, Issue 3), Medline (1966 to May, 2012), and Embase (1980 to May, 2012) through Ovid; China National Knowledge Infrastructure database (1994 to May, 2012), Wanfang Data (1989 to May, 2012), and Vip Information (a full text issues database of china, 1990 to May, 2012). A search strategy to locate studies on gastritis was structured as “Chaihushugan” or “Chaihu Shugan” or “Chai Hu Shu Gan” or “Chaihu Shu Gan”. Eligible RCTs were included regardless of the language of publication. We also scanned bibliographies of relevant studies for possible additional trials.

2.2. Study selection

Two reviewers (F.Q. and J.L.) independently decided which trials fit the inclusion criteria for the meta-analysis. Only RCTs of interventions for CSS in chronic gastritis were considered in this systematic review.

Inclusion criteria: (i) randomized and controlled design; (ii) sample size ≥ 30; (iii) duration of intervention ≥ 2 weeks; (iv) base on strict diagnostic criteria of chronic gastritis; (v) use a suitable control intervention (chemistry); (vi) the diagnoses of chronic gastritis were based on standardized diagnostic criteria, such as the Chinese Consensus on Chronic Gastritis (Chinese Society of Gastroenterology, 2000), Standard of the Diagnosis of 3200 Internal Disease (Bei, 1996), Guiding Principle of Clinical Research on New Drugs of Traditional Chinese Medicine (Zheng, 2002) or other diagnostic criteria for chronic gastritis; and (vii) studies were eligible for inclusion if they reported clear criteria for treatment success, not restricted to single symptoms or by illness severity scores alone.

2.3. Selected outcomes

Patient outcomes were assessed by the number of subjects who complained of adverse events out of the total number of randomized patients. For the meta-analysis, response was defined as > 50% reduction in the total symptom score or similar criterion. Patients with significant improvement of symptoms was > 75% reduction in the score or similar criterion.

2.4. Data extraction

Details abstracted from the reports included the name of the first author, year of the publication, type of chronic gastritis, treatment duration and age of the participants, number of the participants and number of the treatment responses (total effective rate) in each arm. One reviewer extracted data from the trials using a standard data collection form, and the other reviewer checked for accuracy and completeness. All disagreements were resolved by discussion between the two reviewers and by seeking the opinion of a third reviewer when necessary. Where required, it was attempted to obtain additional information through collaboration with the original authors.

Quality assessment of the randomized controlled trials was undertaken using Jadad’s validated score (Jadad et al., 1996). This included the evaluation of randomization, blinding of outcome assessment and patient attrition (including the number of patients lost or excluded, along with reasons).
2.5. Statistical analysis

Statistical analyses were done with Review Manager version 5.0.18 (Cochrane Collaboration) software. The results expressed as risk ratios (RR) and 95% confidence intervals (CI) for dichotomous primary outcomes were calculated by the fixed-effect model. Weighted mean difference with 95% CI was used for continuous outcomes. We used Chi-square statistic to assess the heterogeneity. Fixed-effect model can be appropriate when there is statistical homogeneity (P-value of > 0.1 or an \( \hat{I}^2 \) statistic < 50%) among the studies, and random effect model has to be pursued when statistical heterogeneity (P-value of < 0.1 or an \( \hat{I}^2 \) statistic > 50%) exists in the trials. Publication bias was assessed by the funnel plot.

3. Results

3.1. Description of studies

A total of 256 trials were identified; all of these trials took place in China and were reported in Chinese. Fig. 1 is a flow chart of the trial selecting process. Finally, 21 trials are included in this review, involving a total of 2572 participants (Chai et al., 2006; Deng, 2008; Fu et al., 2009; Huang, 2011; Li, 2009; Li and Wang, 2011; Li and Yuan, 2007; Liu and Yu, 2007; Liu, 2011; Lu, 2009; Pang, 2010; Pang et al., 2012; Wang, 2008; Wen, 2008; Xu et al., 2010; Zhang, 2007; Zhang, 2010; Zhao et al., 2006; Zhao, 2008; Zhao and Song, 2010; Zhu and Ding, 2011). All potentially relevant papers were reviewed by two independent investigators. For the meta-analysis, the terms ‘patients without symptoms’, ‘patients with significant improvement of symptoms’, ‘patients with excellent or good results’ and equivalent expressions were considered successful treatments.

Of the 256 resulting studies, 15 were excluded because they were animal experimental studies. One trial was presented in two papers, therefore this has been considered as one study. Participants, types of gastritis and chemotherapeutic drugs were all described in Table 1. Of the 21 included studies, most were rated for poor-quality RCTs. The studies were conducted between January 2004 and October 2010. The publication years ranged from 2006 to 2012. The patients’ age ranged from 15 to 78 years. The length of the studies ranged from 0.5 to 6 months.

3.2. Comparisons

There were no placebo only groups in any of the included studies. The studies could be conveniently grouped as follows: (a) CSS versus chemotherapy in patients with bile reflux gastritis (BRG); (b) CSS versus chemotherapy in patients with chronic atrophic gastritis (CAG); (c) CSS versus chemotherapy in patients with chronic superficial gastritis (CSG); and (d) CSS versus chemotherapy in patients with chronic erosive gastritis (CEG).

3.3. Risk of bias in included studies

For publication bias estimating, as shown in Fig. 2, we did not observe visual or statistically significant asymmetry according to inverted funnel plot and Egger’s test.

3.4. Assessment the efficacy of CSS vs chemotherapy in various types of chronic gastritis

A total of 15 RCTs tested CSS against chemotherapy in patients with bile reflux gastritis (Chai et al., 2006; Huang, 2011; Li and Yuan, 2007; Li and Wang, 2011; Liu and Yu, 2007; Liu, 2011; Lu, 2009; Pang, 2010; Wen, 2008; Zhang, 2010; Zhao, 2008; Zhu and Ding, 2011). The interventional periods were 3 weeks or more. All trials reported effects in favor of CSS compared to chemotherapy at the end of treatment. A meta-analysis of the 12 trials (n=1313) showed a significant increase of symptom improvement compared to chemotherapy (risk ratios 1.30, 95% CI 1.23–1.37; \( Z_{\text{test}}=9.54, P<0.00001 \)). The Chi-square test for homogeneity of risk ratios are performed to determine whether there are significant differences among the trials (\( \chi^2=5.71, df=11; P=0.89 \)), which indicate that there are no statistical differences in results (Fig. 3).

Five randomized controlled trials tested CSS against chemotherapy in patients with chronic superficial gastritis (Deng, 2008; Pang et al., 2012; Wang, 2008; Zhao et al., 2006; Zhao and Song, 2010). All trials reported effects in favor of CSS compared to chemotherapy at the end of treatment. A meta-analysis of the five trials (n=881) showed a significant increase of symptom improvement compared to chemotherapy (risk ratios 1.20, 95% CI 1.13–1.27; \( Z_{\text{test}}=5.72, P<0.00001 \)). As shown in Fig. 3, the Chi-square test for homogeneity indicate that there are no statistical differences in results among the five trials (\( \chi^2=7.78, df=4; P=0.10 \)) with an \( \hat{I}^2 \) of 49% (\( \hat{I}^2 \) is typically considered low for < 25%, modest for 25–50%, and large for > 50%).

There are only three studies with 167 cases and 141 controls in patients with chronic atrophic gastritis (Fu et al., 2009; Li, 2009; Xu et al., 2010). The interventional periods were 3 months to 6 months. The results showed a significant increase of symptom improvement compared to chemotherapy (risk ratios 1.24, 95% CI 1.12–1.38; \( Z_{\text{test}}=3.99, P<0.0001 \)). As shown in Fig. 3, the Chi-square test for homogeneity indicates that there are no statistical differences in results among the three trials (\( \chi^2=0.74, df=2; P=0.69 \)).

One trial tested CSS against chemotherapy in patients with chronic erosive gastritis (Zhang, 2007). The meta-analysis showed no significant increase of symptom improvement compared to chemotherapy (risk ratios 1.48, 95% CI 1.04–2.10; \( Z_{\text{test}}=2.16, P=0.03 \)).

3.5. Adverse events

Of the 21 papers describing administration of CSS to patients, no trial reported information on adverse events. CSS was impressively effective for chronic gastritis and had no obvious adverse effects. However, spargrosis, irregular menses and hyperprolactinemia were
reported in one trial in chemotherapy group (domperidone, amoxicillin and metronidazole), the rate of adverse events was 7.5% (Lin, 2002). Similar to the result seen in treating depression with CSS (Wang et al., 2012), it was also not observed there be obvious and serious side effects in treating chronic gastritis with CSS.

### 4. Discussion

The present study represents systematic reviewing clinical studies of CSS and determining treatment effects in various types of chronic gastritis with meta-analysis. Unlike previous meta-analyses, in which analyses for CSS were only in chronic superficial gastritis (Huang and Du, 2008), the present study was based on the classification of chronic gastritis, included the RCTs of various types of chronic gastritis. In addition, many trials not included in previous analyses are included in the present study. These advantages should enhance the accuracy of the assessment of the effects of CSS in treating chronic gastritis.

Chronic gastritis is a common disease which is difficult to cure. Current treatments for chronic gastritis main focus on antacids, proton-pump inhibitors, H2 receptor antagonists, cytoprotective agents, antibiotics, prokinetic agents and so on ( Kuipers et al., 2004; van Marrewijk et al., 2009). Antacids (e.g., aluminum hydroxide and magnesium hydroxide) neutralize stomach acid and can provide fast pain relief. H2 antagonists (e.g., cimetidine, ranitidine and famotidine) reduce the amount of acid the stomach produces. Proton-pump inhibitors (e.g., omeprazole and esomeprazole) are

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### Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Classify criteria</th>
<th>Diagnostic criteria</th>
<th>Treatment duration</th>
<th>Age (years)</th>
<th>Percentage of men</th>
<th>Intervention drugs</th>
<th>Symptom improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chai et al. (2006)</td>
<td>BRG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>19–70</td>
<td>67%</td>
<td>CSS (BID)</td>
<td>94.2% (113/120)</td>
</tr>
<tr>
<td>Huang (2011)</td>
<td>BRG</td>
<td>SDD3200/ GPTCM</td>
<td>8 weeks</td>
<td>20–40</td>
<td>57%</td>
<td>Domperidone (10 mg, TID)</td>
<td>93.3% (29/31)</td>
</tr>
<tr>
<td>Li and Yuan (2007)</td>
<td>BRG</td>
<td>SDD3200</td>
<td>4 weeks</td>
<td>20–63</td>
<td>61%</td>
<td>Domperidone (10 mg, TID)</td>
<td>91.9% (31/33)</td>
</tr>
<tr>
<td>Li and Wang (2011)</td>
<td>BRG</td>
<td>SDD3200</td>
<td>8 weeks</td>
<td>24–62</td>
<td>38%</td>
<td>Domperidone (10 mg, TID)</td>
<td>85.0% (34/40)</td>
</tr>
<tr>
<td>Liu and Yu (2007)</td>
<td>BRG</td>
<td>SDD3200/ GPTCM</td>
<td>4 weeks</td>
<td>19–60</td>
<td>48%</td>
<td>Domperidone (10 mg, TID), omeprazole (20 mg, BID)</td>
<td>91.3% (42/46)</td>
</tr>
<tr>
<td>Liu (2011)</td>
<td>BRG</td>
<td>SDD3200</td>
<td>8 weeks</td>
<td>19–72</td>
<td>56%</td>
<td>Domperidone (10 mg, TID), omeprazole (20 mg, BID)</td>
<td>98.2% (110/112)</td>
</tr>
<tr>
<td>Lu (2009)</td>
<td>BRG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>18–67</td>
<td>62%</td>
<td>Domperidone (10 mg, TID), ranitidine (0.3 g, TID)</td>
<td>90.0% (90/100)</td>
</tr>
<tr>
<td>Pang (2010)</td>
<td>BRG</td>
<td>SDD3200</td>
<td>3 weeks</td>
<td>18–70</td>
<td>57%</td>
<td>Domperidone (10 mg, TID)</td>
<td>90.0% (36/40)</td>
</tr>
<tr>
<td>Wen (2008)</td>
<td>BRG</td>
<td>CCCG/ GPTCM</td>
<td>4 weeks</td>
<td>18–65</td>
<td>61%</td>
<td>Domperidone (10 mg, TID), omeprazole (20 mg, BID)</td>
<td>96.8% (30/31)</td>
</tr>
<tr>
<td>Zhang (2010)</td>
<td>BRG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>23–60</td>
<td>57%</td>
<td>Domperidone (10 mg, TID)</td>
<td>94.3% (33/35)</td>
</tr>
<tr>
<td>Zhu and Ding (2011)</td>
<td>BRG</td>
<td>CCCG/ GPTCM</td>
<td>8 weeks</td>
<td>20–66</td>
<td>36%</td>
<td>Domperidone (10 mg, TID)</td>
<td>94.4% (34/36)</td>
</tr>
<tr>
<td>Zhao (2008)</td>
<td>BRG</td>
<td>SDD3200</td>
<td>3 weeks</td>
<td>21–62</td>
<td>51%</td>
<td>Domperidone (10 mg, TID)</td>
<td>89.4% (76/85)</td>
</tr>
<tr>
<td>Deng (2008)</td>
<td>CSG</td>
<td>CCCG/ GPTCM</td>
<td>8 weeks</td>
<td>43 ± 13</td>
<td>51%</td>
<td>Domperidone (10 mg, TID), omeprazole (20 mg, BID)</td>
<td>92.3% (48/52)</td>
</tr>
<tr>
<td>Pang et al. (2012)</td>
<td>CSG</td>
<td>CCCG/ GPTCM</td>
<td>2 weeks</td>
<td>16–64</td>
<td>50%</td>
<td>Domperidone (10 mg, TID), omeprazole (20 mg, BID)</td>
<td>89.1% (34/36)</td>
</tr>
<tr>
<td>Wang (2008)</td>
<td>CSG</td>
<td>CCCG/ GPTCM</td>
<td>6 weeks</td>
<td>16–68</td>
<td>64%</td>
<td>Domperidone (10 mg, TID), vitamin B1 (20 mg, TID), antacid (20 mg, TID)</td>
<td>88.0% (183/208)</td>
</tr>
<tr>
<td>Zhao et al. (2006)</td>
<td>CSG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>18–64</td>
<td>70%</td>
<td>Domperidone (10 mg, TID)</td>
<td>93.3% (56/60)</td>
</tr>
<tr>
<td>Zhao and Song (2010)</td>
<td>CSG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>20–68</td>
<td>67%</td>
<td>Domperidone (10 mg, TID)</td>
<td>94.5% (104/110)</td>
</tr>
<tr>
<td>Fu et al. (2009)</td>
<td>CAG</td>
<td>SDD3200</td>
<td>6 months</td>
<td>22–69</td>
<td>63%</td>
<td>Domperidone (10 mg, TID)</td>
<td>97.1% (66/68)</td>
</tr>
<tr>
<td>Li (2009)</td>
<td>CAG</td>
<td>CCCG/ GPTCM</td>
<td>6 months</td>
<td>29–74</td>
<td>46%</td>
<td>Domperidone (10 mg, TID), vitamin B1 (20 mg, TID), antacid (20 mg, TID)</td>
<td>88.7% (47/53)</td>
</tr>
<tr>
<td>Xu et al. (2010)</td>
<td>CAG</td>
<td>CCCG</td>
<td>3 months</td>
<td>30.4</td>
<td>70%</td>
<td>Domperidone (10 mg, TID)</td>
<td>89.1% (41/46)</td>
</tr>
<tr>
<td>Zhang (2007)</td>
<td>CAG</td>
<td>CCCG</td>
<td>4 weeks</td>
<td>24–65</td>
<td>57%</td>
<td>Domperidone (10 mg, TID)</td>
<td>84.4% (27/32)</td>
</tr>
</tbody>
</table>

CSS, Chaihu-Shugan-San; BRG, bile reflux gastritis; CSG, chronic superficial gastritis; CAG, chronic atrophic gastritis; CEG, chronic erosive gastritis; CCCG: Chinese Consensus on Chronic Gastritis; SDD3200: Standard of the Diagnosis of 3200 Internal Disease; GPTCM: Guiding Principle of Clinical Research on New Drugs of Traditional Chinese Medicine; QD, once a day; BID, twice a day; TID, three times a day; QID, four times a day.
used to limit the amount of stomach acid by shutting down the acid "pumps". Cytoprotective agents (e.g., sucralfate and misoprostol) are designed to help protect the tissues that line the stomach and small intestine. Antibiotics (e.g., amoxicillin) are designed to treat chronic gastritis caused by infection with Helicobacter pylori. Prokinetic agents (e.g., domperidone and cisapride) are used for the treatment of reflux gastritis by stimulating gastric and lower gut motility. However, despite all the standard chemotherapy, many patients continue to experience symptoms of nausea, epigastric burning pain, and bilious vomiting. Some patients cannot tolerate chemotherapy because of undesirable side effects and drug interactions (Cremonini et al., 2002; Kuipers et al., 2004; Stein et al., 1998; van Marrewijk et al., 2009). Therefore, a new agent that possibly works through other pathways could be helpful for patients unable to tolerate standard therapy.

Indeed, as shown in Fig. 3, the present study included 21 related trials involving nearly 2600 patients. The results showed that CSS had produced positive results in chronic gastritis patients compared to chemotherapy. Subgroup analyses further revealed that the effects of CSS were also superior to chemotherapy in various types of chronic gastritis. Moreover, the heterogeneities ($I^2$ values) in two comparisons were 0%, which indicated that these heterogeneities among the studies made the results easy to compare and integrate. RR value observed in bile reflux gastritis (RR = 1.30) and chronic atrophic gastritis (RR = 1.24) were greater than that in chronic superficial gastritis (RR = 1.20), suggesting that the efficacy of CSS seems more robust on bile reflux gastritis and chronic atrophic gastritis than chronic superficial gastritis.

Herbal drugs have been proved to be very effective in treatment of chronic gastritis. Evidence-based approaches in the clinic have to be supplemented by experimental studies to unravel cellular and molecular modes of action of CSS. CSS is a combination of seven crude drugs, which has produced a favorable effect in chronic gastritis (shown in Fig. 3) and depression (Su et al., 2011; Wang et al., 2012). Many pharmacological studies have shown different effects of the single plant extracts. Glycyrrhizae radix has been commonly used for treating stomach disorders (Kim et al., 2008). Liquiritigenin from Glycyrrhizae radix has the cytoprotective effect. Liquiritigenin blocke Cadmium induces cell death by inhibiting the apoptotic processes involving translocation of Bad into mitochondria, decreasing Bcl and cytochrome c in mitochondrial, and poly(-ADP-ribose) polymerase cleavage (Kim et al., 2008). Paeonia has the antimicrobial activity and cytoprotective effect (An et al., 2006; Asai et al., 2011; Papandreou et al., 2002). Paeoniflorin from Paeonia clearly induces heat shock proteins-70 in mouse stomach and has a protective effect on the HCl- and ethanol-triggered gastric mucosal injury (Asai et al., 2011). Fructus Aurantii shows a prokinetic effect on stomach and small intestine (Huang et al., 2011). The cytoprotective effect is related to meranzin hydrate, marmin and nobiletin. Meranzin hydrate can stimulate H1 histamine receptors and promote intestinal transit and gastric emptying (Huang et al., 2011). Marmin and nobiletin possess the effects on maintenance of the mucosal barrier integrity, inhibition of gastric motor activity, and prevention of the endogenous acetylcholine and histamine (Takase et al., 1994). Rhizoma Chuanxiong and Radix Bupleuri also can promote gastric emptying and intestinal motility (Qin et al., 2009b). It is noteworthy that CSS has produced a potential effect of multi-target therapy. The explanation might be that a disease, such as chronic gastritis with most likely a number of various mechanisms involved, is likely to respond to a multi-target treatment.

Our analysis has several potential limitations. First, all the RCTs come from mainland China and are published in Chinese, which are not accessible by the international research community. This is particularly important when sampling frames are restricted to Chinese populations who have distinctive perceptions of CSS treatment. Thus, the differences in expectancies for treatment outcomes should be considered in the interpretation of the study results. Second, although publication biases are not detected in the current study, several potential factors that may cause biases should be addressed. Sample sizes in the majority of RCTs included in the present study are less than 40 subjects in each arm. This may reduce the sensitivity and accuracy of the analyses, and result in either over- or under-estimating the overall treatment effects. Third, quality control was a critical problem for the application and development of herbal prescription, but all trials lacked sufficient information on quality control of the preparation. Accurate
identification of the various components of herbal prescription will go a long way in advancing the validity and convincing the doubting Thomases of the efficacy of herbal prescription in the treatment of diseases (Qin et al., 2011a). Finally, as mentioned in all previous meta-analyses of Chinese traditional medicine (Qin et al., 2011b), a large portion of the trials included in this study did not provide detailed demographic and methodological information, such as durations of illness, number of mood episodes, medication history, random sequence, allocation concealment, intention-to-treat analyses and masking. Moreover, all trials included in the present analysis did not set up blinding conditions and placebo to exclude psychological effects. We could not further determine associations of treatment effects with demographic factors and potential biases derived from methodological flaws.

5. Conclusion

The present study provides further evidence in supporting the viewpoint that herbal prescription CSS is an effective and safe alternative treatment for chronic gastritis. CSS could be considered an alternative option for patients with chronic gastritis. However, the evidence is insufficient because of the low methodological quality of the included trials. The standardization of the herbal preparation would be greatly helpful in improving methodological quality of herbal prescription. Large-scale, well-designed, controlled trials are required to address the effectiveness of CSS therapy for chronic gastritis.

Acknowledgments

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