Acupuncture for the treatment of gastro-oesophageal reflux disease: a systematic review and meta-analysis

Jiajie Zhu,[1,2] Yu Guo,[2] Shan Liu,[3] Xiaolan Su,[2] Yijie Li,[1] Yang Yang,[2] Liwei Hou,[2] Guishu Wang,[1] Jiaxin Zhang,[1] Jiande JD Chen,[4] Qingguo Wang,[3] Ruhan Wei,[5] Wei Wei[2]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/acupmed-2016-011205).

[1]Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing, China
[2]Department of Gastroenterology, Beijing Key Laboratory of Functional Gastrointestinal Disorders Diagnosis and Treatment of Traditional Chinese Medicine, Wangjing Hospital, China Academy of Chinese Medical Sciences, Beijing, China
[3]Basic Medical College, Beijing University of Chinese Medicine, Beijing, China
[4]Division of Gastroenterology and Hepatology, Johns Hopkins University, School of Medicine, Baltimore, Maryland, USA
[5]Cleveland State University, Cleveland, Ohio, USA

Correspondence to
Professor Wei Wei, Beijing Key Laboratory of Functional Gastrointestinal Disorders Diagnosis and Treatment of Traditional Chinese Medicine, Wangjing Hospital, China Academy of Chinese Medical Sciences, No. 6 Wangjing Zhonghuan Road, Chaoyang District, Beijing 100102, China; sxxtyy@sina.com

Accepted 13 May 2017
Published Online First 8 July 2017

To cite: Zhu J, Guo Y, Liu S, *et al*. *Acupunct Med* 2017;**35**:316–323.

ABSTRACT

Background Gastro-oesophageal reflux disease (GORD) is one of the most common diseases presenting to gastroenterology clinics. Acupuncture is widely used as a complementary and alternative treatment for patients with GORD.

Objective To explore the effectiveness of acupuncture for the treatment of GORD.

Methods Four English and four Chinese databases were searched through June 2016. Randomised controlled trials investigating the effectiveness of manual acupuncture or electroacupuncture (MA/EA) for GORD versus or as an adjunct to Western medicine (WM) were selected. Data extraction and quality evaluation were performed by two authors independently and RevMan 5.2.0 was used to analyse data.

Results A total of 12 trials involving 1235 patients were included. Meta-analyses demonstrated that patients receiving MA/EA combined with WM had a superior global symptom improvement compared with those receiving WM alone (relative risk (RR) 1.17, 95% CI 1.09 to 1.26; p=0.03; six studies) with no significant heterogeneity (I^2=0%, p=0.41). Recurrence rates of those receiving MA/EA alone were lower than those receiving WM (RR 0.42,95% CI 0.29 to 0.61; p<0.001; three studies) with low heterogeneity (I^2=7%, p=0.34), while global symptom improvement (six studies) and symptom scores (three studies) were similar (both p>0.05). Descriptive analyses suggested that acupuncture also improves quality of life in patients with GORD.

Conclusion This meta-analysis suggests that acupuncture is an effective and safe treatment for GORD. However, due to the small sample size and poor methodological quality of the included trials, further studies are required to validate our conclusions.

Trial registration number PROSPERO Systematic review registration no. CRD42016041916.

INTRODUCTION

Gastro-oesophageal reflux disease (GORD) is a disorder in which gastric contents reflux recurrently into the oesophagus, causing troublesome symptoms and/or complications.[1] The prevalence of GORD in Western countries is high, ranging from 8.8–40%.[2 3] It is also rising in Asian areas.[4] GORD is associated with chronic cough, laryngitis and asthma[1] as well as obstructive sleep apnoea.[5] In addition to a potentially serious impact on quality of life, GORD imposes a huge burden on society with direct and indirect costs of US$4188 and $8741, respectively, per patient annually in the USA.[6]

While there are several established treatments for GORD, evidence of efficacy remains limited. Since GORD is closely related to lifestyle factors, lifestyle modification forms the basis of clinical management.[1] However, for various reasons, compliance with lifestyle modification is low in most patients.[1] Proton pump inhibitors (PPIs) are perceived to be the most effective treatment; however, long-term courses of treatment increase the risks of osteoporosis, *Clostridium difficile* infection and community-acquired pneumonia.[7] In addition, the economic cost is high; approximately $10 billion are spent on PPIs in the USA annually.[8] Meanwhile, surgery is effective only in a subset of GORD patients, is limited by the experience of surgeons[1] and is not helpful in reducing the risk of development of malignancy in cases of Barrett's oesophagus.[9]

Over the last decade, a pronounced decline has been seen in drug development, accompanied by a dramatic increase in the testing of novel non-medical therapeutic techniques.[10] Acupuncture, an effective alternative therapy, has been widely used in a number of gastrointestinal disorders including GORD. For instance, adding acupuncture to

standard-dose PPI reportedly achieved better results than doubling the PPI dose in patients who had failed standard-dose PPIs.[11] Since then, several other studies have investigated the effectiveness of acupuncture for GORD; however, no consensus has been reached. Moreover, to our knowledge, no systematic review or meta-analysis of trials of acupuncture for GORD has been conducted to date. Accordingly, the aim of this study was to perform a meta-analysis of trials examining the effectiveness of acupuncture for GORD.

METHODS

The protocol for this systematic review was prospectively registered in the PROSPERO (International Prospective Register of Systematic Reviews) database (reference no. CRD42016041916), which is openly accessible at http://www.crd.york.ac.uk/PROSPERO.

Inclusion/exclusion criteria

Types of studies

Randomised controlled trials (RCT) assessing the effectiveness of manual acupuncture (MA) or electroacupuncture (EA) for patients with GORD were included.

Types of participants

Patients diagnosed with GORD aged between 18 and 70 years.

Types of interventions

MA/EA, used alone or combined with Western medicine (WM), needed to have been administered in the treatment groups. Control groups needed to have only received WM, which had to be the same as that provided as an adjunct to MA/EA (where applicable). No limitations were placed on treatment duration.

Types of outcome measures

The primary outcome measurement was global symptom improvement. Secondary outcomes included symptom score, quality of life (measured using the 36-item Short Form Health Survey (SF-36)), recurrence rate and adverse events.

Search strategy

Two researchers searched four English language electronic databases (PubMed, Web of Science, the Cochrane Library and Embase) and four Chinese language electronic databases (Chinese Biomedicine (CBM), China National Knowledge Infrastructure (CNKI), Chinese Scientific Journals Database (VIP) and the WanFang Database) from their inception through June 2016. Conference proceedings and dissertations containing unpublished trials were also searched via the CNKI and WanFang databases. English and Chinese were applied as language restrictions.

The following search terms (and their Chinese equivalents for the Chinese databases) were used individually and in combination, depending on which database was searched: 'acupuncture', 'electroacupuncture', 'erosive esophagitis', 'gastroesophageal reflux disease', 'non-erosive reflux disease', 'GERD', 'GORD', 'gastro oesophageal reflux disease', 'nonerosive esophagitis' and 'endoscopically negative reflux disease'. The search strategy for Pubmed was as follows:

#1 Search (acupuncture(Title/Abstract)) OR electroacupuncture(Title/Abstract)

#2 Search (((((('erosive esophagitis'[Title/Abstract]) OR 'gastroesophageal reflux disease'[Title/Abstract]) OR 'non-erosive reflux disease'[Title/Abstract]) OR GERD[Title/Abstract]) OR GORD[Title/Abstract]) OR 'gastro oesophageal reflux disease'[Title/Abstract]) OR 'nonerosive esophagitis'[Title/Abstract]) OR 'endoscopically negative reflux disease'[Title/Abstract]

#3 Search English (Language).

Study selection and data extraction

Study selection and data extraction were independently carried out by two researchers. Detailed information including population, baseline charact eristics, details of the interventions and outcome measurements were extracted to form a conclusive table. Any divergences were resolved by discussion and consensus with a third researcher.

Assessment of risk of bias

Using the Cochrane risk of bias tool, the methodological qualities of the included trials were evaluated by two researchers.[12] The contents included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, selective reporting, incomplete outcome data and 'other bias'. For the latter, diagnostic/inclusion/exclusion criteria and baseline comparability were considered. Risk of bias was classified as low, high or unclear. Disagreements were resolved through discussion and consensus with a third researcher.

Data synthesis and analysis

RevMan 5.3 (Cochrane, London, UK) was used to analyse the data. Dichotomous data were expressed as relative risk (RR) and continuous variables as mean difference (MD) with 95% CI. Both the χ^2 test and I^2 statistics were used for the assessment of heterogeneity.[13] A fixed effects model was used if there was no obvious heterogeneity (I^2 <50% or $p>0.1$) and a random effects model was used if significant heterogeneity existed (50% <I^2<80% or $p<0.05$). A descriptive analysis was implemented if the heterogeneity was substantial (I^2 >80% or $p<0.01$).[14] Subgroup analyses for different treatment methods were performed when the necessary data were available.

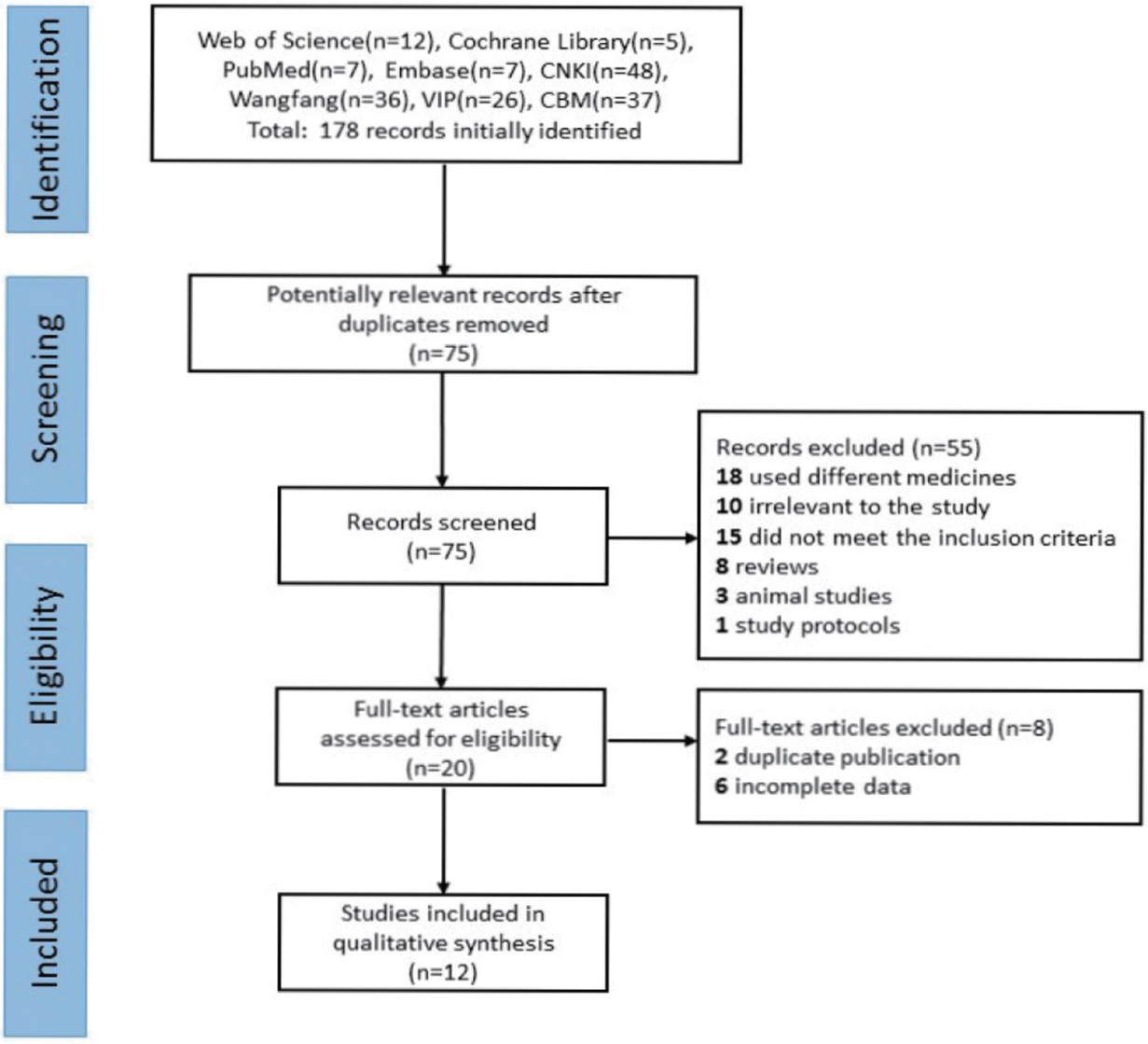

Figure 1 Flow chart and study selection. CBM, Chinese Biomedicine; CNKI, China National Knowledge Infrastructure; VIP, Chinese Scientific Journals Database.

RESULTS

Study selection

A total of 178 citations were identified during the initial search and 12 articles were finally selected (figure 1).

Study characteristics

The 12 articles included 11 journal papers[11 15–24] and one dissertation[25] with a total of 1235 patients (640 and 595 in the treatment and control groups, respectively). Among them, two studies (one conducted in the USA[11] and one in China[20]) were published in English. The remaining studies were all conducted in China and published in Chinese. All of the trials had two arms, except one trial[16] that had three arms, namely EA, WM and a combined group (EA+WM). Six studies[15 17 22–25] used MA and the other six studies[11 16 18–21] utilised EA. Five studies[15 18 20 21 25] applied MA/EA alone in the trial groups, while six studies[11 17 19 22–24] combined MA/EA with WM and one[16] included both types of comparison in view of its three-arm design, as described above. Detailed information is provided in table 1 and table S1 (see online supplementary material).

Methodological quality

All articles included in the analysis were designed as randomised studies. Five studies[11 18 20 21 25] used random number tables or lists, while the others did not detail the specific methods of randomisation. An attempt to contact the authors to clarify the method did not generate any responses. As there was no sham intervention in any of the included studies, participant blinding was not deemed to be applicable.

Table 1 Characteristics of the included studies

Authors	Number	Age (years)		Interventions		Duration	Outcome measurements
	T/C	T	C	T	C	(weeks)	
Dickman 2007[11]	15/15	52.7±10.8	48.9±8.1	EA+WM	Omeprazole 20 mg twice daily	4	1. Symptom scores; 2. SF-36 score; 3. Adverse events
Feng 2016[15]	30/30	48.9±16.07	44.7±15.26	MA	Rabeprazole 20 mg as needed	4	1. Global symptom improvement; 2. RDQ scores; SAS; SDS
Guo 2007[24]	31/30	22–62	21–63	MA+WM	Famotidine 20 mg twice daily, domperidone 10 mg three times daily	5	Global symptom improvement
Lan 2008[23]	40/36	45.3±16.7	44.1±14.5	MA+WM	Lansoprazole 30 mg twice daily, domperidone 10 mg threee times daily	4	Global symptom improvement
Liu 2007[25]	59/60	44.6±14.26	45.8±12.96	MA	Omeprazole 20 mg once daily	8	1. Global symptom improvement; 2. Symptom score; 3. Recurrence rate; 4. Endoscopic grading score; 5. Adverse events
Liu 2015[17]	34/34	40.4±4.36	42.3±5.01	MA+WM	Omeprazole 40 mg once daily, itopride 50 mg three times daily	5	1. Global symptom improvement; 2. Adverse event
Wang 2015[16]	40/20	43.6±1.8	43.4±1.5	EA	Rabeprazole 20 mg once daily	2	1. Global symptom improvement; 2. RDQ score; 3. Gastrin level
Xiang 2014[18]	31/31	44.4±24.67	44.1±25.25	EA	Mosapride 5 mg three times daily	4	1. Global symptom improvement; 2. Symptom scores
Yu 2011[22]	28/28	42.3	43.5	MA+WM	Lansoprazole 30 mg once daily, mosapride 5 mg three times daily	4	1. Global symptom improvement; 2. Recurrence rate
Zhang 2012a[21]	120/120	43±9	42±13	EA	Pantoprazole 20 mg twice daily, mosapride 5 mg three times daily	6	1. Oesophageal impedance-pH monitoring; 2. Global symptom improvement; 3. Endoscopic grading score; Symptom score; 4. SF-36 scores; 5. Adverse events
Zhang 2012b[20]	122/123	42.4±11.7	41.7±18.2	EA	Omeprazole 20 mg twice daily, mosapride 5 mg three times daily, amitriptyline 25 mg twice daily	6	1. Oesophageal impedance-pH monitoring; 2. Global symptom improvement; 3. Endoscopic grading score; 4. Symptom score; 5. SF-36 scores; 6. Adverse events
Zhang 2013[19]	50/50	41.1	39.8	EA+WM	Pantoprazole 40 mg once daily	5	1. Global symptom improvement; 2. Recurrence rate; 3. Adverse events

C, control group; EA, electroacupuncture; MA, manual acupuncture; RDQ, Roland-Morris isability Questionnaire; SAS, Self-rating Anxiety Scale; SDS, Self-rating Depression Scale; T, trial group; SF-36, 36-item Short Form Health Survey; WM, Western medicine.

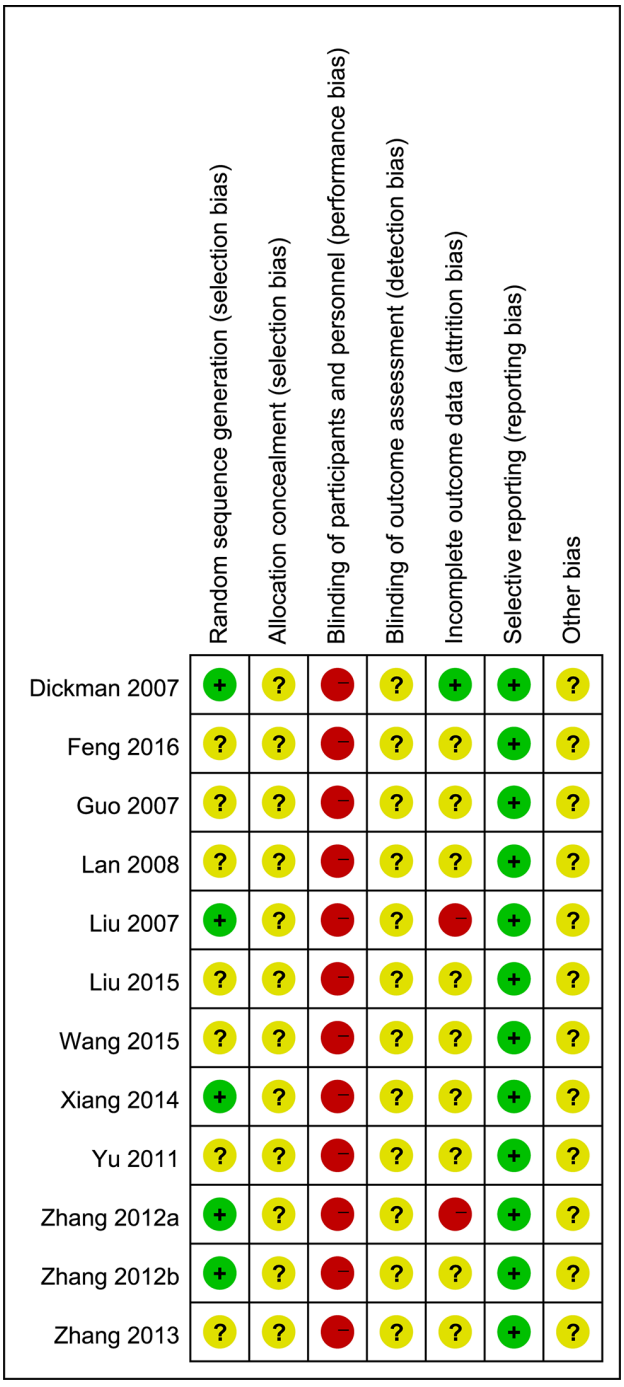

Figure 2 Methodological quality assessment of the risk bias for each included study.

Two trials[21 25] reported dropout rates of patients but failed to perform intention-to-treat (ITT) analyses (figure 2). All trials reported all outcome measurements mentioned in the Methods, and were therefore deemed to be at low risk of attrition bias. For other sources of bias, all studies were rated as unclear risk because of the lack of registration information.

Global symptom improvement

All 12 trials[11 15–25] reported on the primary outcome measure. A total of 1205 patients (625 and 580 in the treatment and control groups, respectively) were included in the analysis. Figure 3 shows the results of the meta-analyses of trials comparing MA/EA versus WM and MA/EA as an adjunct to WM, respectively. There were 402 patients in total that used MA/EA alone. The pooled results showed that MA/EA was equivalent to WM at treating GORD (RR 1.05, 95% CI 0.98 to 1.12; p=0.15) with low heterogeneity (I^2=21%, p=0.28). When MA/EA combined with WM was compared against use of WM alone, a significant improvement in global symptom score was observed (RR 1.17, 95% CI 1.09 to 1.26; p=0.03) with no significant heterogeneity (I^2=0%, p=0.41).

Symptom score

Three studies[20 21 25] used symptom scores to assess the severity of GORD. As detailed in figure S1 (see online supplementary material), the pooled results demonstrated that MA/EA was equivalent to WM in terms of its effect on symptom scores (SMD −0.02, 95% CI −0.18 to 0.14; p=0.84) with no significant heterogeneity (I^2=0%, p=0.87).

Recurrence rate

Three studies[19 22 25] reported on recurrence rate. As shown in figure 4, compared directly with WM, MA/EA reduced the recurrence rate of GORD (RR 0.42, 95% CI 0.29 to 0.61; p<0.001) with low heterogeneity (I^2=7%, p=0.34).

Quality of life

Three studies[11 20 21] evaluated quality of life using the SF-36; however, the presence of substantial heterogeneity prevented pooling of results. Dickman *et al*[11] found that the scores of all eight dimensions of the SF-36 with the single exception of vitality were improved by treatment with MA, whereas treatment with double-dose PPI was only associated with a slight improvement in physical and social function. Inter-group comparison also demonstrated that the MA treatment was associated with superior improvements in general health (55.0±18.0 vs 41.9±20.0, p=0.025) and body pain (57.0±31.1 vs 40.9±19.3, p=0.020) scores. Zhang *et al*[21] found that EA treatment had equivalent effects to WM treatment at the end of the intervention period, but superior effects during the 48 week follow-up period, with greater improvements in role physical (67±13 vs 55±21), role emotional (72±36 vs 64±18), vitality (71±23 vs 62±41) and body pain (84±20 vs 64±50) scores (all p<0.05). The results of the second study Zhang *et al*[20] were similar, with superior improvements in role physical (66.52±13.29 vs 54.87±11.34), role emotional (71.59±35.54 vs 63.55±27.74) and body pain (83.56±19.92 vs 73.85±39.51) scores (all p<0.05).

Adverse events

Adverse events were reported in five of the studies. Zhang *et al*[20] reported mild diarrhoea in three patients receiving WM during the initial stages of treatment,

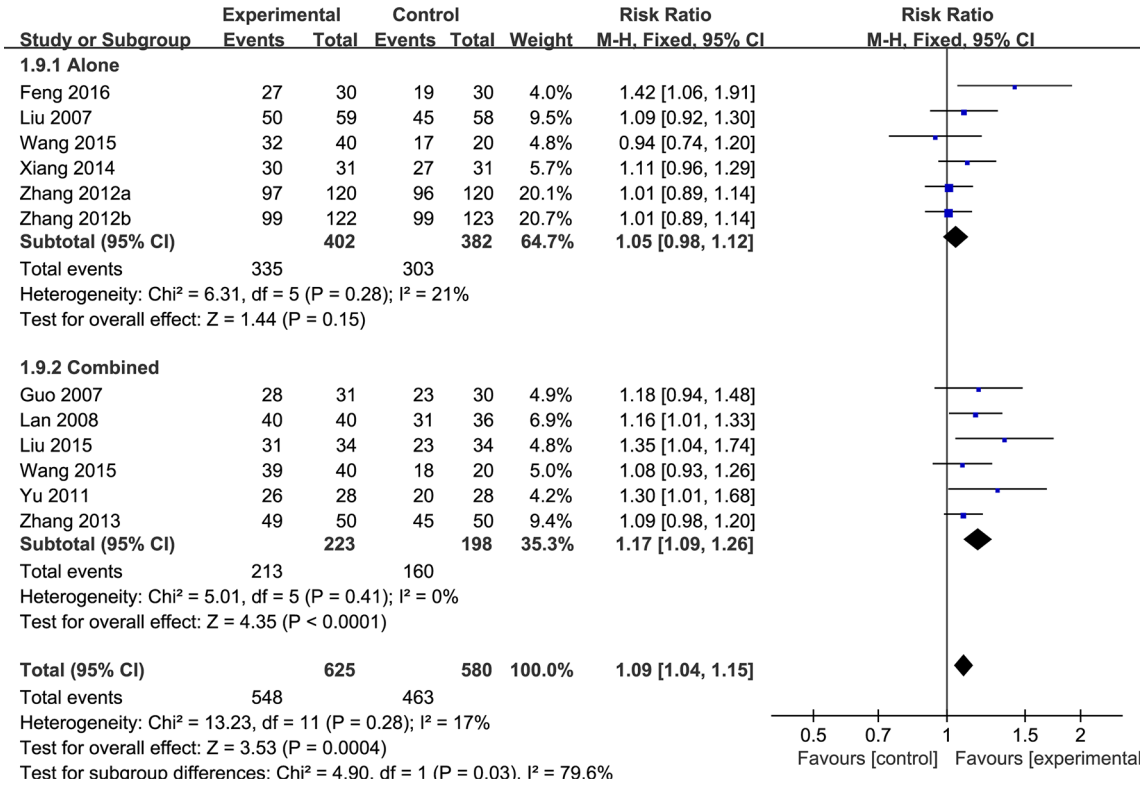

Figure 3 Forest plots of global symptom improvement in subgroups of patients with gastro-oesophageal reflux disease (GORD) treated with manual acupuncture or electroacupuncture (MA/EA) compared with Western medicine (WM) (1.9.1), and patients treated with MA/EA as an adjunct to WM (1.9.2), respectively.

which spontaneously resolved within 5 days. Zhang *et al*[21] also identified two cases of mild diarrhoea in the WM group that improved spontaneously. One patient in the WM group withdrew from the study by Liu *et al*[25] due to nausea and abdominal pain. Dickman *et al*[11] mentioned a case of mild wrist pain that resolved within 2 weeks without any specific treatment in the MA group. By contrast, Liu *et al*[17] and Zhang *et al*[19] reported no adverse events.

Publication bias

As shown in figure S2, our funnel plot analysis suggested that there may be a slight publication bias among the included studies (see online supplementary material).

DISCUSSION

Main findings

This meta-analysis investigated the effectiveness of MA/EA (used alone or combined with WM) in the treatment of GORD relative to WM. The results showed that MA/EA was associated with a lower recurrence rate of symptoms (RR 0.42) and higher quality of life when directly compared with WM and that there were minimal reported adverse events. Furthermore, when MA/EA was combined with WM there was a significant increase in global symptom improvement. The results also suggest that MA/EA alone is equivalent to WM in terms of both global symptom improvement and reduction of symptom scores (with no significant differences observed between the two groups),

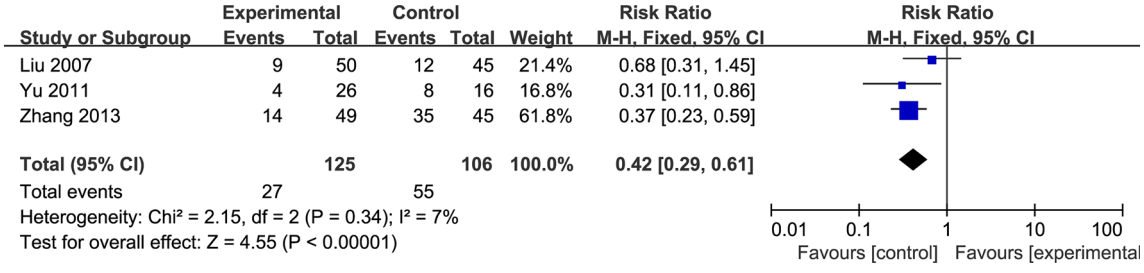

Figure 4 Forest plot of recurrence rate in patients with gastro-oesophageal reflux disease (GORD) treated with manual acupuncture or electroacupuncture (MA/EA) compared with Western medicine (WM).

although we cannot be certain of this fact because the included RCTs were designed as superiority trials rather than equivalence trials.

Interpretation

Dysfunctional motility, reflected by decreased lower oesophageal sphincter pressure (LESP), increased transient lower oesophageal relaxation (TLESR) and decreased oesophageal clearance capacity, is believed to contribute greatly to the development of GORD.[26] EA has been shown to have a regulatory effect on oesophageal motility. In cats with lower oesophageal sphincter myotomy, an increase in LESP and peak amplitude of oesophageal peristalsis was seen after EA at ST36.[27] In normal cats, EA at PC6 also led to a significant reduction in the frequency of TLESR induced by gastric distension.[28] In addition, a clinical study demonstrated that the frequency of TLESR was reduced by approximately 40% following EA at PC6.[29]

Acidity is another major cause of GORD and is closely related to the frequency of symptoms and severity of oesophagitis.[30] Zhang *et al*[20] used oesophageal pH monitoring to show that the duration of oesophageal acid exposure (pH <4) was significantly decreased from 18% to 10% after 6 weeks of EA treatment.

In the past, acid reflux was thought to be the major contributor to GORD. With more modern testing techniques, oesophageal hypersensitivity has gained increasing attention and is considered to be a key reason for failure to respond to PPIs.[31] In addition, several publications have focused on the effects of MA/EA on visceral hypersensitivity in irritable bowel syndrome.[32 33] It is believed that MA/EA has a modulatory effect on oesophageal sensory thresholds,[28] but the specific mechanisms involved are in need of further study.

Strengths and limitations

There are several strengths to our study. To the best of our knowledge, this is the first published systematic review and meta-analysis to investigate the effectiveness and safety of acupuncture in the treatment of GORD. Several outcome measures were used to comprehensively evaluate effectiveness and safety. Furthermore, a standardised protocol was developed *a priori* and registered in the PROSPERO database. However, there are also limitations to this meta-analysis. First, the trials included in the analysis were limited and the sample sizes were relatively small. Second, 11 out of 12 trials were carried out in China and 10 studies were published in Chinese. Accordingly, there is a high risk of publication bias (as suggested by our funnel plot analysis). Last, but not least, the methodological quality of the included studies was generally poor.

Implications for further research

Based on this meta-analysis, several issues need be addressed in order to improve the methodological quality of future clinical studies. First, a sample size calculation should be performed before enrolment. Second, an attempt at double-blinding could be made using sham MA/EA, in order to control for non-specific effects of needling and placebo effects. Third, the randomisation procedure, allocation concealment and blinding methods should be explicitly described and fully reported. Fourth, withdrawal/dropout during the study should be clearly reported and an ITT analysis should be used. Finally, all clinical trials should be prospectively registered and a link to the protocol should be provided in the published article.

CONCLUSION

This meta-analysis suggests that MA and EA improve recurrence rates compared with WM when used alone, and lead to greater global symptom improvement when used as an adjunct to WM in patients with GORD. They may also have a positive impact on quality of life. Although there is evidence to support the use of MA/EA alone, greater therapeutic gains may be achieved when combined with WM. Due to the generally small sample size and poor methodological quality of the included studies, a definitive conclusion is not possible and hence our findings should be interpreted with caution. Further studies with improved design, larger sample sizes and longer periods of follow-up are needed.

Contributors JZ and YG contributed equally to this research. WW, JZ and YG designed the review protocol. JZ, YG, SL and YL carried out the literature search. XS, YY, LH, GW and JZ contributed to data extraction. JZ, YG and WW contributed to quality assessment. JZ and YG performed the analyses and drafted the paper. JJDC, QW, RW and WW revised the paper.

Funding This research was supported by the Fund Sponsorship of the Capital Public Health Project (grant no. Z151100003915144), National Natural Science Foundation of China (grant no. 81573806 and 81403389).

Competing interests None declared.

Patient consent This is a systematic review and meta-analysis.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Fock KM, Talley NJ, Fass R, *et al*. Asia-Pacific consensus on the management of gastroesophageal reflux disease: update. *J Gastroenterol Hepatol* 2008;23:8–22.
2 El-Serag HB, Sweet S, Winchester CC, *et al*. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2014;63:871–80.
3 Poh CH, Navarro-Rodriguez T, Fass R. Review: treatment of gastroesophageal reflux disease in the elderly. *Am J Med* 2010;123:496–501.

4 Tan VP, Wong BC, Wong WM, *et al*. Gastroesophageal reflux disease: cross-sectional study demonstrating rising prevalence in a Chinese population. *J Clin Gastroenterol* 2016;50:e1–e7.
5 Demeter P, Pap A. The relationship between gastroesophageal reflux disease and obstructive sleep apnea. *J Gastroenterol* 2004;39:815–20.
6 Wagner JS, DiBonaventura MD, Balu S, *et al*. The burden of diurnal and nocturnal gastroesophageal reflux disease symptoms. *Expert Rev Pharmacoecon Outcomes Res* 2011;11:739–49.
7 Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2013;108:308–28.
8 Shaheen NJ, Hansen RA, Morgan DR, *et al*. The burden of gastrointestinal and liver diseases, 2006. *Am J Gastroenterol* 2006;101:2128–38.
9 Corey KE, Schmitz SM, Shaheen NJ. Does a surgical antireflux procedure decrease the incidence of esophageal adenocarcinoma in Barrett's esophagus? A meta-analysis. *Am J Gastroenterol* 2003;98:2390–4.
10 Maradey-Romero C, Kale H, Fass R. Nonmedical therapeutic strategies for nonerosive reflux disease. *J Clin Gastroenterol* 2014;48:584–9.
11 Dickman R, Schiff E, Holland A, *et al*. Clinical trial: acupuncture vs. doubling the proton pump inhibitor dose in refractory heartburn. *Aliment Pharmacol Ther* 2007;26:1333–44.
12 Higgins J, Green S. Cochrane handbook for systematic reviews of interventions. Cochrane Collaboration, Version 510 (updated 2011). http://handbookcochraneorg.
13 Higgins JP, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
14 DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
15 Feng JX, Chen CM. Clinical research in governor vessel daogi needling method for treatment of non-erosive reflux disease. *ShiZhen Medicine and Materia Medical Research* 2016;27:138–40.
16 Wang Y, Peng W. Clinical study of electroacupuncture combining rabeprazole treatment for GERD and its influence on gastrin. *Mod J Integ Tradit Chin West Med* 2015;24:720–1.
17 Liu LM, Shang HS. Clinical trial of acupuncture using harmonizing stomach to descending adverse qi method in the treatment of GERD. *Mod Tradit Chin Med* 2015;35:32–3.
18 Xiang YM, Hou ZP, Wang J, *et al*. Clinical observation of gastroesophageal reflux disease by electroacupuncture at the old 10-needles. *J Liaoning University of TCM* 2014;16:19–21.
19 Zhang YF, Liang GZ, Zhang Z. The efficacy of electroacupuncture combining with pantoprazole in patients with reflux esophagitis: clinical trial. *Med Innovat Chin* 2013;10:93–4.
20 Zhang C, Guo L, Guo X, *et al*. Clinical curative effect of electroacupuncture combined with zhizhukuanzhong capsules for treating gastroesophageal reflux disease. *J Tradit Chin Med* 2012;32:364–71.
21 Zhang CX, Guto LK, Guo BR. Clinical efficacy of electroacupuncture combined with dalitong granule for gastroesophageal reflux disease and its mechanism. *Zhongguo Zhen Jiu* 2012;32:491–8.
22 Lansoprazole YDH. Mosapride combined with acupuncture in treating non-erosive reflux disease: a clinical trial. *Chin Comm Doct* 2011;13:177–8.
23 Lan AZ. Clinical research of acupuncture combined with proton pump inhibitor treatment on GERD. *Jiangsu J Tradit Chin Med* 2008;40:58–9.
24 Guo Y. Clinical research of acupuncture combined with western medicine treatment on RE. *J Centr Plains Med* 2007;34:59–60.
25 Liu XH. *Clinical research on treating RE with the Qingweijiangni medicine and acupuncture*: HeBei Medical University, 2007.
26 Xing J, Chen JD. Alterations of gastrointestinal motility in obesity. *Obes Res* 2004;12:1723–32.
27 Shuai X, Xie P, Liu J, *et al*. Different effects of electroacupuncture on esophageal motility and serum hormones in cats with esophagitis. *Dis Esophagus* 2008;21:170–5.
28 Wang C, Zhou DF, Shuai XW, *et al*. Effects and mechanisms of electroacupuncture at PC6 on frequency of transient lower esophageal sphincter relaxation in cats. *World J Gastroenterol* 2007;13:4873–80.
29 Chang FY, Chey WY, Ouyang A. Effect of transcutaneous nerve stimulation on esophageal function in normal subjects-evidence for a somatovisceral reflex. *Am J Chin Med* 1996;24:185–92.
30 Hoeij F, Weijenborg PW, Weerman M, *et al*. Mucosal integrity and sensitivity to acid in the proximal esophagus in patients with gastroesophageal reflux disease. *Am J Physiol Gastrointest Liver Physiol* 2016;311:G117–G122.
31 Bashashati M, Hejazi RA, Andrews CN, *et al*. Gastroesophageal reflux symptoms not responding to proton pump inhibitor: GERD, NERD, NARD, esophageal hypersensitivity or dyspepsia? *Can J Gastroenterol Hepatol* 2014;28:335–41.
32 Li H, He T, Xu Q, *et al*. Acupuncture and regulation of gastrointestinal function. *World J Gastroenterol* 2015;21:8304–13.
33 Liu HR, Fang XY, Wu HG, *et al*. Effects of electroacupuncture on corticotropin-releasing hormone in rats with chronic visceral hypersensitivity. *World J Gastroenterol* 2015;21:7181–90.