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Author: Mei Wang Yun-Hai Gao Jie Xu Yuan Chi Xiao-Bing Wei George Lewith Jian-Ping Liu

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Highlights:

1. 30 RCTs with 2,967 participants were involved to evaluate the preventive effect of ST36 acupoint injections with various agents for POI

2. ST36 acupoint injection demonstrated a shortened time to first flatus, bowel sounds recovery and first defecation compared to usual care alone.

3. Neostigmine, vitamin B1 and metoclopramide are the commonly used agents for ST36 acupoint injection.

Zusanli (ST36) acupoint injection for preventing postoperative ileus: a systematic review and meta-analysis of randomized clinical trials

Mei Wang[a], Yun-Hai Gao[b], Jie Xu[a], Yuan Chi[a],
Xiao-Bing Wei[b], George Lewith[c], Jian-Ping Liu[a,d*]

[a] School of Preclinical Medicine, Liaoning University of Traditional Chinese Medicine, 79 Chong Shan Dong Lu, Huanggu District, Shenyang, 110847, China;
[b] Department of general surgery, Affiliated Hospital of Liaoning University of Traditional Chinese Medicine, 33 Bei Ling Street, Huanggu District, Shenyang, 110032, China;
[c] Primary Care, Faculty of Medicine, University of Southampton, Hampshire, SO16 5ST, UK
[d] Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, 11 Bei San Huan Dong Lu, Chaoyang District, Beijing, 100029, China

[*] Corresponding author: Jian-Ping Liu, MD, PhD, 1961-12-20, Professor, PhD supervisor. Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, 11 Bei San Huan Dong Lu, Chaoyang District, Beijing 100029, China. Tel: 0086-10-64287002; Fax:0086-10-64286871

Email addresses:
MW:linhan616@126.com

YHG:gaoyh-573@163.com

JX: xujie729@yeah.net

YC: chemcy@mail.dlut.edu.cn

XBW:weixiaobing1314@126.com

GL: glewith@scmrt.org.uk

JPL:jianping_l@hotmail.com

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Summary

Objective: To evaluate the preventive effect of Zusanli (ST36) acupoint injections with various agents, for postoperative ileus (POI).

Methods: We searched electronic databases for randomized controlled trials from inception to 1st February 2015 evaluating ST36 acupoint injection for preventing POI. Revman 5.2.0 was used for data analysis with effect estimates presented as mean difference (MD) with 95% confidence interval (CI). Statistical heterogeneity was tested using I^2 (defined as significant if I^2>75%). We used a random effects model (REM) for pooling data with significant heterogeneity.

Results: Thirty trials involving 2,967 participants were included. All trials were assessed as high risk of bias (poor methodological quality). For time to first flatus, meta-analysis favored ST36 acupoint injection of neostigmine (MD -20.70 hrs, 95% CI -25.53 to -15.87, 15 trials, I^2=98%, REM), vitamin B1 (MD -11.22 hrs, 95% CI -17.01 to -5.43, 5 trials, I^2=98%, REM), and metoclopramide (MD -15.65 hrs, 95% CI -24.77 to -6.53, 3 trials, I^2=94%, REM) compared to usual care alone. Meta-analysis of vitamin B1 favored ST36 acupoint injection compared to intra-muscular injection (MD -17.21 hrs, 95% CI -21.05 to - 13.36, 4 trials, I^2=89%, REM). Similarly, for time to bowel sounds recovery and first defecation, ST36 acupoint injection also showed positive effects.

Conclusions: ST36 acupoint injections with various agents may have a preventive effect for POI. Safety is inconclusive as few of included trials reported adverse events. Due to the poor methodological quality and likely publication bias further robust clinical trials are required to arrive at a definitive conclusion.

Keywords: ST36 acupoint injection; postoperative ileus; systematic review; meta-analysis; randomized controlled trial

Introduction

Postoperative ileus (POI), is a common condition after abdominal surgery that presents with discomfort, pain, nausea, vomiting, and abdominal distension. It is a major contributory factor to extended hospitalization and increased costs.[1-3] POI is generally defined as a transient impairment of bowel motility after abdominal surgery or other injury.[1] Duration of POI varies from a few hours to several weeks. Recent studies show that, on average, patients with a diagnosis of POI stay 5 days longer in hospital after abdominal surgery than patients without POI.[4] In the US the economic consequences of POI are estimated to surpass one billion dollars each year.[5]

Currently, no effective techniques are available for the management of POI.[1,6] Usually, after abdominal surgery, current practice is to withhold oral feeding until POI resolves,[7,8] but the evidence for this has been questioned recently.[1] Several strategies, including minimizing intestinal trauma during surgery, using midthoracic epidural anaesthesia and minimizing the need for opioids in pain management, do shorten the time of POI but it remains a major problem.[6] Pharmacological approaches including metoclopramide, erythromycin, beta blockers, laxatives, neostigmine, and naloxone, have limited clinical efficacy and safety for treating POI.[9-11] Gum chewing is associated with improved gastrointestinal function for preventing POI, but it is limited using in sleepy, drowsy, or older patients or in patients without teeth.[12] Further research is urgently needed to identify and develop new interventions for the prevention of POI.

Acupoint injection therapy emerged in 1950s in China; it originated from intra-muscular injection in western medicine and was gradually integrated into traditional Chinese medicine.[13] After its initial development acupoint injection therapy is widely used in China for a variety of indications including POI, pain, vomiting, nausea and

retention of urine.[14] Acupoint injection is an acupoint stimulating technique in which a liquid agent is injected to prevent and/or treat disease. The agents usually used for acupoint injection include bee venom, Chinese herbal extractions, western medications, vitamins, and normal saline.[15] The commonly used acupoint in treating gastrointestinal diseases is Zusanli (ST36).[16,17] ST36 is located on the Stomach Meridian and its action, harmonizes *qi* and blood, adjusts the spleen and stomach, and improves general weakness; its traditional therapeutic properties are ideally suited to treating POI.[18] Electroacupuncture at ST36 at a specific frequency can improve gastrointestinal functional diseases.[19] Agents administrated in acupoints, through the meridians, are thought to play a synergistic effect with acupoint stimulation, and are thought to have a more sustained effect than traditional acupuncture needling or simple intra-muscular injection.[20] ST36 acupoint injections with various agents have been widely used as a preventative method for POI in China for many years but have not been part of standard of postoperative care in clinical practice due to a lack of systematic evidence demonstrating its efficacy and safety. We therefore performed a systematic review and meta-analysis of randomized clinical trials to evaluate the preventive effect of ST36 acupoint injections with various agents for POI.

Methods

Registration number

The protocol of this systematic review was registered in the PROSPERO database (http://www.crd.york.ac.uk/PROSPERO_REBRANDING/display_record.asp?ID=CRD42014007443).

Search strategy

We searched PubMed, the Cochrane CENTRAL, EMBASE, China National Knowledge Infrastructure (CNKI), VIP Database, Chinese Biomedical Database (SinoMed), and Wanfang Database from inception to 1st February 2015. We searched: MeSH term "postoperative"; key words: "postoperative ileus" or "POI" or "gastrointestinal function recovery" or "gastrointestinal disorder" and "ST36" or "zusanli" and "acupuncture" or "aquapuncture" or "*point injection" or "acupoint block" and "randomiz*". Clinical trials were set as a limitation for searching. We also searched relevant ongoing trials from the US equivalent Clinical Trials register (http://www.clinicaltrials.gov).

Inclusion/exclusion criteria

Types of studies

Randomized clinical trials (RCTs) were included. Quasi-RCTs (clinical trials allocated participants based on alternation, such as date of birth, hospital medical record number) were excluded. We excluded case series, case reports, reviews and animal studies. There was no limitation on language or type of publication.

Types of participants

Participants who underwent elective or emergent abdominal surgery without experiencing POI or any complications were included. There were no limitations on age, gender, original abdominal disease or type of surgery. We excluded postoperative patients who failed to have flatus within a prespecified duration of time.

Types of interventions

ST-36, is located 3 *cun* below the lower border of the patella, 1 fingers' breadth lateral

to the anterior crest of the tibia, in the tibialis anterior musle.[21] *Cun* is defined according to the rules of traditional acupuncture as the width of the interphalangeal joint of the patient's thumb.[22] When the needles are inserted into ST36 acupoint, patients feel *deqi* (a sensation of dull, aching, and spreading),[23] and then agents are slowly injected. *Deqi* or needling sensation is the traditional acupuncture term used to describe the supposed connection between acupuncture needles and the acupuncture meridians.[24] Agents that are injected at ST36 acupoint as part of a therapeutic approach designed to sustain and amplify the effects of simple needling. These agents included vitamins, normal saline (as a therapy), various pharmaceutical medications and herbal extracts. There was no limitation on sensation of *deqi* and how located the acupoint. Single or combination of the agents to be injected was included. The controls included usual care (stomach decompression, nasogastric tube, mobilization from bedrest and maintaining body fluid balance), placebo, or the same medication used in the acupoint injection given through another method (e.g. routine intra-muscular injection). We excluded trials comparing ST36 acupoint injection with other type of ST36 acupoint stimulation such as manual acupuncture, electro-acupuncture, or acupoint paste, which could not manifest the holistic effect of acupoint and agents.

Types of outcome measures

The primary outcome was time to first flatus. Secondary outcomes were time to bowel sounds recovery, time to first defecation, length of hospital stay, abdominal distention, time to recovery of oral dietary intake and adverse events. Bowel sounds were recorded at four quadrants of the abdomen with a standard interval (often every 2 hrs) after ST36 acupoint injection until heard three times per minute. This suggested bowel sounds recovery. We excluded trials with missing outcome data or not available

for analysis.

Study selection and data extraction

Two review authors (MW and YHG) selected studies independently. Two of the four authors (MW, JX, XBW and YC) extracted data using a self-developed data form from the included trials independently. Extracted information included: sample size, demographic characteristics of participants, intervention details, withdrawals, and clinical outcomes. A consensus was reached by discussion with JPL in case of disagreement.

Assessment of risk of bias in included studies

Two authors (MW and YHG) independently assessed the methodological quality of included trials, and a consensus was reached by discussion with JPL in case of disagreement. We assessed methodological quality of RCTs according to the risk of bias tool in the Cochrane handbook for systematic reviews of interventions.[25] The following items were assessed: random sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, selective reporting and other bias. The risk of bias was categorized as low, unclear, or high risk of bias.

Data analysis

We used mean difference (MD) with 95% CI for effect estimates. We applied RevMan 5.2.0 software for data analyses. Heterogeneity was assessed using the I^2 (defined as significant if I^2>75%). We used random effects model (REM) for pooling data with significant heterogeneity. Funnel plots were generated to detect publication bias. When the data were available, subgroup analysis was done for different injected

agents and different outcomes.

Results

Our search identified 689 citations, and 30 RCTs were eligible, as summarized in the flow chart (Fig. 1).

Description of studies

Table 1 summarized the characteristics of 30 included trials. All trials were conducted in China, and published in Chinese. A total of 2,967 abdominal postoperative participants (1,519 in intervention group and 1,448 in control group) were included with an average number of 99 per trial (ranging from 30 to 266).

The experimental interventions were agents administered through ST36 acupoint injection plus usual care. The injected agents included neostigmine (15 trials, 50%), vitamin B1 (9 trials, 30%), metoclopramide (3 trials, 10%), normal saline (1 trial), *Astragalus membranaceus* extracts (1 trial), vitamin B1 plus vitamin B12 (1 trial). Nine trials (33.33%, 9/30) reported the details of how to locate ST36 acupoint,[26,29,31,32,37,38,44,45,54] and 17 trials (56.67%, 17/30) reported *deqi* sensation (needling feeling which is felt as dull, aching, and spreading).

The controls included usual care in 23 trials; intra-muscular injection (the same agents as given for ST36 acupoint injection) in five trials; and other medicines in two trials (oral mosapride, domperidone; castor oil via gastric tube). Comparing the same agents administrated through ST36 acupoint injection with intra-muscular injection, the controls were initiated at same time and given at same dosage as the interventions. Most trials had two-arms, five trials had three arms, [30,31,33,36,55] and two trials had four arms[26,29]. For trials involving multi-arms, we included the arms of usual care or intra-muscular injection, and excluded arms of acupoint stimulation based on our

predefined inclusion/exclusion criteria for controls. No trial used a placebo as a control.

All trials reported the time to first flatus, 12 trials reported time to bowel sounds recovery with clear reporting standards, and eight trials reported time to first defecation. No trials reported serious adverse events. No trial reported the length of hospital stay or time to dietary intake.

Risk of bias assessment

All of the included trials were assessed to be of high risk of bias in general suggesting poor methodological quality according to the predefined quality criteria (Fig.2). Although 'random allocation' was mentioned in all trials, only eight (26.67%, 8/30) trials described the methods for random sequence generation as a random number table,[30,34,36,42,43,45,58,59] the others only mentioned that 'patients were randomly divided into two groups' without detailed information. No trial reported allocation concealment and drop-outs or mentioned intention-to-treat analysis. There was no evidence of appropriate blinding of participants or study personnel performed in any of the included trials. Although no blinding of outcome assessment was performed in any trials, we considered this was probably a low risk of bias because the time to first defecation was the participants' self-reported outcome. Since the protocols of the included trials were not available, we assessed the selective outcome reporting by comparing the outcome measures described in the methods section with the actual reporting in the results. In total, two trials were assessed as high risk of bias for selective reporting. Two trials reported sample size calculation.[33, 36]

Effects of interventions

We did subgroup analyses based on different agents injected at ST36 acupoint.

Primary outcome

Time to first flatus

All trials reported outcomes of time to first flatus. Meta-analysis showed ST36 acupoint injections of neostigmine (MD -20.70 hrs, 95% CI -25.53 to -15.87, 15 trials, I^2=98%, REM), vitamin B1 (MD -11.22 hrs, 95% CI -17.01 to -5.43, 5 trials, I^2=98%, REM), and metoclopramide (MD -15.65 hrs, 95% CI -24.77 to -6.53, 3 trials, I^2=94%, REM) plus usual care demonstrated a better effect than usual care alone. Meta-analysis showed better effects from ST36 acupoint injection of vitamin B1 on shortening the time to first flatus than intra-muscular injection (MD -17.21 hrs, 95% CI -21.05 to - 13.36, 4 trials, I^2=89%, REM). The forest plots for outcome of time to first flatus are shown in Fig 3.

Secondary outcomes

1.Time to bowel sounds recovery

Twelve trials reported the time to bowel sounds recovery with clearly predefined criteria for assessment. Meta-analysis of neostigmine (MD - 6.11 hrs, 95% CI -8.26 to -3.96, 2 trials, I^2=54%, REM), and vitamin B1 (MD -8.99 hrs, 95% CI -14.70 to -3.28, 4 trials, I^2=96%, REM) ST36 acupoint injection plus usual care showed a better effect than usual care alone in shortening the time to bowel sounds recovery. Meta-analysis of ST36 acupoint injection of metoclopramide plus usual care showed no significant difference compared with usual care alone (MD -13.43 hrs, 95% CI -32.92 to 6.07, 2 trials, I^2=94%, REM). Meta-analysis showed better effects for ST36 acupoint injection of vitamin B1 on shortening the time to bowel sounds recovery than intra-muscular injection (MD -14.89 hrs, 95% CI -21.36 to -8.43, 2 trials,

I^2=95%, REM). The detailed effect estimates are presented in Table 2.

2.Time to defecation

Eight trials reported the time to first defecation. Meta-analysis of ST36 acupoint injection of neostigmine (MD -27.46 hrs, 95% CI -41.69 to -13.23, 3 trials, I^2=96%, REM) and metoclopramide (MD -19.65 hrs, 95% CI -34.15 to -5.14, 2 trials, I^2=94%, REM) plus usual care compare with usual care alone showed a better effect. The detailed effect estimates are presented in Table 2.

3. Adverse events

Of the 30 trials, 28 trials did not mention information on adverse events; two trials reported that no adverse events occurred. [44,47]

Funnel plot analysis

A funnel plot analysis of 30 RCTs for the outcome of time to first flatus was performed to explore publication bias (Fig 4). The plot was asymmetrical suggesting the existence of publication bias.

Discussion

Main findings

Our review of 30 RCTs with 2,967 participants evaluated the preventive effect of ST36 acupoint injections with various agents for POI. This demonstrated a shortened time to first flatus, bowel sounds recovery and first defecation. Neostigmine, vitamin B1 and metoclopramide are the most frequently used agents for ST36 acupoint injection. The safety of ST36 acupoint injections for these agents is unclear.

Limitation of the systematic review

Several limitations existed in this review. The methodological quality of the included studies was generally poor as they reported limited information about the generation of allocation sequence, allocation concealment, and blinding.

Secondly, all trials were conducted and published in China. In addition, our testing of funnel plot showed asymmetry and therefore, publication bias may exist in this review. No trial was registered and no protocol was available so we are unable to analyse whether the trials have a selective reporting and /or incomplete outcome reporting.

Thirdly, there is significant heterogeneity in most meta-analyses of the included trials. This could be explained by their clinical heterogeneity: (1) the participants' characteristics, such as age, sex, original diseases; (2) a variety of surgical protocols (laparoscopy and laparotomy), study locations, surgical procedures/duration, and type of anesthesia; (3) differences in ST36 acupoint injection protocols, such as the initial time, variations in agents, dosage, frequency and sensation of *deqi*; (4) diverse postoperative care protocols among the included trials, including stomach decompression, insertion and removal of nasogastric tubes, maintaining body fluid balance and anti-inflammatory medication protocols. The time and frequency of mobilization from bedrest also may affect gastrointestinal recovery; (5) the outcome of time to first flatus was highly dependent the participants self-reporting, which may not reflect the exact duration of flatus recovery. Adequate definitions of resolution and an internationally acknowledged outcome measures are required for the future study of preventing POI.

Fourthly, only two in the included trials reported the information of adverse events. Therefore, we could not estimate the safety of ST36 acupint injections with various agents. The normal clinical use of neostigmine in postoperative patients may

cause adverse effects including abdominal cramps, excess salivation, vomiting and bradycardia.[56] Although no serious adverse events were reported in a few trials, the safety of ST36 acupoint injections with various agents is unclear because of a lack of data.

Implications for future research

In this review, no study reported hospital stay and time to recovery of oral dietary intake. Future trials with rigorous design and large sample size are necessary to confirm the preventive effect of ST36 acupoint injections with various agents on shortening the duration of abdominal distention, hospital stay, recovery of oral dietary intake and to evaluate the presence of adverse effects. Such trials should consist of participants with similar original conditions utilizing generally accepted surgery protocols and postoperative care. These clinical trials should be prospectively registered in an international trial registry. We also suggest that reporting for these trials should follow the Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) to explicitly and transparently explain the therapeutic processes involved.[57]

Acupuncture is widely accepted in China as an effective therapy for preventing POI. A recent study showed that electro-acupuncture reduced the duration of POI after laparoscopic surgery for colorectal cancer compared with no or sham acupuncture;[22] in this study patients received general anesthesia. However, previous studies showed that acupuncture alone is not effective in preventing POI,[16,58] especially when using epidurals. The use of epidural anesthesia blocks the relevant afferent and efferent pathways for acupuncture.[16] In our review, ST36 acupoint injection demonstrated effectiveness for preventing POI and the effect appears not to be modified by anesthetic type.

Neostigmine, vitamin B1, and metoclopramide are the commonly used agents for ST36 acupoint injection. One of the explanations for the preventive effect is supposed that the agents injected into the acupoint play a role in amplifying and sustaining the effects of simple needling. Therefore, normal saline used through acupoint injection could enhance acupoint stimulation and is not considered as placebo in this context. In traditional Chinese medicine, ST36 is traditionally considered to be an effective acupoint in treating many gastrointestinal diseases. However, no high-quality clinical trials have been conducted to explore whether other acupoints have similar effects. Further RCTs comparing ST36 acupoint injection with non-acupoint or other acupoint injection should be encouraged. Meanwhile, high quality RCTs comparing different agents used in ST36 acupoint injection are also needed to determine the comparative effectiveness of the agents in preventing POI.

Conclusion

This review suggests that ST36 acupoint injections with various agents may have preventive effect for POI. However, these positive findings should be interpreted with caution due to the poor methodological quality for the included trials and likely publication bias. The commonly used agents are neostigmine, vitamin B1, and metoclopramide. Based on the limited trials reporting adverse events, the safety of ST 36 acupoint injection is inconclusive. Neostigmine should be used with caution for ST36 injection in postoperative patients due to the adverse effects which limit its conventional use in POI. Further rigorous trials are needed to establish the evidence base to support the clinical use of ST36 acupoint injection therapy.

Competing interests

The authors declare they have no competing interests.

Authors' contributions

JPL conceived and designed the study. MW conducted study search and identification with YHG, and conducted inclusion/exclusion, study selection, data extraction, quality assessment with JX, YC and XBW. MW wrote the first draft of the manuscript. WM contributed to data analysis. MW, GL, JPL and YHG participated in the revision of subsequent draft.

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LEGENDS

FIGURES

Figure 1. Flow-chart of study selection (PDF)

Figure 2. Risk of bias summary (PDF)

Figure 3. Forest plot of time to first flatus (PDF)

Figure 4. Funnel plot of time to first flatus (PDF)

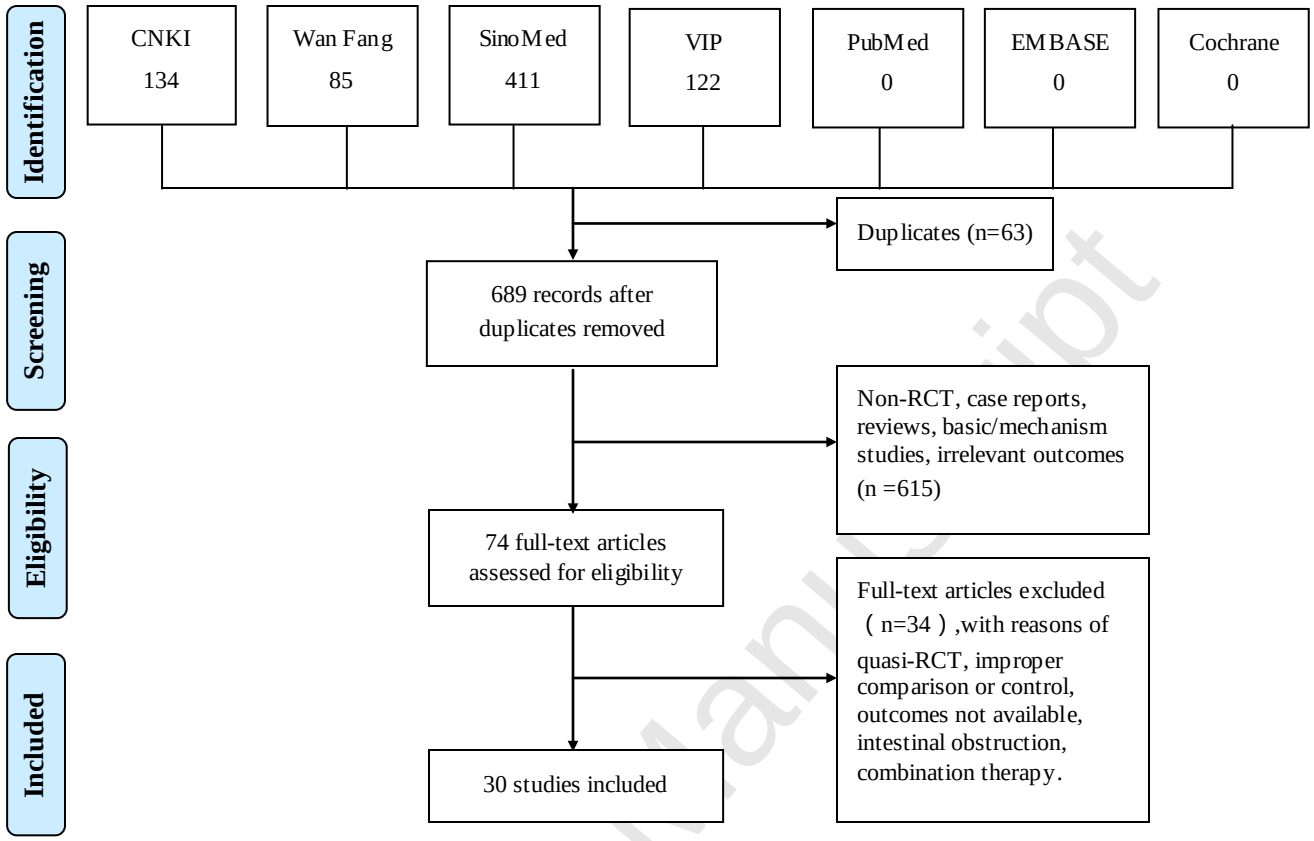
TABLE

Table 1. Characteristics of included studies on ST36 acupoint injection for preventing POI (DOCX)

Table 2. Effect estimates of ST36 acupoint injection for preventing POI (DOCX)

SUPPOTING INFORMATION

Appendix file PRISM checklist (DOCX)



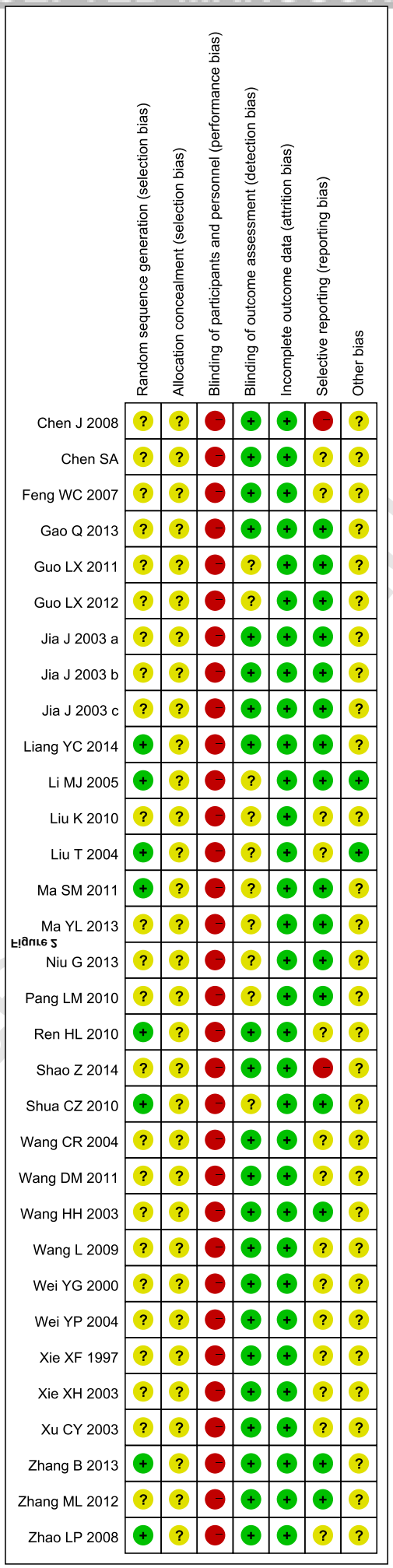
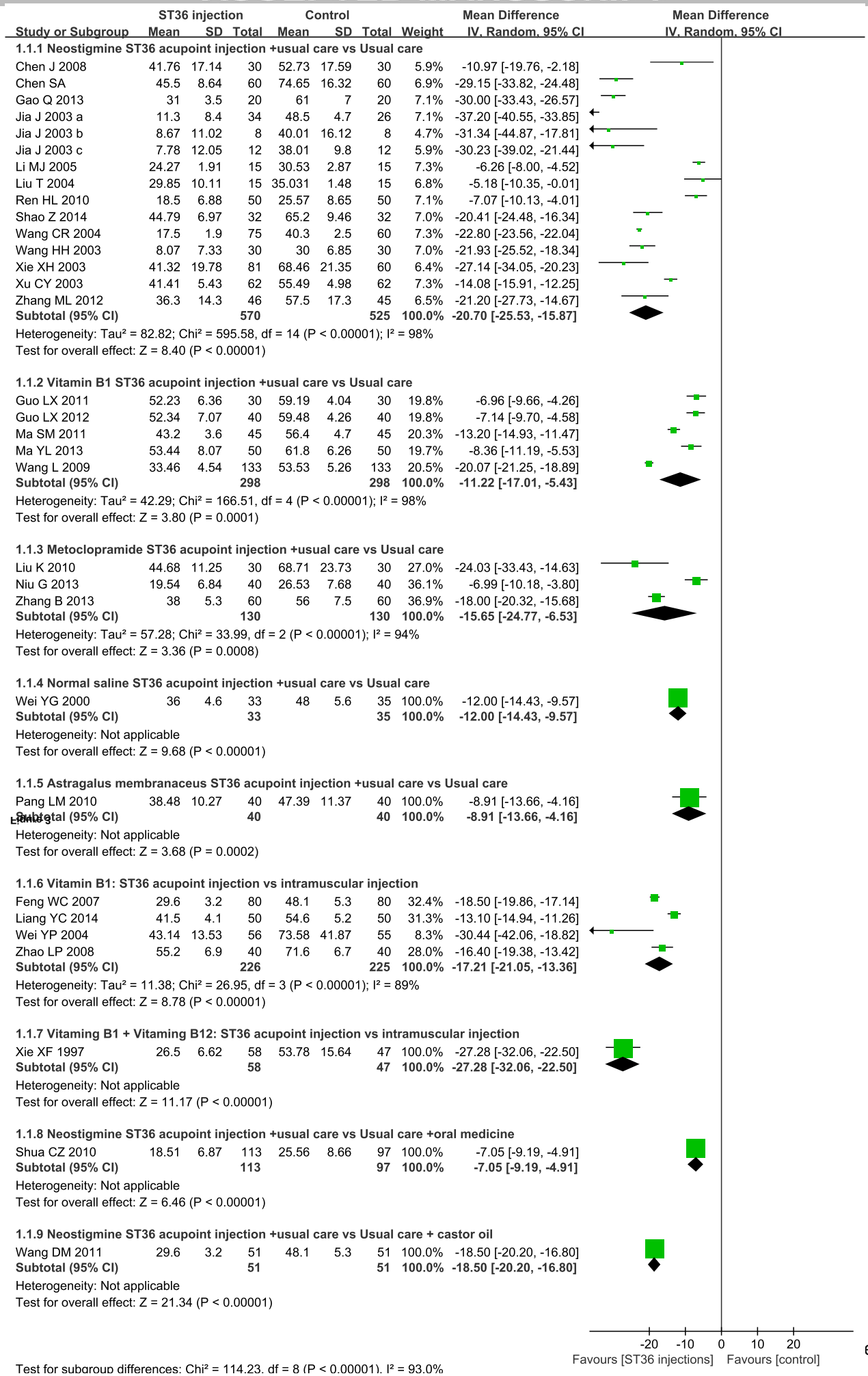


Figure 2



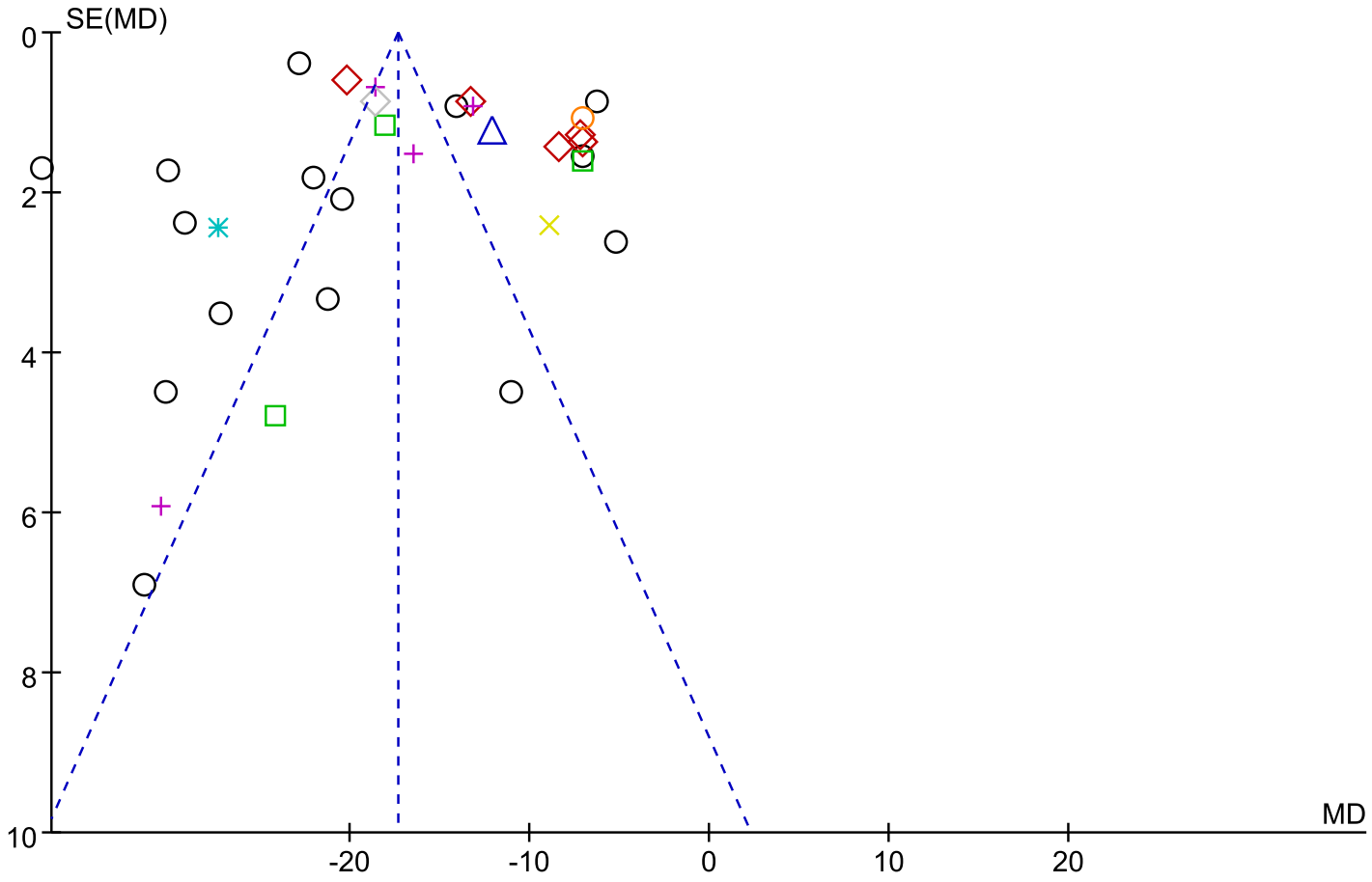


Table 1 Characteristics of included studies on ST36 acupoint injection for preventing POI.

Study ID	No. (M/F)	Mean age (years)	Participants (Surgery site)	Type of anesthesia/ duration of surgery	Intervention (ST36 acupoint injections)	Control	Outcome measure
Chen J 2008[26]	I: 30 (16/14) C: 30 (11/19)	I:NA C: NA	Appendix, gallbladder, stomach, intestine, colon, spleen	General and epidural anesthesia	Neostigmine, 0.5mg*2=1mg, 8h after surgery, once daily, depth of insertion 1.5 *cun*[*].	Usual care	TFF, TFD (day) BSC, BT
Chen SA 2011[27]	I: 60 (38/22) C: 60 (30/30)	I: 53 (27-82) C: 58 (40-75)	Rectum	NA	Neostigmine, 0.25mg*2=0.5mg, twice daily (5:00,13:00) until flatus, *deqi*[#].	Usual care	TFF
Gao Q 2013[29]	I: 20 (15/5) C: 20 (11/9)	I: 45.0±23.0 (28-68) C: 40.0±30.0 (30-70)	T:Stomach (n=6), colon (n=10), rectum (n=4); C:Stomach (n=6), colon (n=6), rectum (n=8);	General anesthesia I: (168.0±33.0) min C: (180.0±22.0) min	Neostigmine, 0.5mg, 6h after surgery, once daily.	Usual care	BPR, TFF

					daily, depth of insertion 2.5-3.0cm, *deqi*[#].			
Niu G 2013[39]	I:40 C:40	I:NA C:NA	Gallbladder	NA	Metoclopramide, 20mg, back to the ward postoperative.	Usual care	TBSR, TFF, TFD, V	
Zhang B 2013[53]	I: 60 (26/34) C: 60 (22/38)	I: 46.8 (26-71) C: 43.4 (24-68)	Gallbladder	NA	Metoclopramide, 1ml, 1h after surgery, twice daily, depth of insertion 1 *cun*[*], *deqi*[#].	Usual care	TFF, ABD, SM	
Pang LM 2010[40]	I: 40 (25/15) C: 40 (19/21)	I: 33.8±12.6 C: 31.4±14.7	T:Gallbladder (n=13), appendix (n=27); C:Gallbladder (n=9), appendix (n=31)	I: (0.7±0.3) h C: (0.8±0.3) h	*Astragalus membranaceus*, 1ml*2=2ml, once daily, for 3 days, *deqi*[#].	Usual care	TBSR, TFF, TFD, S, FR	
Wei YG 2000[48]	I:33 C:35	I:NA C:NA	Stomach, intestine	NA	Normal saline, 2ml*2=4ml, 6h after surgery, once daily, for 3 days.	Usual care	TFF, TFD	
Liang YC 2014[34]	L:50 C:50	I:NA C:NA	Gallbladder and biliary tract (n=94), spleen	NA	ST36 acupoint injection: vitamin B1, 100mg, 12h	Intramuscular injection: Vitamin	TFF, TBSR, ABD	

Notes: M, male; F, female; I, intervention group; C, control group; NA, not available; h, hours; TFF, time to first flatus; BSC, bowel sounds change; BT, body temperature;

TBSR, time to bowel sounds recovery; TFD, time to defecation; S, symptoms; FR: flatus rate; CR: cure rate; AE, adverse events; BPR, bowel peristalsis recovery; ABD, abdominal distention; SM, serum motilin; VIP, vasoactive intestinal peptide; TFBS, time to first bowel sound; V, vomiting; GFR, gastrointestinal function recovery.

[*]*cun*, defined according to the rules of traditional acupuncture as the width of the interphalangeal joint of the patients's thumb.

[#]*deqi*: the traditional acupuncture term used to describe the connection between acupuncture needles and the energy pathways of the body.

Table 2 Effect estimates of ST36 acupoint injection for preventing POI.

Outcomes and comparisons	Study ID	Number of participants (I/C)	Effect estimates (95%CI)
Time to bowel sounds recovery（hours）			
1. ST36 acupoint injections + usual care *vs* usual care			
1.1 Neostigmine	Li MJ 2005[33]	130(65/65)	MD -6.11 [-8.26, -3.96]
	Ren HL 2010[41]		I^2=54%,REM
1.2 Vitamin B1	Guo LX 2011[30]	330(165/165)	MD -8.99 [-14.70, -3.28]
	Guo LX 2012[31]		I^2=96%,REM
	Ma SM 2011[37]		
	Ma YL 2013[38]		
1.3 Metoclopramide	Liu K 2010[35]	140(70/70)	MD -13.43 [-32.92, 6.07]
	Niu G 2013[39]		I^2=94%,REM
1.4 *Astragalus membranaceus*	Pang LM 2010[40]	80(40/40)	MD -7.64 [-12.02, -3.26]
2. The same agents: ST36 injection *vs* intramuscular injection			
2.1Vitamin B1	Zhao LP 2008[54]	180(90/90)	MD-14.89 [-21.36, -8.43]
	Liang YC 2014[34]		I^2=95%,REM
3. ST36 acupoint injections *vs* oral medications			
3.1 Neostigmine	Shua CZ 2010[43]	210(113/97)	MD -7.56 [-9.41, -5.71]
Time to first defecation（hours）			

1. ST36 acupoint injections + usual care *vs* usual care			
1.1 Neostigmine	Ren HL 2010[41]	376(206/170)	MD -27.46 [-41.69, -13.23]
	Wang CR 2004[44]		I^2=96%,REM
	Xie XH 2003[51]		
1.2 Metoclopramide	Liu K 2010[35]	140(70/70)	MD -19.65 [-34.15, -5.14]
	Niu G 2013[39]		
1.3 Normal saline	Wei YG 2000[48]	68(33/35)	MD -14.00 [-17.71, -10.29]
1.4 *Astragalus membranaceus*	Pang LM 2010[40]	80(40/40)	MD -14.67 [-21.05, -8.29]
2. ST36 acupoint injections *vs* oral medications			
2.1Neostigmine	Shua CZ 2010[43]	210(113/97)	MD -14.89 [-18.04, -11.74]

Notes: I, intervention group; C, control group; CI, confidence interval; MD, mean difference; REM, random effect model.