Acupoint Stimulation for Postoperative Ileus Following Gastrointestinal Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Abstract

Introduction: Postoperative ileus is a common complication of gastrointestinal surgery, which leads to unsatisfactory outcomes with current therapies. In this review, we examined whether acupoint stimulation after gastrointestinal surgery can help hasten postoperative recovery of the digestive system.

Methods: A literature search for relevant studies (published as of April 2017) was conducted across eight biomedical databases. Randomized controlled trials (RCTs) which compared acupoint stimulation with placebo, no treatment, sham acupuncture, or standard care, in adults with postoperative ileus were eligible for inclusion. Trials which compared a combination of acupoint stimulation and standard care with standard care were also included. The Cochrane risk of bias was used to evaluate study quality. Outcomes were summarized using risk ratio (RR) and mean difference (MD) for binary and continuous variables, respectively.

Results: Fourteen RCTs (combined n=1299) that investigated the role of acupoint stimulation in postoperative ileus after cholecystectomy or colorectal cancer (both open and laparoscopic surgery) were identified and included Chinese and English publications. Most of the trials were found to have a high risk of bias. Results of meta-analysis showed that treatment with acupuncture, moxibustion, electroacupuncture, auriculotherapy, and acupoint injection plus standard care was associated with shorter time to passage of first flatus as compared to that with standard care alone. Acupuncture plus standard care was associated with shorter time to first defecation as compared to that with standard care alone.

Conclusions: There is a paucity of high-quality evidence to recommend the use of acupoint stimulation for treatment of postoperative ileus. Randomized trials with adequate sample size, appropriate blinding and rigorous randomization methods should be undertaken to compare acupuncture with both sham and no acupuncture to generate high-quality evidence on this treatment.

Keywords: Acupoint stimulation; Postoperative ileus; Systematic review; Randomized controlled trial

Abbreviations: CENTRAL: Cochrane Central Register of Controlled Trials; CINAHL: Chlna Network Knowledge Infrastructure; TND: Time to Return to Normal Diet; CI: Confidence Intervals; RRs: Risk Ratios; TFD: Time To First Defecation

Introduction

Postoperative ileus is a type of bowel dysmotility that may occur after surgery. It is a particularly common occurrence after abdominal surgery and is characterized by bloating due to accumulation of fluid and flatus in the bowel, pain, nausea, vomiting, intolerance to solid food, and delayed passage of flatus and formed stool [1]. The incidence of postoperative ileus among patients who underwent colectomy in United States in the year 2004 was 17.4% [2]. The etiopathogenesis of postoperative ileus is not completely understood; however, surgical manipulation, inflammatory response, and inhibitory neural reflexes are believed to be involved in its causation [3-5]. Postoperative ileus accounts for a considerable morbidity and economic burden and has a detrimental effect on patient satisfaction [6-7]. Acupuncture and moxibustion are traditional Chinese medical modalities that have been in use over the past 2000 years. Acupuncture involves piercing of meridian points (acupoints) on the body with needles for therapeutic purposes. Moxibustion involves the application of smoldering moxa cones or sticks directly or indirectly on acupoints. With advances in acupuncture techniques, other methods for therapeutic stimulation of acupoints on the basis of meridian theory have emerged, including auriculotherapy (puncture of certain reactive spots on the auricle), electroacupuncture (EA; a combination of needling and electrostimulation), acupoint injection (AI; injection of certain Chinese and/or Western pharmaceutical agents into acupoints), acupressure (application of pressure over acupoints instead of needles), and catgut embedment at the acupoints (CE; implantation of chromic catgut into acupoints for continuous stimulation).
Both animal experiments and clinical studies have shown that acupuncture can induce gastrointestinal transit after abdominal surgery and normalize gastrointestinal function [8-11]. Moreover, EA has been found to promote colonic motility and prevent formation of postoperative intra-abdominal adhesions [12,13]. Moreover, EA stimulation of acupuncture was shown to enhance peristalsis after surgery [14,15], and acupuncture was shown to alleviate intra-abdominal adhesions, accelerate postoperative recovery of mitochondrial and rough endoplasmic reticulum function in the intestinal cells, and to increase the small intestinal transit rate in rats [16-18]. To our knowledge, the currently available evidence pertaining to the effects of acupuncture stimulation on postoperative ileus has not been systematically appraised. In this review, we sought to examine whether acupuncture stimulation can reduce the duration of postoperative ileus in patients who have undergone open or laparoscopic gastrointestinal surgery.

Methods

Search strategy

A literature search for relevant studies was conducted on the following online biomedical databases: the Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; EMBASE; CINAHL; China Network Knowledge Infrastructure; Wan Fang Database; VIP Database for Chinese Technical Periodicals; and Chinese Biomedical Database. Studies published as of April 2017 were eligible for inclusion. A combination of the following key words were used for the literature search: “ileus”, “postoperative”, “acupuncture”, “moxibustion”, “auriculotherapy”, “electroacupuncture”, “acupoint injection”, “acupressure”, and “catgut embedding at acupuncture”. Titles and abstracts of all retrieved articles were independently screened by two reviewers (XTG and GNL) using a novel data extraction form developed for this review. Two other reviewers (GY and JL) then checked and entered the data into the Review Manager 5 software.

Data extraction

From the selected studies, data were independently extracted by two reviewers (XTG and GNL) using a novel data extraction form developed for this review. Two other reviewers (GY and JL) then checked and entered the data into the Review Manager 5 software.

Data pertaining to the following variables related to acupuncture treatment were extracted: type of acupuncture stimulation, treatment frequency, treatment duration, length of each treatment session, and number of points used. Other extracted data elements included author details, title of study, year of publication, study design, disease, sample size, treatment, type of control interventions, TFD, TFF, LOS, and complications related to acupuncture stimulation.

Assessment of risk of bias

All studies were independently evaluated for risk of bias by four reviewers (XTG, GNL, JL, and GY). The risk of bias was categorized as low, high, or unclear using the criteria specified in the Cochrane Risk of Bias Tool. Disagreements, if any, among the reviewers were resolved by consensus. Bias with regard to random sequence generation, concealment of allocation, blinding (or masking), incomplete outcome data, selective reporting of outcomes, and other sources of bias were evaluated.

Data analysis

Statistical analyses were conducted using Review Manager 5. Continuous variables are presented as mean differences (MDs) with 95% confidence intervals (CI), and dichotomous data as risk ratios (RRs) with 95% CI. Trials were included in the meta-analysis if they were reasonably homogeneous with regard to study design, participants, interventions, control, and outcome measures.

Results

Description of studies

A total of 2688 articles (CENTRAL, 14; MEDLINE, 16; EMBASE, 121; CINAHL, 4; CNKI, 1477; VIP, 376; WanFang, 389; CBM, 291) were retrieved on initial search; of these, 878 records were retained after elimination of duplicates. Of these, 878 records were screened for relevance; 121; CINAHL, 4; CNKI, 1477; VIP, 376; WanFang, 389; CBM, 291) were retrieved on initial search; of these, 878 records were...
and abstracts, 816 trials were excluded. Full-texts of 62 articles were reviewed, of which 48 studies were excluded. Finally, only 14 studies qualified for inclusion in this review (Figure 1).

Details of these 14 trials [20-33] are listed in Table 1. Three RCTs incorporated three treatment arms each [24, 28, 32]. All of the studies had similar design and were conducted after laparoscopic or open surgery for cholecystectomy or colorectal cancer. Twelve articles [20-26, 29-33] were published in Chinese language and two [27, 28] in English language between 2008 and 2016. All trials were single-center trials.

These 14 trials included a total of 1299 participants. All cases of postoperative ileus were treated in hospital. Gastrointestinal surgery included cholecystectomy and surgery for colorectal cancer. Study sample sizes ranged from 40 to 216 patients; age of patients ranged from 18 to 85 years. Patients were recruited based on clinical presentation of delayed passage of first flatus and defecation, and intolerance to solid food after gastrointestinal surgery. Only one study protocol [28] was reviewed by an institutional review board and reported study participation with informed consent from patients (Table 1).

Acupoint stimulation in treatment groups included acupuncture [27, 30], moxibustion [23, 24], EA [31, 28], auriculotherapy [22, 25, 33], AI [20, 24, 32], acupressure [21, 32], and CE [29], all of which were accompanied by standard care and compared with the same standard of care in the control group. Only SS Ng et al. [28] compared EA and SA. None of the studies compared acupoint stimulation with placebo or acupoint stimulation with no treatment. There were no reports of mortality or adverse events related to acupoint stimulation in any of the studies included in this review. Detailed information on acupoint stimulation is presented in Table 2.

Methodological quality

The 14 studies included in the review were of poor methodological quality (Figure 2). Three studies [25, 26, 33] reported using a random number table or coin toss, and were accordingly judged as having a low risk of bias. No information on randomization of subjects was specified for the other 11 studies; these were deemed to have a potentially high risk of bias. Only SS Ng et al. [28] reported the use of sealed envelopes for treatment allocation and was judged as having a low risk of bias. However, no information on allocation concealment was reported for the remaining 13 trials; these were judged as having an unclear risk of detection bias. Blinding is not possible for acupoint stimulation, especially in China, as most individuals are familiar with acupuncture. However, study by SS Ng et al. [28] had low risk of performance bias as patients were randomized to EA or SA groups and were blinded to the treatment allocation. Qian [29] & Ng [28] reported blinding of statisticians during statistical analyses; these studies were judged as having a low risk of analysis bias. For the remaining 12 studies, no information related to blinding of participants or personnel was reported; accordingly, these were categorized as having an ‘unclear’ risk of performance bias. There were no missing outcome data in the 14 studies included in the review, and thereby, there is a low risk of attrition bias. As protocols for 13 studies were not available, the risk of reporting bias was categorized as ‘unclear’. Only 1 article reported sample size calculation and was judged to be at a low risk of bias.

Effects of interventions

Primary outcome

a. Time to passage of first flatus: All trials reported data on time to passage of first flatus. Results of meta-analysis showed that treatment with acupuncture (MD: -17.33h, 95% CI, -19.40 to -15.26; 3 trials, I² = 0%, REM), moxibustion (MD: -10.35h, 95% CI, -12.12 to -8.58; 2 trials, I² = 0%, REM), auriculotherapy (MD: -12.80h, 95% CI, -21.09 to -4.5; 3 trials, I² = 0%, REM) and EA (MD: -16.02h, 95% CI, -21.55 to -10.49; 2 trials, I² = 0%, REM) plus SC was associated with shorter TFF as compared to that with SC alone. SC plus SA was associated with shorter TFF as compared to that with SC alone. However, no significant difference in TFF was observed between EA versus SA, and acupuncture plus SC versus SC arms. The forest plot is presented in Figure 3.

Secondary outcomes

a. Time to first defecation: Five trials reported data pertaining to time to first defecation (TDF). Results of meta-analysis showed that treatment with acupuncture (MD: -10.16h, 95% CI, -19.01 to -1.32, 3 trials, I² = 77%, REM) plus SC was associated with shorter TFF as compared to that with SC alone. Auriculotherapy plus SC and CE plus SC were associated with shorter TDF as compared to that with SC alone (Table 3).
### Table 1: Characteristics of the included studies.

| Reference | Country | Design | No. of Patients (TG/CG) | Mean Age (Years) (TG/CG) | Surgery |
|-----------|---------|--------|------------------------|--------------------------|---------|
| Chen [21] | China   | two-arm parallel group randomized trial | 40 (24/16) | 58/58 | colon cancer and rectal cancer surgery |
| Yang [31] | China   | two-arm parallel group randomized trial | 62 (32/30) | 68.59±2.44/69.97±1.59 | cholecystectomy |
| Kou [27]  | China   | two-arm parallel group randomized trial | 40 (20/20) | 58±21/58±11 | gallstone surgery |
| Guo [23]  | China   | three-arm parallel group randomized trial | 50 (25/25) | NR | colorectal cancer |
| Cai [20]  | China   | two-arm parallel group randomized trial | 78 (39/39) | 57.3/56.4 | cholecystectomy |
| Guo [24]  | China   | two-arm parallel group randomized trial | 90 (30/30/30) | NR | colorectal cancer |
| Fu [22]   | China   | two-arm parallel group randomized trial | 60 (30/30) | 48/47 | benign gallbladder polyps, gallstone |
| Qian [29] | China   | two-arm parallel group randomized trial | 62 (31/31) | NR | colorectal cancer surgery |
| Zhang ML [32] | China | three-arm parallel group randomized trial | 136 (46/45/45) | 63/64/61 | gastrointestinal surgery |
| Jin [25]  | China   | two-arm parallel group randomized trial | 216 (108/108) | 42.42±12.58/43.48±11.38 | cholecystectomy |
Table 2: Detailed information on acupoint stimulation.

| Reference | No. of Patients (TG/CG) | Age (Years) (TG/CG) | Interventions                                                                 | Outcomes                                                                 |
|-----------|-------------------------|---------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Chen [21] | 40 (24/16)              | 58/58               | Acupressure at Zusanli (ST36) and Hegu (LI4) bilaterally for 20 min at 6 h postoperatively and thereafter repeated once every 4–6 h until first flatus. | The same routine postoperative care as the intervention group, excluding acupressure, TFF |
| Yang [31] | 62 (32/30)              | 68.59±2.44/69.97±1.59 | Electroacupuncture at Zusanli (ST36) and Sanyinjiao (SP6) bilaterally 4 h postoperatively for 20 min and thereafter repeated every 4 h until first flatus. | The same routine postoperative care as the intervention group, excluding EA, TFF |
| Kou [27]  | 40 (20/20)              | 58±21/58±11         | Acupuncture with filiform needles (0.3 mm diameter, 40 mm length) on alternate days bilaterally at Zusanli (ST 36), Shangjuxu (ST 37), Xiajuxu (ST 39), and Yanglingquan (GB 34). On detection of needling sensation, the doctor performed 20 s of reinforcing-reducing technique, followed by needling manipulation every 5–10 min with retention for 20–30 min. | The same routine postoperative care as the intervention group, excluding Acupuncture, TFF, TFD |
| Author | Study Size | Comparator | Intervention | Result |
|--------|------------|------------|--------------|--------|
| Guo [23] | 50 (25/25) | NR | Moxibustion, circling moxibustion 2 minutes, then bird-pecking moxibustion 1 minute, and along the facial nerves go and back 2 minutes until the feeling disappear | The same routine postoperative care as the intervention group, excluding moxibustion |
| Cai [20] | 78 (39/39) | 57.3/56.4 | Acupoint injection with neostigmine methylsulfate 1 mL into Zusanli (ST36) and Shangjuxu (ST37) at 6 h postoperatively | The same routine postoperative care as the intervention group, excluding AI |
| Guo [24] | 90 (30/30/30) | NR | Group 1 received moxibustion at Zhongwan (CV12), Tianshu (ST25), Shangjuxu (ST37), and Zusanli (ST36), first at 6 h postoperatively and thereafter once daily until recovery of bowel movement (>3 bowel sounds per minute on auscultation). Group 2 received acupoint injection of Vitamin B1 100 mg bilaterally into Zusanli bilaterally, first 6 h postoperatively and thereafter once daily until recovery of bowel movement. | The same routine postoperative care as the intervention group, excluding acupoint injection and moxibustion |
| Fu [22] | 60 (30/30) | 48/47 | Auriculo therapy using Semen Vaccariae administered at CO4, CO7, CO6, and CO17 at 4 h postoperatively and pressed for 5 min until heat sensation was elicited and thereafter repeated every 2 hours until the first flatus | The same routine postoperative care as the intervention group, excluding acupoint injection and moxibustion |
| Qian [29] | 62 (31/31) | NR | Catgut 1.5 cm implanted into Zusanli (ST36) for continuous stimulation at 6 h postoperatively | The same routine postoperative care as the intervention group, excluding CE |
| Zhang ML [32] | 136 (46/45/45) | 63/64/61 | Group 1 Acupoint injection with neostigmine methylsulfate 0.5 mL into Zusanli (ST36), every 12 hours at a time; Group 2 acupressure at Zusanli (ST36) for 10~15 min each time and thereafter repeated once every 4 hours. | The same routine postoperative care as the intervention group, excluding acupoint injection and Acupressure |
| Author   | Study Design          | Sample Size   | Results/Interventions                                                                 | Control Group                                    | Outcomes measure(s)       |
|----------|-----------------------|---------------|---------------------------------------------------------------------------------------|--------------------------------------------------|--------------------------|
| Jin [26] | Auricular acupuncture | 216 (108/108) | 42.42±12.58/43.48±11.38                                                                 | TFF, TND                                         | The same routine postoperative care as the intervention group, excluding auriculotherapy |
| Zhang P  | Auriculotherapy        | 60 (30/30)    | NR                                                                                     | TFD, TFF                                         | The same routine postoperative care as the intervention group, excluding auriculotherapy |
| Ng [28]  | Electroacupuncture    | 165 (55/55/55)| NR                                                                                     | TFD, TND, LOS                                    | The same routine postoperative care as the intervention group, excluding EA.            |
| Sun [30] | Acupuncture           | 90 (30/30/30) | NR                                                                                     | TFD, TFF                                         | The same routine postoperative care as the intervention group, excluding acupuncture   |
| Jin [26] | Acupuncture           | 150 (75/75)   | 52.0±12.5/51.0±10.4                                                                    | TFD, TFF                                         | The same routine postoperative care as the intervention group, excluding acupuncture   |

TFD: Time To Passage of First Flatus; TFFL: Time to First Defecation; LOS: Length Of Hospital Stay; TND: Time To Return To Normal Diet; TG: Treatment Group; CG: Control Group; NR: Not Reported; SC: Standard Care; EA: Electroacupuncture; SA: Sham Acupuncture; AI: Acupoint Injection; CE: Catgut Embedding At Acupoints
Table 3: Effect estimates of the secondary outcomes for postoperative ileus.

| Interventions and Outcomes | Study ID | Sample Size (I/C) | Effect Estimates (95% CI) |
|---------------------------|----------|-------------------|--------------------------|
| **Time to First Defecation** |          |                   |                          |
| Acupuncture+SC vs. SC     | Jin [26] | 150 (75/75)       | MD: -10.16 [-19.01, -1.32] |
|                           | Kou [27] | 40 (20/20)        |                          |
|                           | Sun [30] | 60 (30/30)        | \(I^2=77\%), REM         |
| Auriculotherapy+SC vs. SC | Zhang P [33] | 60 (30/30) | MD: -24.48 [-30.52, -18.44] |
| CE+SC vs. SC              | Qian [29] | 62 (31/31)        | MD: -12.86 [-21.34, -4.38] |
| **Length of Hospital Stay** |          |                   |                          |
| EA+SC vs. SC              | Ng [28]  | 110 (55/55)       | MD: -2.00 [-3.40, 0.60]   |
| EA vs. SA                 | Ng [28]  | 110 (55/55)       | MD: -0.30 [-1.03, 0.43]    |
| CE+SC vs. SC              | Qian [29] | 62 (31/31)        | MD: -2.43 [-5.24, 0.38]    |
| **Time to Return to Normal Diet** |          |                   |                          |
| EA+SC vs. SC              | Ng [28]  | 110 (55/55)       | MD: -19.20 [-33.68, -4.72] |
| EA vs. SA                 | Ng [28]  | 110 (55/55)       | MD: -2.40 [-11.03, 6.23]   |
| Auriculotherapy+SC vs. SC | Jin [25] | 216 (108/108)     | MD: -6.48 [-6.79, -6.17]   |
| CE+SC vs SC               | Qian [29] | 62 (31/31)        | MD: -13.44 [-36.54, 9.66]  |

REM: Random Effects Model; MD: Mean Difference; SC: Standard Care; EA: Electroacupuncture; SA: Sham Acupuncture; CE: Catgut Embedding At Acupoints; I/C: Intervention/Control

b. **Length of hospital stay**: Data pertaining to LOS were available only for two trials. Treatment with EA plus SC was associated with shorter LOS as compared to that with SC alone. However, no significant difference was observed in this respect between EA and SA or between CE plus SC and SC groups (Table 3).

c. **Time to return to normal diet**: Data pertaining to time to return to normal diet (TND) was available only for three trials. No significant difference was observed with respect to TND between CE plus SC and SC groups or between EA and SA groups. However, treatment with auriculotherapy plus SC and EA plus SC was associated with significantly shorter TND as compared to that with SC alone (Table 3).

d. **Mortality**: None of the trials reported data on mortality.

e. **Adverse events**: None of the trials reported data on adverse events.

**Discussion**

**Main findings**

A total of 14 studies with a combined study population of 1299 patients were included in this review. The selected studies investigated the role of acupoint stimulation in patients who developed postoperative ileus after cholecystectomy or surgery for colorectal cancer (both laparoscopic and open surgery). In most of the studies, acupoint stimulation was associated with significant shortening of TFD and TFF as compared to that associated with standard care.

**Limitation**

Firstly, the included studies showed significant clinical heterogeneity with respect to age and sex of patients, preoperative preparation, surgical anesthesia, postoperative analgesia, intraoperative bleeding, routine postoperative care,
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Comparison with other Reviews

Wang et al. [35] reviewed the use of acupoint injection with different medicines for prevention of postoperative ileus. In their meta-analysis, acupoint injection of neostigmine, vitamin B1, or metoclopramide compared to usual care showed a beneficial effect on the time to recovery of bowel sounds, TFD or TFF. The outcome was similar to that used in the present study. However, due to poor methodological quality, definitive conclusions could not be derived [34].

Conclusion

The evidences included in this review have a lot of unclear risk of bias because of lack of sufficient information. Moreover, none of the studies provided information on adverse events related to acupoint stimulation. Therefore, this treatment for patients with postoperative ileus needs to be further studied in terms of efficacy and safety.

High-quality randomized controlled trials of acupoint stimulation for treatment of postoperative ileus are required. These should employ adequate sample size, rigorous randomization methods and appropriate binding techniques.
Moreover, in this modality of treatment, blinding of assessors and statisticians would be more realistically feasible.

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**Authors Contribution**

LSW: protocol development, literature search, quality assessment of trials, development of final review.

XTG: literature search, assessment of trials, data extraction, data entry.

GN L: development of final review.

JL: literature search, assessment of trials, data extraction.

GY: data input.

**Conflict of Interest**

All authors declare that they have no conflict of interests.

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