The effectiveness of acupuncture in postoperative ileus - A systematic review and meta-analysis

by

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Background: Postoperative ileus (POI), also known as postoperative functional gastrointestinal disorder, is generally defined as transient inhibition of normal gastrointestinal motility, which typically last 3-5 days after surgery. It can selectively affect the stomach, small intestine, or colon, each with a different mechanism and clinical presentation, and was managed differently. Due to the disappointing results and side effects of drugs therapy, the use of acupuncture as supplementary and alternative has been of increasing interest. Objective: This paper included a systematic review and meta-analysis on the effectiveness of acupuncture and common acupoints selection in POI. GRADE was used for quality evaluation for meta-analysis; while each trial was evaluated with CONSORT and STRICTA for TCM. Methods: Randomised controlled trials (RCTs) comparing acupuncture with non-acupuncture treatment in POI were identified from databases PubMed, EBSCO, Ovid, CNKI and Wanfangdata. Eligible studies were included, data was extracted and meta-analysis was performed using RevMan 5.2. Results were expressed as RR for dichotomous data, and 95% CI were calculated. Results: Of the 69 studies identified, 4 RCTs, 123 patients in the intervention group and 124 patients in the control group met the inclusion criteria for meta-analysis. Meta-analysis results showed that the number of cured and improvement for acupuncture vs. control (no acupuncture) was significantly more in the intervention than control group (RR 1.09, 95%CI 1.01, 1.18; P=0.02). However, the quality of study was generally low in these studies where blinding was not emphasized in most trials. Conclusions: Acupuncture might be beneficial for the management of POI, the evidence justifies future high-quality studies. Study registration: This research is registered under PROSPERO with registration number CRD42013005485.

Keywords: postoperative postoperative ileus; acupuncture; acupoint; systematic review; meta-analysis

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BACKGROUND

Ileus is the absence of intestinal peristalsis without mechanical obstruction. Postoperative ileus (POI), also known as postoperative functional gastrointestinal disorder (FGID) refers to the time after surgery before coordinated electromotor bowel function resumes[1]. It is generally defined as transient inhibition of normal gastrointestinal motility, which typically last 3-5 days after surgery[2]. It can selectively affect the stomach, small intestine, or colon, each with a different mechanism and clinical presentation, and was managed differently[1].

Acute colonic pseudo-obstruction (colonic ileus) is often seen in elderly hospitalized patients with multiple medical comorbidities[1]. It often occurs after surgery to parts of the body other than the abdomen, such as after orthopedic procedures[1]. In abdominal surgery, it usually takes 2-4 days to recover[3]. The small bowel normally resumes activity several hours after surgery, the stomach 24-48 hours after surgery, and the colon 3-5 days after surgery[1]. POI which persists longer than this can be considered pathologic and is sometimes called paralytic ileus[1].

Clinical consequences of POI include worsened postoperative pain, nausea and vomiting, delay in resuming enteral nutrition and prolonged hospitalization. Other postoperative complications include deconditioning, malnutrition, and increased risk of nosocomial infections and pulmonary complications, may also be increased[2]. Prolonged hospital stay increases the risk of hospital-acquired infections, deep vein thrombosis and other conditions[1]. The mean hospital length of stay was 9.3 days in patients with POI vs. 5.3 days in those without[1]. The costs and economic burden is considerable[1].

Neural and chemical factors may lead to POI. Sympathetic-parasympathetic imbalance, chemical mediators such as nitric oxide, vasoactive intestinal peptide, substance P, calcitonin gene-related peptide, and endogenous opioids, inflammation, narcotic analgesics are important risk factors[1].

Opiates delay colonic transit in postoperative patients, which effect can be reversed by narcotic antagonist naloxone (Narcan)[1]. Nonsteroidal anti-inflammatory drugs (NSAID) such as ketorolac (Toradol) are attractive alternatives to opiate analgesics, both for their anti-inflammatory effect and opiate sparing properties[1]. However, it can cause bleeding, renal insufficiency, and gastritis, that limit their applicability and duration of use[1].

Many strategies have been applied to prevent and manage POI, ranging from changes in surgical technique, supportive care, and patient-initiated activities, to pharmacologic intervention[1]. It has been shown that epidural anesthesia shortens ileus and reduces the need for narcotics[1]. The level of the epidural placement is important: a thoracic epidural is needed to effectively block these sympathetic pathways[1]. It has been shown that thoracic epidural
analgesia hasten the return of bowel function by 1-2 days and to reduce the need for opiates compared to systemic opioids alone[1].

Laparoscopic surgery is less traumatic and has several advantages over open surgery[1]. The systemic inflammatory response appears to be less vigorous after laparoscopic surgery than after open surgery, as measured by circulating levels of interleukin 1, interleukin 6, and C-reactive protein[1]. The length of stay after a laparoscopic procedure is shorter than after an open procedure, and a shorter duration of POI[1].

Numerous studies have evaluated the utility of prokinetic agents in POI with mainly disappointing results. Metoclopramide has failed to improve postoperative bowel motility in several randomized trials. Cisapride showed promise in some prospective trials but has since been withdrawn from the U.S. market due to cardiovascular side effects[2]. Erythromycin has been ineffective in two prospective trials in shortening postoperative ileus[2]. Domperidone, has not been evaluated in the postoperative setting and is not currently available in the U.S[2]. Laxatives are another potential agent. However, larger, randomized trials need to be performed before its use becomes a routine part of postoperative patient care[2].

NSAID may decrease the duration of POI due to their anti-inflammatory effects, and decrease the amount of opiates needed for postoperative pain control. However, physicians must be wary of potential side effects, including antiplatelet effects, increased risk of gastrointestinal bleeding, and adverse renal effects[2]. Cyclooxygenase (COX)-2 selective inhibitors have been reported to be effective in reducing ileus in a recent small study, and may decrease the risk of bleeding associated with the nonselective COX inhibitors[2]. A standardized treatment with minimal side effects awaits further trials.

Acupuncture is widely accepted in China as well as throughout the world as an effective treatment option for the management of postoperative nausea and vomiting and various functional gastrointestinal disorders[4]. However, its role in treating POI is less clear, and data from the Chinese as well as the Western literature are scarce[4].

Acupuncture, acupoint injection, auricular acupressure, abdominal acupuncture, electro-acupuncture and catgut embedment had been used for therapy[5]. Acupoints selection included single acupoint of ST36, ST25; lower confluent acupoint (bilateral lower confluent acupoint with ST36, ST37 and ST39, GB-34; distance acupoints (bilateral LI4, ST36, ST37 and ST39) and combination of near and distance acupoints (CV12, ST25, CV4, CV6, TE6, ST36 and ST37; CV12, ST25, ST36, SP9 and BL20). Other methodology used included warm needle therapy, combination of acupuncture with oral Chinese herbs and combination of acupuncture with topical Chinese medicine[5].
In view of the potential of acupuncture as an alternative and complementary treatment, this study is carried out to evaluate the efficacy of acupuncture for the treatment of POI, common acupoint(s) selection, manipulation technique, side effects and use of rescue anti-emetics.

MATERIALS AND METHODS

Search criteria: We combined the following MeSH and text words with filters:

1. English phrase: postoperative, ileus, functional gastrointestinal disorder, gastrointestinal dysfunction, gastrointestinal function, acupoints, acupressure, transcutaneous electric nerve stimulation, electrical acustimulation, electroacustimulation, electro-acupuncture, auricular acupuncture, moxibustion, sticking therapy


Supplementary search: http://www.google.cn and http://www.clinicaltrials.gov; to search for articles which could not be assessed from the database via the university library website and to check for any left out trials.

Unpublished trials were not included.

Any uncertainties were clarified by contacting the respective corresponding authors of the studies.

Selection criteria

Inclusion criteria: 1. type of research: randomised controlled clinical trials; 2. patients underwent surgery regardless of age, gender, ethnic, type of anaesthesia or surgery; 3. all forms of acupuncture (manual needling, electro-acupuncture, acupressure, etc.) 4. publications within 1986 to 30 Jun 2013, full text articles in English or Chinese.
Outcome measures

Primary outcome: to evaluate the efficacy of acupuncture for the treatment of POI and acupoint(s) selection.

Secondary outcome: to evaluate the manipulation technique, side effects and use of rescue anti-emetics with acupuncture therapy.

Exclusion criteria: 1. non-randomised trials; 2. non clinical trials; 3. patients with other co-existing acute or chronic illness; 4. patients taking medication before operation; 5. articles not in English or Chinese; 6. duplicate articles; 7. articles which data or analysis were not complete.

Data collection and analysis

Published articles were evaluated independently by 2 authors (KBC & JPZ). Relevant, full articles were sorted and cross-examined. Any discrepancies were discussed or further evaluated by a 3rd author (YH). Data was collected in a standardised form including title of journal, authors, year of publication, type of randomisation, type of anaesthesia and surgery, type of intervention, sample size, age and gender of participants, time and technique of intervention, needle retention, depth of needle insertion, duration of intervention and follow up, results, conclusion and side effects.

All trials satisfying the inclusion criteria were included in the initial analysis (Figure 1). Trials whose protocols varied significantly from other studies were excluded.

Data was collected using MS Excel 2010. Collection of randomised controlled clinical trials data was divided into subgroups according to type of intervention. Control groups consisted of usual care and/or medication, depending on the availability of studies.

Meta-analysis was performed using RevMan 5.2. Analysis was presented as RR (relative risk) for dichotomous data and 95%CI with P<0.05 as significant level. Heterogeneity of the data was assessed with I² values. I² values of 25%, 50%, and 75% represent low, moderate, and high heterogeneity. Funnel plots were performed to check the existence of bias (outcome level). If heterogeneity showed P<0.1 or I²>50, sensitivity analysis would be carried out and any outlier would be examined the cause of differences.

Quality of studies was evaluated using GRADE with GRADE profiler version 3.6. Items evaluated included:
1. risk of bias/study limitations (study level), inconsistency, indirectness, imprecision and publication bias (downgrade quality of evidence)

2. large effect, plausible confounding and dose response gradient (upgrade quality of evidence)

According to GRADE Working Group grades of evidence[6], quality of studies was graded as high, moderate, low or very low:

1. High quality: Further research is very unlikely to change our confidence in the estimate of effect.

2. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

3. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

4. Very low quality: We are very uncertain about the estimate.

All trials were evaluated using CONSORT[7] and STRICTA[8] for TCM according to the standard guideline. Items evaluated included title and abstract, introduction, methods, discussion and other information for CONSORT; acupuncture rationale, details of needling, treatment regimen, other components of treatment, practitioner background and control or comparator interventions for STRICTA.

All trials were also evaluated using CONSORT and STRICTA for TCM according to the standard guideline. Results were accumulated and summarized.

RESULTS

Of the 69 studies reviewed, finally a total of 4 studies, 247 participants[9,10,11,12] met the criteria for meta-analysis (Fig 1). Data was summarized in Table 1.

Acupuncture vs. control (usual care)

The proportion of recovery for the 4 pooled trials was 95.93% (118/123) for acupuncture and (87.90%) 109/124 for control. Pooled RR was 1.09 (1.01, 1.18), P=0.02. The number of cured and improvement from POI was significantly more in the intervention group (P<0.05) compared to control group (no acupuncture) (Figure 2A).
Funnel plot were shown in Figure 2B.

Results of meta-analysis showed low to moderate heterogeneity, with $P>0.1$ and $I^2<50$ (Fig 2A). No bias was demonstrated (Funnel plots, Figure 2B).

**Type of intervention**

Four studies[9,10,11,12] included involved the use of manual acupuncture, 1 of the studies applied fast track programme[12].

**Acupoint(s) selection**

For manual acupuncture, ST36 and ST37[9,10,11,12] were the common acupoints selected. In addition, ST39[9,10,11], GB34[9], PC6 and SP4[12] were used in some studies.

**Manipulation technique**

A study on open cholecystectomy performed single finger insertion bilaterally with reinforcing reducing technique for 20s, with 0.30mm x 40mm filiform needle. Needle was left for 20-30min, manipulated once at 5-10min interval, once daily, for 2 times[9]. Another study on appendectomy performed rapid penetration with lift, thrust, twirl, rotation, reinforcing and reducing bilaterally for 30s, followed by needle retention 20min, manipulated once at 10min interval with 0.30mm x 40mm filiform needle within 8h post-operation[10].

One study on appendectomy applied rapid penetration with lift, thrust, twirl, rotation, reinforcing and reducing technique bilaterally for 30s with 0.30mm x 40mm filiform needle, followed by needle retention 20min, manipulate once at 10min interval within 8h post-operation[11]. In another study on colon resection and Dxion procedure, manual acupuncture was performed at postoperative 24h using lift, thrust, twirl and rotation technique, rapid penetration and slow into the depth of 0.8 inch at PC6 and SP4 with 32# x 1 inch filiform needles and into the depth of 1-1.5 inch at ST37 and ST36 with 32# x 1.5 inch filiform needles. Needles were left for 30min, performed once daily for 5 days[12].
Side effects and use of rescue anti-emetics

Three studies reported no side effects[9,10,11] while 1 study did not report whether there was any side effects occurred[12]. There was no reported use of anti-emetics in any of the studies.

QUALITY EVALUATION
GRADE

All studies (Table 1) demonstrated low quality of evidence. None of the studies reported blinding and precision was not reported in the study outcome(s).

CONSORT AND STRICTA FOR TCM

CONSORT: Of the 4 studies, 1(25.00%) reported demographic baseline, 0(0.00%) reported sequence generalization randomisation, 1(25.00%) reported allocation concealment, 0(0.00%) reported details of blinding (Figure 3A).

STRICTA: Of the 4 studies, 4(100.00%) reported the style of acupuncture, 3(75.00%) reported acupoint locations, 1(25.00%) reported depth of needle insertion, 3(75.00%) reported response sought, 4(100.00%) reported needle stimulation, 4(100.00%) reported duration of needle retention and 4(100.00%) reported needle type (Figure 3B).

DISCUSSION

Type of intervention

Meta-analysis showed that the number of cured and improvement for acupuncture vs. control (no acupuncture) was significantly more in the intervention than control group.

Postoperative ileus is a common complication after abdominal surgery, its risk factors include type of surgery, use of perioperative opioid, postoperative analgesia and other related factors. Patients usually present with abdominal distension, nausea, vomiting, absence of bowel sounds, not passing flatus, absence of defaecation, abdominal pain and fever, hiccups and other reactions[9].

The longer the duration of gastrointestinal dysfunction, the more the accumulation of gas and luminal fluid and the less likely recovery would occur. This can even cause adhesions,
intestinal obstruction, anastomotic hernia and other serious complications. The early recovery of the gastrointestinal function, the earlier the patient would be able to consume food. The speed of recovery of the gastrointestinal function is important for the patients’ health[10,11].

The use of drugs to stimulate gastrointestinal motility not only fails to treat the root of the disease, but also increase the burden of the gastrointestinal tract. Acupuncture helps to balance the disharmony of blood and qi and function of the internal organ without addition burden. It can effectively promote the recovery of gastrointestinal function[10,11]. Previous study given acupuncture simultaneously with enteral nutrition support showed that acupuncture could effectively relieve abdominal pain, bloating, nausea, vomiting, diarrhea and other gastrointestinal disorders symptoms, helped the progress of enteral nutrition support to be carried out smoothly, speed up post-surgery early energy consumption and patients’ recovery[13].

A study applied the use of manual acupuncture in “fast track surgery”[12] and found to be more effective than usual care alone. This programme consist of firstly pre-surgery education; secondly optimization use of intraoperative anaesthesia, good insulation measures, minimal invasive surgical technology, minimise postoperative complication and pain and thirdly attention and strengthen postoperative recovery, ambulation and early nutritional support. This programme received attention from home country and abroad and was promoted for various diseases and had proved to be successful in rectal surgery[12].

Chinese medicine believes abdominal surgery causes poor qi, qi stagnation, internal organ qi transportation disorders, disharmony of qi within stomach and spleen in which yang and yin deficiency is the key to this disease. Acupuncture treatment mainly based on regulating the smooth transport of qi within stomach, small and large intestine[9]. Acupuncture therapy at the Stomach Meridian of Foot-Yangming helps to regulate gastrointestinal motility, acid-base balance, fluid secretion, hormones and blood[12].

**Acupoint(s) selection**

ST36 and ST37 were the common acupoints used in manual acupuncture[9,10,11,12]. Acupuncture at ST36 of Foot-Yangming meridian adjust and harmonies qi and blood of the spleen and stomach and complement weakness. ST37 is the lower He-Sea point of the Large Intestine Meridian and Point of the Sea of Blood. In a study on open cholecystectomy[9], ST39 and GB34 were used in addition. ST39 is the Lower He-Sea point of the Small Intestine Meridian and Sea of Blood point. ST37 and ST39 regulate qi of the large and small intestine respectively[3],[9]. GB34 is the He-sea point of the Gall Bladder Meridian of Foot-Shaoyang and Converging point of Sinews. It smooths the qi of gall bladder and prevents the regurgitation of gallbladder qi[3]. The integrated application of the above points can activate the flow of qi and blood, regulate the function of stomach and intestines, and then help the movement of
intestines and relieve bloating\cite{3,9}. It shortened the recovery period of gastrointestinal function after open cholecystectomy\cite{9}. Study done by the same author 2011\cite{3}, acupuncture at the lower He-Sea points shorten the healing time of gastrointestinal function after cholecystectomy. Due to its convenience and lack of side effects, its application is suggested to be used widely in clinical practice.

Two studies on appendectomy performed manual acupuncture on bilateral ST36, ST37 and ST39\cite{10,11} while another study on colon carcinoma resection, PC6 and SP4 were selected in addition to ST36 and ST37\cite{12}. Recent research found that PC6 adjusts gastrointestinal function, inhibits gastric acid secretion and regulate intestinal motility\cite{12}. SP4 is the Luo-connecting point of the Spleen Meridian and master point of the Chong Mai vessel (couple with PC 6). It strengthens the spleen, harmonizes Middle Jiao and regulates Chong Mai.

**Manipulation technique**

Commonly used technique in manual acupuncture included lift, thrust, twirl, rotation, reinforcing and reducing for 20-30s, rapid penetration and slow to the depth of 0.8-1.5 inch insertion with needle retention varied from 20-30min. Three studies reported the use of bilateral acupoint\cite{9,10,11}.

**Side effects and use of rescue anti-emetics**

Overall there were no side effects reported and no reported use of anti-emetics in the studies.

**QUALITY EVALUATION**

**GRADE, CONSORT AND STRICTA FOR TCM**

All studies were conducted in mainland China. Details of blinding and allocation concealment were not emphasised.

Although high quality evidence doesn’t necessarily imply strong recommendations, and strong recommendations can arise from low quality evidence\cite{6}, studies in the future should follow the standard guideline for better quality of evidence.

Future studies should be carried out according to recommendations for better quality of evidence.
LIMITATIONS

There were limitations in this paper due to lack of studies of the same type of intervention(s) to form subgroup for meta-analysis:

1. Efficacy of other forms of acupuncture such as electro-acupuncture, acupressure, acupoint injections, warm needle therapy, auricular acupuncture, auricular acupressure, sticking therapy and moxa-moxibustion could not be elicited.

2. Efficacy of combination of different type of acupuncture intervention(s) could not be elicited.

3. Efficacy of acupuncture vs. anti-emetics could not be elicited.

CONCLUSION

Acupuncture for treatment of POI is worth popularising for its efficacy, safe, cost effectiveness and benefits. Acupuncture might be beneficial for the management of POI, the evidence justifies future high-quality studies.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHOR’S CONTRIBUTION

KBC – study design, data collection and evaluation, data analysis and manuscript writing

JPZ – data collection and evaluation

YH – study design and data evaluation

AUTHOR’S INFORMATION

KBC - MBBS, MMedSc, MPhil; PhD candidate of the integrative Chinese and Western Medicine

JPZ - Undergraduate student
YH - BMed, MMed, PhD; Professor, Chief Physician, Doctoral Supervisor, with her present research mainly on mechanisms underlying the therapeutic effect of acupuncture.

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We would like to express our thanks and gratitude for the contribution.
REFERENCES


Table 1. Data summary and GRADE quality of the 4 studies included in meta-analysis for POI

<table>
<thead>
<tr>
<th>Author, Year Country</th>
<th>Study Population</th>
<th>Type, duration of surgery</th>
<th>Type, duration of anaesthesia</th>
<th>Experimental events</th>
<th>Control events</th>
<th>Rescue anti-emetics</th>
<th>Side effects</th>
<th>GRADE</th>
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<tr>
<td>Kou XR, 2010 Tianjin, China [9]</td>
<td>Adult: M/F 5/13 35-77 (58±21) yo C: M/F 4/15 27-74 (58±11) yo</td>
<td>Open cholecystectomy I:(86.05±29.30) min C:(86.47±30.57) min</td>
<td>Combined intravenous inhalation I:(108.61±98.84) min C:(108.82±99.72) min</td>
<td>Manual acupuncture at bilateral ST36, ST37, ST39, GB34 (n-20)</td>
<td>Usual care (n=20)</td>
<td>Nil</td>
<td>Nil</td>
<td>LOW</td>
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<tr>
<td>Zhang Y, 2011 Tianjin, China [10]</td>
<td>Adult: M/F 32/28 17-72(44)yo C: M/F 29/31 21-73(49)yo</td>
<td>Appendectomy</td>
<td>N/A</td>
<td>Manual acupuncture at bilateral ST36, ST37, ST39 + usual care (n=60)</td>
<td>Usual care (n=60)</td>
<td>Nil</td>
<td>Nil</td>
<td>LOW</td>
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<td>Zhao XF, 2010 Tianjin, China [11]</td>
<td>Adult: M/F 16/14 17-72(44)yo C: M/F 14/16 21-73(49)yo</td>
<td>Appendectomy</td>
<td>N/A</td>
<td>Manual acupuncture at bilateral STS6, ST37, ST39 + usual care (n=30)</td>
<td>Usual care (n=30)</td>
<td>Nil</td>
<td>Nil</td>
<td>LOW</td>
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<td>Wang HM, 2011 Nanjing, China [12]</td>
<td>Adult: M/F 11/4 39-80 (60.40±11.01) yo C: M/F 9/6 41-78</td>
<td>Left colon carcinoma resection, right colon carcinoma resection, Dxion procedure, sigmoid colon</td>
<td>General anaesthesia + continuous epidural anaesthesia</td>
<td>Manual acupuncture at PC6, SP4, ST37, ST36 + usual care (fast track programme) (n=15)</td>
<td>Usual care (fast track programme) (n=15)</td>
<td>Nil</td>
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Abbreviations: I – Intervention  
C – Control
LEGENDS

Figures

1. Figure 1. PRISMA Flow diagram for data collection and analysis.
2. Figure 2. Number of cured and improvement from POI for acupuncture vs. control.
3. Figure 3. Quality assessment graph evaluated using CONSORT and STRICTA for TCM.

Table

1. Table 1. Data summary and GRADE quality of the 4 studies included in meta-analysis for POI
Figure 1. PRISMA Flow diagram for data collection and analysis.
Figure 2A. Acupuncture vs. control (no acupuncture).

Figure 2B. Funnel plot for acupuncture vs. control (no acupuncture).

Figure 2. Number of cured and improvement from POI for acupuncture vs. control.
Figure 3A. Percentage of important items reported (evaluated with CONSORT).

Figure 3B. Percentage of important items reported (evaluated with STRICTA).

Figure 3. Quality assessment graph evaluated using CONSORT and STRICTA for TCM.
Additional files provided with this submission:

Additional file 1: PRISMA 2009 Checklist for POI.docx, 29K
http://www.biomedcentral.com/imedia/3540591681135880/supp1.docx