Effect of Acupuncture on Postoperative Ileus after Distal Gastrectomy for Gastric Cancer

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ABSTRACT

Purpose: Acupuncture has recently been accepted as a treatment option for managing postoperative ileus (POI) and various functional gastrointestinal disorders. Therefore, we conducted a prospective randomized study to evaluate the effect of acupuncture on POI and other surgical outcomes in patients who underwent gastric surgery.

Materials and Methods: Thirty-six patients who underwent distal gastrectomy for gastric cancer from March to December 2015 were randomly assigned to acupuncture or non-acupuncture (NA) groups at 1:1 ratio. The acupuncture treatment was administered treatment once daily for 5 consecutive days starting at postoperative day 1. The primary outcome measure was the number of remnant sitz markers in the small intestine on abdominal radiograph. The secondary outcome measure was the surgical outcome, including the times to first flatus, first defecation, start of water intake, and start of soft diet, as well as length of hospital stay and laboratory findings.

Results: The acupuncture group had significantly fewer remnant sitz markers in the small intestine on postoperative days 3 and 5 compared to those in the NA group. A significant difference was observed in the numbers of remnant sitz markers in the small intestine with respect to group differences by time (P<0.0001). The acupuncture group showed relatively better surgical outcomes than those in the NA group, but the differences were not statistically significant.

Conclusions: In this clinical trial, acupuncture promoted the passage of sitz markers, which may reflect the possibility of reducing POI after distal gastrectomy.

Keywords: Acupuncture; Paralytic ileus; Sitz marker; Stomach neoplasms; Gastrectomy

INTRODUCTION

Ileus occurring immediately after surgery in the absence of precipitating factors is referred to as postoperative ileus (POI) [1]. It is commonly associated with surgery, and may adversely influence patient recovery and prolong hospital stay.

In POI, patients have diffuse discomfort but no sharp colicky pain or distended abdomen. They often have a quiet abdomen with few bowel sounds on auscultation. Stasis and progressive accumulation of gastric and intestinal secretions and gas result in abdominal
distension, pain, nausea, vomiting, and obstipation. Delayed gastric emptying also increases the risk of aspiration in patients during the early postoperative period.

The precise mechanism and etiology of POI are not completely understood. After an abdominal surgical procedure, POI may interfere with or alter the contractile activity of the small bowel, which is governed by a complex interaction between the enteric nervous system, central nervous system, hormones, and local molecular and cellular inflammatory factors [2].

Successful management for reducing POI is challenging. Although chewing gum, epidural local anesthetics, prokinetic agents, and opioid antagonists have been used to shorten the recovery time of intestinal function [3,4], the duration of POI is still reported to be as long as 4 days [5].

Additional treatment modalities are needed to reduce POI because prompt recovery of bowel function after surgery is of major importance, not only for patient well-being, but also for reducing healthcare costs; prolonged ileus can also lead to other complications that prolong hospital stay.

Acupuncture is a minimally invasive integrative oncological modality with a very low incidence of side effects [6]. It has been used in China since thousands of years to treat a variety of gastrointestinal (GI) problems [7] and has recently been used as a treatment option for reducing POI and various functional GI disorders [5,8,9]. Although the role of acupuncture in reducing POI is less clear, several studies have shown accelerated motility and increased contractility of the bowel via parasympathetic and cholinergic pathways after acupuncture treatment [10,11].

Unfortunately, to our knowledge, no clinical studies have confirmed the therapeutic potential of acupuncture in stimulating intestinal transit and resolving paralytic ileus after surgery. Therefore, we conducted a prospective randomized study to evaluate the efficacy of acupuncture in reducing the duration of POI and other surgical outcomes in patients who underwent distal gastrectomy for treatment of gastric cancer.

MATERIALS AND METHODS

Patients
We conducted prospective, randomized controlled, phase III study of patients who underwent distal gastrectomy for histologically proven gastric cancer at the Daegu Catholic University Medical Center from March to December 2015. The inclusion criteria were as follows: patients undergoing elective distal gastrectomy for gastric cancer who were older than 18 years of age, with American Society of Anesthesiologists grades I–III physical status, and who provided written informed consent. We excluded patients with a history of major abdominal or pelvic surgery, those with contraindications to electrical stimulation devices (pacemaker or implantable defibrillator), and those who were allergic to acupuncture needles. This study was approved by the Clinical Research Ethics Committee of Daegu Catholic University Medical Center (DCMC-CR-14-002), and informed consent was obtained from all patients.

Study design
Patients potentially eligible for the study were informed by the principal investigator, regarding the study details on the day before their scheduled surgery, and a standard
perioperative protocol was followed. All surgeries were performed under general anesthesia. The patients were randomized before surgery using simple randomization to either the acupuncture (A) or non-acupuncture (NA) groups in 1:1 ratio. According to our prospective randomized pilot study, the difference in remnant sitz markers in the small intestine between groups on postoperative day 3 was 10.6, with a standard deviation of 9.6; a sample size of 18 patients in each group was needed to yield a power of 90% with a significance level of 0.025 (2 pair-wise comparisons). Thus, a sample size of 40 patients was required for the current study, assuming a 10% dropout rate. All patients in both groups received the same postoperative management. Every patient received intravenous patient-controlled analgesia for pain control immediately after operation and did not receive epidural analgesia. Early ambulation was encouraged from the day after operation. Physical examination including abdominal auscultation was performed daily, and sips of water were started upon audible bowel sounds. When the patient could tolerate water intake without symptoms or adverse events, a liquid diet was started from the next day. Similarly, a soft diet was started from the next day after tolerable intake of the liquid diet. Patients were discharged when they tolerated a solid diet and were fully ambulatory.

**Acupuncture interventions**

The acupuncture treatments were administered at Daegu Catholic University Medical Center by Korean traditional medicine doctors. The acupuncture treatment in the A group was given once daily for 5 consecutive days starting on postoperative day 1. Each session lasted 25 to 30 minutes, starting from the moment the first needle was inserted. Single-use, sterile, disposable acupuncture needles (stainless steel, 0.20 mm in diameter and 40 mm in length) were used. The acupoints used in this study were based on traditional Korean medicine and other studies [5,10,11]. During each acupuncture session, each patient received 16 acupuncture needles at bilateral ST-36 (Zusanli), SP-6 (Sanyinjiao), LI-4 (Hegu), TE-6 (Ziaogou), LV-3 (Taichong), LI-11 (Quchi), and unilaterally at GV-20 (Baihui), EX-HN3 (Yintang), GV-26 (Shuigou), and CV-24 (Chengjiang). The tip of the acupuncture needle was located in the muscle layer. The acupuncture needles were inserted perpendicular to the acupoints in the extremities to a depth of approximately 20 mm from the skin surface. Acupoints located in the head, such as GV-20, EX-HN3, GV-26, and CV-24, were incapable of being accessible at 20-mm depth; therefore, we inserted acupuncture needles 5 mm deep at an angle of 30 degrees to the skin. Electrical stimulation (ES-160; Ito Co., Ltd., Tokyo, Japan) at a frequency of 100 Hz was applied at bilateral ST-36, SP-6, LI-4, and TE-6. No acupuncture treatment was performed in the NA group, but other perioperative management strategies were evenly applied with those in the A group.

**Outcome evaluation**

Detecting the end of POI remains controversial, and studies have used various endpoints. We evaluated as the primary endpoint the numbers of remnant sitz markers in the small intestine that did not pass through the ileocecal valve, as measured radiographically. We inserted a sitz marker capsule (20 sitz markers/capsule) into just the distal part of anastomosis, and radiographs were obtained for every patient on postoperative days 1, 3, 5, and 7. The remnant sitz markers were counted by a single specialized radiologist to reduce bias. Fig. 1 shows representative abdominal radiographs of patients in the A and NA groups.

The secondary outcomes of this study included time to first flatus, start of sips of water, start of soft diet, and hospital stay. Other secondary endpoints included white blood cell (WBC) count and C-reactive protein (CRP) level to assess changes in acute inflammatory reaction.
Statistical analysis
A descriptive analysis was used to summarize the characteristics and operative outcomes using means (standard deviation) for quantitative variables and frequencies (percent) for qualitative variables. Comparisons of the characteristics and operative outcomes between the A and NA groups were analyzed using 2-sample t-tests for quantitative variables and chi-square tests for qualitative variables. The transit analysis of the sitz markers and laboratory parameters by time and group interaction (group differences by time) effects were performed using a repeated-measure two-factor analysis of variance. Contrasts were used for multiple comparisons. All tests were 2-sided, and P<0.05 were considered significant. IBM SPSS Statistics ver. 19.0 (IBM Co., Armonk, NY, USA) was used for the analyses.

RESULTS
Patient demographics
Forty patients were enrolled and randomly assigned to either the A (n=20) or NA (n=20) groups. Two patients in each group were withdrawn due to discontinued intervention or
refusal to participate in this study. Thus, 36 recruited patients were available for the analyses of primary and secondary outcomes. No complications or adverse events related to the use of acupuncture were reported.

The study groups were similar with respect to demographic data and surgical details (Table 1). The patient characteristics were well balanced between the groups with respect to age, sex, body mass index, operation method, tumor size, postoperative stage, retrieved lymph nodes, and combined resection. Gastroduodenostomy was performed after distal gastrectomy in all patients. Each group had one patient who underwent combined resection, both of which were cholecystectomies for gall bladder stones. No patient stayed in the intensive care unit.

**Outcome measures**

The comparison between the numbers of remnant sitz markers in the small intestine between the A and NA groups is shown in Table 2 and Fig. 2. The A group had significantly fewer remnant sitz markers in the small intestine on postoperative days 3 and 5 compared with those in the NA group (3.22±4.26 vs. 14.17±4.02, P<0.001; 0.00±0.00 vs. 5.89±3.18, P<0.001). A significant difference was also observed between the numbers of remnant sitz markers in the small intestine with respect to time and group interaction (group difference by time) effects (P<0.001).

Table 3 shows the comparison of surgical outcomes between the A and NA groups. The A group had significantly faster time to first flatus than those in the NA group (2.33±0.49 vs. 2.94±0.80 days, P=0.009). The A group also tended to show relatively faster time to first defecation (2.94±0.64 vs. 3.39±0.69 days), earlier ingestion of water (3.22±0.65 vs. 3.67±0.59 days), earlier consumption of a soft diet (4.61±0.92 vs. 4.83±0.86 days), and shorter hospital stay (9.72±2.29 vs. 10.17±2.38 days) than those shown by the NA group, but the differences were not statistically significant (P=0.054, 0.055, 0.458, and 0.572, respectively).

### Table 1. Clinicopathological characteristics of the acupuncture and non-acupuncture groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acupuncture group (n=18)</th>
<th>Non-acupuncture group (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>60.94±9.43</td>
<td>60.06±13.18</td>
<td>0.817</td>
</tr>
<tr>
<td>Sex (male:female)</td>
<td>16 (88.9):2 (11.1)</td>
<td>16 (88.9):2 (11.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.76±3.89</td>
<td>22.39±3.56</td>
<td>0.650</td>
</tr>
<tr>
<td>Operation method (open:laparoscopy)</td>
<td>15 (83.3):3 (16.7)</td>
<td>16 (88.9):2 (11.1)</td>
<td>0.630</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>3.49±1.93</td>
<td>4.52±2.33</td>
<td>0.181</td>
</tr>
<tr>
<td>Stage (I:II:III)*</td>
<td>10 (55.6):4 (22.2):4 (22.2)</td>
<td>7 (38.9):6 (33.3):5 (27.8)</td>
<td>0.594</td>
</tr>
<tr>
<td>Retrieved lymph node</td>
<td>41.72±10.94</td>
<td>40.22±6.94</td>
<td>0.626</td>
</tr>
<tr>
<td>Combined resection</td>
<td>1 (5.6)</td>
<td>1 (5.6)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*Classification according to the American Society of Anesthesiologists grades.

Values are presented as mean±standard deviation or number (%).

### Table 2. Comparison of numbers of remnant sitz markers in the small intestine between the acupuncture and non-acupuncture groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acupuncture group (n=18)</th>
<th>Non-acupuncture group (n=18)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>19.56±0.78</td>
<td>20.00±3.00</td>
<td>0.950</td>
</tr>
<tr>
<td>3</td>
<td>3.22±4.26</td>
<td>14.17±4.02</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>5</td>
<td>0.00±0.00</td>
<td>5.89±3.18</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>7</td>
<td>0.00±0.00</td>
<td>1.50±2.53</td>
<td>0.317</td>
</tr>
<tr>
<td>Time and group interaction</td>
<td></td>
<td></td>
<td>P&lt;0.001* (1&gt;3, 5, 7)</td>
</tr>
</tbody>
</table>

*Statistically significant difference (P<0.05). †Result of repeated-measures two-factor analysis of variance. ‡Result of multiple comparisons by contrast.

Values are presented as mean±standard deviation.
The comparison of laboratory outcomes between the A and NA groups is shown in Table 4. Postoperative WBC counts increased gradually and were significantly lower on postoperative day 5 and 7 (P<0.001 and P<0.001, respectively). Significantly fewer remnant sitz markers are detected in the A group than in the NA group with respect to the time and group interaction (P<0.001).

*Statistically significant difference (P<0.05).

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**Table 4.** Comparison of acute inflammatory parameters between the acupuncture and non-acupuncture groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acupuncture group (n=18)</th>
<th>Non-acupuncture group (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cells</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative day</td>
<td>8.73±3.14</td>
<td>8.57±4.19</td>
<td>0.897</td>
</tr>
<tr>
<td>Postoperative day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12.09±2.62</td>
<td>12.61±2.83</td>
<td>0.576</td>
</tr>
<tr>
<td>3</td>
<td>13.15±2.51</td>
<td>14.37±4.74</td>
<td>0.340</td>
</tr>
<tr>
<td>5</td>
<td>8.33±1.79</td>
<td>11.00±2.34</td>
<td>0.001*</td>
</tr>
<tr>
<td>7</td>
<td>7.94±1.71</td>
<td>9.93±2.33</td>
<td>0.006*</td>
</tr>
<tr>
<td>Time and group interaction</td>
<td></td>
<td></td>
<td>P&lt;0.273</td>
</tr>
</tbody>
</table>

C-reactive protein

<table>
<thead>
<tr>
<th>Variable</th>
<th>Acupuncture group (n=18)</th>
<th>Non-acupuncture group (n=18)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative day</td>
<td>2.75±2.01</td>
<td>2.81±2.69</td>
<td>0.941</td>
</tr>
<tr>
<td>Postoperative day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>84.84±91.04</td>
<td>83.32±45.34</td>
<td>0.943</td>
</tr>
<tr>
<td>3</td>
<td>141.62±45.88</td>
<td>139.95±60.81</td>
<td>0.927</td>
</tr>
<tr>
<td>5</td>
<td>84.19±41.34</td>
<td>109.91±74.36</td>
<td>0.211</td>
</tr>
<tr>
<td>7</td>
<td>69.44±47.27</td>
<td>99.61±72.99</td>
<td>0.152</td>
</tr>
<tr>
<td>Time and group interaction</td>
<td></td>
<td></td>
<td>P&lt;0.585</td>
</tr>
</tbody>
</table>

Values are presented as mean±standard deviation.

*Statistically significant difference (P<0.05).

Values are presented as mean±standard deviation.

*P<0.05, statistically significant difference. ¹Result of repeated-measures two-factor analysis of variance. ²Result of multiple comparisons by contrast.
day 5 and 7 in the A group than those in the NA group (P=0.001 and P=0.006), but the difference was not significant for the time and group interaction (group difference by time) effects (P<0.273). Postoperative CRP levels in both groups increased gradually and decreased on postoperative days 5 and 7, but the difference was not statistically significant (P<0.585).

DISCUSSION

Acupuncture has been used as a minimally invasive integrative modality for GI motility disorders in China and Korea for thousands of years and is now being accepted by clinicians and patients in the West as an effective treatment option for various functional GI disorders. Acupuncture improves GI motility in laparotomy animal models [12-15] and has a positive effect on GI motility in healthy volunteers, patients with diabetic gastroparesis, and those who have undergone transabdominal hysterectomy and colonic surgery [16-21]. However, the role of acupuncture for reducing POI is less clear, and data from Chinese and Western literature are scarce.

To date, 3 properly conducted randomized controlled trials for preventing POI after surgery using acupuncture have been published in the English literature. Meng et al. [21] randomly assigned 90 patients with prolonged POI to receive electro-acupuncture or no acupuncture after surgery but failed to show significant differences in time to first bowel movement and pain scores between the 2 groups. Deng et al. [22] randomized 81 patients to receive true acupuncture or sham acupuncture after colonic surgery, but true acupuncture did not reduce POI more compared to sham acupuncture. Ng et al. [5] randomly assigned 165 patients who underwent elective laparoscopic surgery for colonic and upper rectal cancer to receive electro-acupuncture or sham or no acupuncture after surgery. In their study, electro-acupuncture reduced the duration of POI, time to ambulation, and postoperative analgesic requirements compared with those in the no or sham acupuncture groups. However, to our knowledge, no other studies have been conducted on patients who underwent gastric surgery.

The selection of acupoints for our study was based on expert consensus provided by qualified and experienced acupuncturists. The most commonly used acupoint for treating POI in clinical studies is ST-36 [20,21]. Electro-acupuncture at ST-36 with 100 Hz of electrical stimulation reduces the postoperative analgesic requirement and associated side effects in patients undergoing lower abdominal surgery [23]. We also used other acupoints, such as SP-6, LI-4, and TE-6 with electrical stimulation, which is effective in patients with POI [5] and LV3 and LI-11, which are widely used acupoints to treat GI disorders. The combined therapeutic effects of electro-acupuncture at these acupoints contribute to accelerated recovery from POI via parasympathetic and cholinergic pathways [19,20].

It is important to define specific parameters when evaluating a patient for POI. One commonly used parameter is time to recover GI function (GI-3), which is a 3-component composite endpoint that includes time until the patient first tolerates solid food and the time until the patient first passes either flatus or shows bowel movement [24]. In this study, the A group had significantly faster time to first flatus than did the NA group (2.33±0.49 vs. 2.94±0.80 days, P=0.009). However, flatus is often regarded as an insensitive parameter [25], and the time to resume diet can be influenced by the patient’s perception and can be easily manipulated by the attending clinician.
Two techniques have been used to evaluate GI motility, such as transit of sitz (plastic) markers viewed radiographically and transit of radioisotope detected by gamma camera (scintigraphy) [26,27]. Sitz markers have been used longer and are widely available because they are simple and clearly identifiable markers. In this study, we inserted a sitz marker capsule (20 sitz markers/capsule) into distal bowel at the anastomosis and counted the remnant numbers of markers visible in the small intestine radiograph every other day. This method provided quantitative data for POI. Therefore, we adopted the numbers of remnant sitz markers in the small intestine as the single primary outcome measure for this study because it was more objective and could be readily recorded by the assessor without bias.

Preventing POI, a major cause of delayed discharge after abdominal surgery, is the most important objective of Enhanced Recovery After Surgery (ERAS) protocols. The term ERAS is often used to describe a multimodal perioperative care program that was previously called “fast-track surgery” [28]. This program comprises several evidence-based perioperative care elements that are individually beneficial, and result in substantially improved surgical outcomes when used together. Several factors are included in ERAS protocols, including gum chewing, mid-thoracic epidural analgesia, oral magnesium oxide, and bisacodyl suppositories to promote bowel motility after abdominal surgery [29,30]. These protocols reduce time to a bowel movement by 1 to 2 days. In this study, we demonstrated that acupuncture can be easily and safely applied to enhance recovery of bowel motility and may be useful as a potential factor in ERAS protocols.

This study has several limitations. First, although same postoperative management was applied in both groups, the A group received more attention for at least 25 to 30 minutes per each day as part of the acupuncture treatment compared to the NA group. Because sham acupuncture was not used in this study, the lack of interaction between physician and patient in the NA group could have affected the results. Second, this study was conducted on patients who had undergone open as well as laparoscopic gastrectomies; however, there were only 5 laparoscopic gastrectomies in the study population. Although there was no significant difference in operative method between the treatment groups, the possibility remains that the duration of POI was influenced by whether the patients underwent open or laparoscopic surgery. Finally, the small number of patients may have been insufficient to compare the surgical outcomes. However, we observed more favorable results for each of these surgical outcomes in the A group than those in the NA group, even though there were no statistical significances (Table 3). Therefore, further large-scale studies are warranted to validate and generalize these findings.

In conclusion, this study showed that acupuncture could promote the passage of sitz markers in the small intestine. This result may reflect the potential effect of acupuncture on reducing the duration of POI after gastric cancer surgery, by earlier recovery of small bowel movement. Although further studies are warranted to validate these findings, acupuncture could reduce POI and be used as an ERAS protocol method for patients undergoing gastric cancer surgery.

REFERENCES


