

Combined Therapeutic Value of Acupuncture and Parecoxib Sodium Therapy for Bowel Function Recovery after Laparoscopic Cholecystectomy

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Xiao *et al.*: Acupuncture and Parecoxib Sodium Therapy for Bowel Function Recovery

The main objective of this study is to investigate the added therapeutic value of acupuncture+parecoxib sodium therapy on bowel function recovery after laparoscopic cholecystectomy. According to the calendar periods of the hospital admission, we retrospectively included 173 patients who received laparoscopic cholecystectomy, some of whom received acupuncture at Zusanli, Yanglingquan, and Taichong combined with parecoxib sodium therapy. Of the 173 patients included, 53 (30.6 %) received postoperative acupuncture plus parecoxib sodium therapy. There was no statistically significant difference in baseline characteristics of the patients ($p>0.05$). Gastrointestinal symptoms and time taken for first anal exhaust or first defecation after the surgery were studied as outcomes to evaluate the recovery of bowel function. Patients who received acupuncture plus parecoxib sodium therapy experienced fewer gastrointestinal symptoms including bloating (11.3 % vs. 25.8 %, $p=0.032$) and constipation (13.2 % vs. 27.5 %, $p=0.040$), a shorter time to first anal exhaust (37.7 ± 11.3 h vs. 44.2 ± 14.6 h, $p=0.005$) and time to first defecation (60.3 ± 18.7 h vs. 68.4 ± 21.1 h, $p=0.017$), and fewer prescriptions of gastric prokinetic agents (28.3 % vs. 45.8 %, $p=0.030$) compared to those patients, who did not receive any acupuncture treatment (parecoxib sodium monotherapy). In addition to standard care, acupuncture at Zusanli, Yanglingquan, and Taichong+parecoxib sodium therapy facilitates the recovery of bowel function after laparoscopic cholecystectomy.

Key words: Acupuncture, parecoxib sodium, laparoscopic cholecystectomy, gastrointestinal disorders, bowel function

Laparoscopic Cholecystectomy (LC) is one of the most commonly performed abdominal surgical procedures^[1,2] and has been considered as a standard surgical treatment for gallstone diseases including cholelithiasis, acalculous cholecystitis, gallbladder polyp, and porcelain gallbladder^[3,4]. The procedure itself was a mature operative technique^[5], which usually can be performed under general anesthesia within a short duration of time. Along with that healthy and reliable patients with good home support can leave the hospital shortly after the surgery^[6,7]. Although serious postoperative complications (including bile duct injury, bile leaks, bleeding and bowel injury) may still occur, which are often related to surgeon's experience and patient selection^[8-13]. The adverse incidences are rare, which includes <2 % for biliary duct

injuries^[14], up to 3 % for bile leaks^[15], <1.5 % for receiving transfusion rates of blood components^[16], and <1 % for bowel injury^[17]. However, changes in bowel function after LC are rather common (>30 %)^[18], including decrease in bowel movements, flatulence, eructation, indigestion and constipation, although these complications are usually related to the side effects of pain medications, anesthesia and a lack of mobility, instead of the procedure itself^[19,20]. The gastrointestinal symptoms are usually unspecific and mild, but patients with impaired bowel function may experience worse quality of life, longer hospital stays, higher hospital costs and higher risk of readmission^[21-23]. Although some pharmacologic interventions seems to recovery from postoperative ileus, the therapeutic effects are not satisfying in trials

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and may accompany by side effects^[24]. As a non-pharmacologic intervention, acupuncture has been used as additional treatment for recovery of gastrointestinal function^[25] in patients who received LC, although the therapeutic effects are still in doubt due to poor quality of evidence, limited data, and clinical heterogeneity of acupuncture methods. Parecoxib sodium is a Cyclooxygenase-2 (COX-2) inhibitor with anti-inflammatory and anti-oxidative stress actions, which mainly plays its role by inhibiting inflammatory cytokines and reducing Reactive Oxygen Species (ROS), and lipid peroxide levels^[26,27]. It is primarily used for its analgesic effects in patients undergoing LC, which not only helps in reducing the amount of morphine used after surgery, but also has some certain safety benefits^[28,29].

However, limited data is available regarding the effect of acupuncture+parecoxib sodium on bowel function recovery of patients after LC. In order to provide more evidence about the clinical value of acupuncture+parecoxib sodium therapy, the study aimed to investigate the added therapeutic value of this combination therapy on recovery of bowel function of patients undergoing LC.

MATERIALS AND METHODS

Study participants:

We retrospectively included 173 patients who were admitted and received LC in the Department of General Surgery of Hanchuan People's Hospital from January 2017 to December 2019 by using medical data collected from the hospital information system. The current study was approved by the Ethical Committee of Hanchuan People's Hospital and was conducted in accordance with the Declaration of Helsinki.

Inclusion criteria:

Patients who were admitted to the department of general surgery of Hanchuan People's Hospital between January 2017 and December 2019; patients who received elective LC during the hospitalization and length of hospital stay ≥ 72 h were included in the study.

Exclusion criteria:

Patients with prior history of abdominal surgery; patients who received other procedures during the LC, including those switched to open cholecystectomy; patients who had any other

gastrointestinal diseases, except for gallstone diseases and patients who had cancer or other severe chronic diseases, such as end-stage renal disease were excluded from the study.

LC and standard care:

Abdominal ultrasonography and/or computed tomography scan were always performed for patients with suspected gallstone diseases. One of the deputy chief physicians or chief physicians in the department of general surgery would evaluate the examinations and make a decision whether LC is needed or not for the patients, who were usually the same surgeons who will perform the procedure if it was indicated. During the study period, all the indicated patients were given a standard 3-port-technique LC under general anesthesia, as well as an intravenous administration of 40 mg of parecoxib sodium diluted to 2 ml by 0.9 % sodium chloride at the end of the pneumoperitoneum. The surgeon who performed the surgery will make the decisions regarding intraoperative cholangiograms, switch to open cholecystectomy, or placement of drain after the procedure. After the LC, the patients would generally stay for a few days, during which they would receive standard post-operation care, including rest for the first 24 h, diet (i.e., starting with clear liquids and then advancing to a regular low-fat diet), wound care, and medications for pain control or antibiotics (which were indicated by the treating physicians). We retrospectively collected few variables as baseline characteristics of the patients, which includes age, sex, Body Mass Index (BMI), smoking history, hypertension, diabetes, duration of LC, length of hospitalization, prescriptions of medications for pain control or antibiotics during the hospitalization.

Routine care for recovery of bowel function after LC:

All patients after LC would be monitored for bowel function until they were discharged. A nurse would visit the patients every day to collect information about gastrointestinal symptoms, and time taken for first anal exhaust and first defecation. All the information was reported to the treating physician of the patient, who would visit the patient at least once a day. Based on that information, the physician might prescribe gastric prokinetic agents (domperidone or mosapride) or laxative (mainly lactulose oral solution). We retrospectively collected few variables to evaluate

the recovery of bowel function, which includes abdominal pain, bloating, constipation, diarrhea, time taken for first anal exhaust, time to first defecation, and prescriptions of gastric prokinetic agents or laxatives.

Acupuncture treatment:

As collaboration with the Department of Traditional Chinese Medicine of Hanchuan People's Hospital, acupuncture treatment was performed on the 2nd d after the surgery for all the admitted patients unless contraindicated or patients disagreed to participate. Acupuncture was all given by the experienced physiotherapists using disposable, stainless steel acupuncture needles (0.25×40 mm) and the acupuncture points were Zusanli (ST36), Yanglingquan (GB34), and Taichong (LR3)^[30]. A single 20 min acupuncture treatment was provided to each patient. During the acupuncture treatment, the response of the patients was monitored by the treating physiotherapists.

Statistical analysis:

We used International Business Machines (IBM) Corporation Statistical Package for Social Sciences (SPSS) software (version 22) to perform all the statistical analyses. Baseline characteristics of the patients were presented as mean±standard deviations or frequency and proportions, and

compared between the two groups of patients. Student's t-test or Chi-square (χ^2) test was used to examine the difference between the two groups. Recovery of bowel function after LC was studied as the outcomes and compared between the two groups, which were evaluated by gastrointestinal symptoms, frequencies of bowel sounds and prescriptions of prokinetic agents or laxatives. Statistical results were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

According to the inclusion and exclusion criteria, a total of 173 patients were included. The mean age was (52.5±13.8) y and 56.6 % (98/173) were male patients. The mean BMI was (23.6±4.3) kg/m² and 30.1 % (52/173) patients had smoking history. Prevalence of hypertension and diabetes were 11.6 % (20/173) and 22.5 % (39/173), respectively. The mean duration of LC was (64.9±8.8) min and all patients were treated with parecoxib sodium before surgery.

After the surgery, 53 (30.6 %) patients received acupuncture treatment and 120 (69.4 %) patients did not receive acupuncture treatment. There were no statistically significant difference in the above baseline characteristics ($p > 0.05$) between the two groups (Table 1).

TABLE 1: BASELINE CHARACTERISTICS OF THE INCLUDED PATIENTS

Characteristics	Patients (n=173)	Patients who didn't received acupuncture treatment (n=120)	Patients who received acupuncture treatment (n=53)	p value
Age (years)	52.5±13.8	52.2±13.3	53.1±15.1	0.682
Sex				
Male	98 (56.6 %)	71 (59.2 %)	27 (50.9 %)	0.314
Female	75 (43.4 %)	49 (40.8 %)	26 (49.1 %)	
BMI (kg/m ²)	23.6±4.3	23.9±4.3	22.8±4.0	0.121
Smoking history	52 (30.1 %)	38 (31.7 %)	14 (26.4 %)	0.487
Hypertension	20 (11.6 %)	13 (10.8 %)	7 (13.2 %)	0.653
Diabetes	39 (22.5 %)	25 (20.8 %)	14 (26.4 %)	0.418
Duration of LC (minutes)	64.9±8.8	64.8±8.8	65.1±8.7	0.867
Prescriptions of medications for pain control	106 (61.3 %)	68 (56.7 %)	38 (71.7 %)	0.061
Prescriptions of antibiotics	15 (8.7 %)	12 (10.0 %)	3 (5.7 %)	0.35

Patients who received acupuncture treatment were less likely to experience bloating (11.3 % vs. 25.8 %, $p=0.032$), constipation (13.2 % vs. 27.5 %, $p=0.040$), and had a shorter time to first anal exhaust (37.7 ± 11.3 h vs. 44.2 ± 14.6 h, $p=0.005$) and time to first defecation (60.3 ± 18.7 h vs. 68.4 ± 21.1 h, $p=0.017$) when compared to those who did not receive acupuncture treatment, while no significant difference was observed in length of hospitalization, abdominal pain and diarrhea ($p>0.05$) (Table 2). Meanwhile, fewer gastric prokinetic agents were prescribed to patients who received acupuncture treatment than those who did not receive acupuncture treatment (28.3 % vs. 45.8 %, $p=0.030$), but regarding the prescription of laxatives there was no significant difference between the two groups.

Although the recovery is usually quicker for laparoscopic surgery than open surgery as it is less traumatic^[31] but postoperative functional gastrointestinal disorder is rather common after abdominal surgery. Acupuncture therapy is observed to provide potential therapeutic effect on recovery of gastrointestinal function after cholecystectomy, but evidence from available studies is not conclusive due to poor quality evidence, limited data and clinical heterogeneity

of acupuncture methods^[25]. Parecoxib sodium has been shown to relieve and inhibit acute or chronic pain and opioid dependence, but little is known about its effect on postoperative gastrointestinal function recovery. In this study, we performed a retrospective study which included 173 patients who received LC to evaluate the added therapeutic value of acupuncture+parecoxib sodium therapy on post-LC bowel function recovery. We found patients who received acupuncture treatment had fewer gastrointestinal symptoms including bloating, constipation, a shorter time to first anal exhaust, time to first defecation and fewer prescriptions of gastric prokinetic agents, compared to those who did not receive acupuncture treatment. These results confirm the added therapeutic effect of acupuncture+parecoxib sodium therapy on bowel function recovery after LC. Although our study is an observational study, the assignment of acupuncture treatment in our study was based on calendar period. Such a design increased the strength of our study, which greatly alleviated concern about combination therapy^[32]. Therefore, our findings provide new support for the use of acupuncture+parecoxib sodium treatment for patients who received LC to help recover bowel function.

TABLE 2: RECOVERY OF BOWEL FUNCTION AFTER LC

Variables	Patients (n=173)	Patients who didn't received acupuncture treatment (n=120)	Patients who received acupuncture treatment (n=53)	p value
Length of hospitalization (days)	8.2±3.6	8.6±3.6	7.5±3.5	0.063
Abdominal pain	17 (9.8 %)	13 (10.8 %)	4 (7.5 %)	0.503
Bloating	37 (21.4 %)	31 (25.8 %)	6 (11.3 %)	0.032
Constipation	40 (23.1 %)	33 (27.5 %)	7 (13.2 %)	0.04
Diarrhea	24 (13.9 %)	19 (15.8 %)	5 (9.4 %)	0.262
Time to first anal exhaust (Hours)	42.2±14.0	44.2±14.6	37.7±11.3	0.005
Time to first defecation (Hours)	65.9±20.7	68.4±21.1	60.3±18.7	0.017
Prescriptions of gastric prokinetic agents	70 (40.5 %)	55 (45.8 %)	15 (28.3 %)	0.03
Prescriptions of laxative	21 (12.1 %)	16 (13.3 %)	5 (9.4 %)	0.469

In the study, the selected acupoints were ST36, GB3, and LR3. ST36 is the most common acupoint in the similar studies^[24]. According to the therapy of traditional Chinese medicine, ST36 is located along the stomach meridian of foot-Yangming, and is the lower He-sea point of the stomach. Acupuncture at ST36 is believed to regulate gastrointestinal movement and therefore help recovery of bowel function after LC. A meta-analysis included 30 trials involving 2967 participants supported potential preventive effect of ST36 acupoint injections with various agents for postoperative ileus^[33]. In the study of Zhang *et al.* multimodal analgesia, including parecoxib sodium intervention, not only reduced postoperative pain and avoided the increased risk of postoperative complications in patients undergoing radical gastrectomy, but also promoted the recovery of gastrointestinal function^[34]. Our study also found that the acupuncture group was less likely to experience bloating, constipation and fewer gastric prokinetic agents were prescribed compared to the non-acupuncture group, which was consistent with other studies. GB34 is the lower He-sea point of the gall bladder and is located along the gall bladder meridian of foot-Shaoyang, an acupuncture point which is commonly selected together with ST36. Acupuncture at GB34 is believed to disperse stagnant liver qi, promotes bile flow, smooth the flow of gallbladder qi, and prevents regurgitation^[24]. LR3 is the source (yuan) point for the liver meridian, where the vital energy of the organs (Zang-Fu organs) pass through and acupuncture at LR3 is believed to stimulate or spread the vital energy of the other meridians and regulate the function of other organs^[35]. Our findings demonstrated that acupuncture at the above three acupoints did speed up the recovery of bowel function after LC. Firstly, our study is a retrospective study, so we were not able to introduce strict standards regarding the selection of the patients and the procedures involved in LC. We were also unable to evaluate the study outcomes more strictly. Instead, we could only identify the relevant symptoms from the medical records. It is possible that these symptoms were not recorded using the same criteria. These limitations may impair the validity of our findings and should be validated in prospective studies. Second, our study is still at risk of residual confounding, although this may not be a great concern because the assignment

of acupuncture treatment was according to calendar periods. Last but not least, there were several other forms of acupuncture; it remains unknown whether other techniques of acupuncture would provide the same or better therapeutic effect on recovery of bowel function after LC.

Acupuncture at ST36, GB34 and LR3 combined with parecoxib sodium therapy facilitates bowel function recovery after LC in addition to standard care, but more studies are needed to confirm our findings.

Author contributions:

Hui Xiao has contributed in data curation, formal analysis, methodology, investigation and writing the original draft. Lan Xiao has contributed in conceptualization, methodology, supervision, reviewing and editing the manuscript.

Conflict of interests:

The authors declared no conflict of interests.

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