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BRIEF ARTICLE

Effect of implanting fibrin sealant with ropivacaine on pain after laparoscopic cholecystectomy

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Abstract

AIM: To investigate the safety and efficacy of implanting fibrin sealant with sustained-release ropivacaine in the gallbladder bed for pain after laparoscopic cholecystectomy (LC).

METHODS: Sixty patients (American Society of Anesthesiologists physical status was Ⅰ or Ⅱ and underwent LC) were randomly divided into three equal groups: group A (implantation of fibrin sealant in the gallbladder bed), group B (implantation of fibrin sealant carrying ropivacaine in the gallbladder bed), and group C (normal saline in the gallbladder bed). Postoperative pain was evaluated, and pain relief was assessed by visual analog scale (VAS) scoring.

RESULTS: The findings showed that 81.7% of patients had visceral pain, 50% experienced parietal, and 26.7% reported shoulder pain after LC. Visceral pain was significantly less in group B patients than in the other groups ($P < 0.05$), and only one patient in this group experienced shoulder pain. The mean VAS score in group B patients was lower than that in the other groups.

CONCLUSION: Visceral pain is prominent after LC and can be effectively controlled by implanting fibrin sealant combined with ropivacaine in the gallbladder bed.

Key words: Analgesia; Fibrin sealant; Laparoscopic cholecystectomy; Pain; Ropivacaine

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INTRODUCTION

Since the widespread adoption of laparoscopic cholecystectomy (LC) in the late 1980s, LC has become the gold standard for chronic cholecystitis[1]. Postoperative pain after LC is generally less than that after open cholecystectomy, however, the postoperative pain experienced by patients still causes preventable distress. Treating postoperative pain is an important and primary objective, because it affects patients' comfort, postoperative morbidity, and, inevitably, social costs due to prolonged hospitalization and work inactivity. Pain after LC can be divided into three components, namely, visceral, parietal, and shoulder pain, with different intensities and time courses[2]. LC is mainly associated with visceral pain[3] which may refer to the shoulder in 35% to 60% of cases[4,5]. Various treatments have been proposed to make this surgery as pain-free as possible[6-8]. The main objective of this study was to assess the effectiveness of implanting fibrin sealant combined with ropivacaine in the gallbladder bed for pain control after LC.

MATERIALS AND METHODS

The study was designed as a single-center, randomized trial. Of the 78 patients who underwent LC from October 2008 to August 2009, 60 patients (42 women, 18 men) were enrolled in this study, which was performed after approval was received from the Ethics Committee of Beijing Tongren Hospital, Capital Medical University. All patients whose American Society of Anesthesiologists (ASA) physical status were Ⅰ or Ⅱ underwent diagnostic abdominal ultrasound, liver function tests, and coagulation profile along with hematologic and biochemical investigations. Patients with previous major upper abdominal surgeries, choledocholithiasis, acute

cholecystitis, or conversion to open cholecystectomy were excluded from the study. Patients with a body mass index higher than 35, and those with diminished liver and kidney functions were not evaluated in this study. The visual analog pain evaluation scale (VAS) was introduced to the patients before surgery and the details of the study were explained to the patients. All patients stated that they understood the VAS. Patients who were unable to comprehend the scale were not included in the study. Only patients who were suitable and compatible with the study design were included. The patients were randomly divided into 3 equal groups with the help of computer-generated randomization numbers.

All patients underwent LC under a standard general anesthetic technique for premedication and during the intraoperative period. The anesthetist performed intraoperative, noninvasive monitoring. Ventilation was adjusted to maintain an end-tidal CO_2 pressure below 38 mmHg. Second-generation cephalosporin (cefoxitin) 1 g was injected intravenously before the induction of anesthesia. LC was carried out using the standard three-port technique, and CO_2 pneumoperitoneum pressure was maintained at 14 mmHg throughout the procedure. The procedures were performed by the same experienced surgeon. After complete hemostasis and the gallbladder bed washed with normal saline, the different treatments were performed according to the different groups. Group A: Fibrin sealant (5 mL) (Guangzhou Bioseal Biotech, Guangzhou, China) was implanted in the gallbladder bed. Group B: Fibrin sealant (5 mL) combined with ropivacaine (1 mg/kg body weight) was implanted in the gallbladder bed. Group C: The gallbladder bed was douched with normal saline only.

Following LC, carbon dioxide was evacuated through the ports by applying gentle pressure all over the abdomen. Gallbladders were taken out of the peritoneal cavity *via* the umbilical incision. Rescue analgesia (intramuscular dolantin 50 mg) or rescue antiemetic (intramuscular ondansetron 8 mg) was administered if the VAS was higher than 10 or the patient complained of vomiting. The amount of dolantin used was noted.

The degree of postoperative pain was assessed every 4 h in the first 12 h after surgery and then every 12 to 48 h, using a VAS (0 = no pain, 10 = worst possible pain), by nursing staff who were unaware of the perioperative intervention. The character of the pain was also assessed simultaneously. Visceral pain was defined as deep-seated pain located in the right hypochondrium or referred to the shoulder. Parietal pain was defined as incisional pain located at the trocar sites.

Statistical analysis

Data were expressed as the mean ± SE. All data were prepared and compiled using SPSS 16.0 software. Statistical differences were determined by ANOVA using the Dunnet procedure in non-repeated measures obtained by the mean postoperative VAS scores for the various groups. Categorical variables were recorded as numbers (percentages) and compared by using the χ^2 test with Yates correction. The threshold for statistical significance was considered $P < 0.05$.

Table 1 Patient characteristic data (mean ± SE)

Variables	Group A	Group B	Group C
Age (yr)	41.6 ± 16.1	42.2 ± 14.7	40.8 ± 17.6
Weight (kg)	62.6 ± 18.3	65.3 ± 16.8	64.7 ± 19.1
Sex (M/F)	14/6	14/6	14/6
Duration of anesthesia (min)	106.7 ± 21.4	98.2 ± 24.3	103.7 ± 25.7
Duration of surgery (min)	66.4 ± 20.1	62.8 ± 19.5	68.5 ± 18.3

Table 2 Multiple comparisons of visual analog scale (VAS) scores for various groups *vs* group C (the control) (mean ± SE)

Time (h)	Group	*n*	VAS	*P* value
4	G1	20	7.2 ± 2.8	0.547
	G2	20	4.3 ± 1.2	0.007
	G3	20	8.3 ± 3.5	
8	G1	20	6.5 ± 3.7	0.435
	G2	20	3.4 ± 1.6	0.008
	G3	20	7.0 ± 3.1	
12	G1	20	5.1 ± 1.9	0.327
	G2	20	2.5 ± 0.8	0.001
	G3	20	5.9 ± 2.0	
24	G1	20	3.5 ± 1.3	0.264
	G2	20	1.8 ± 0.9	0.001
	G3	20	4.0 ± 1.8	
36	G1	20	2.7 ± 1.2	0.362
	G2	20	1.2 ± 0.6	0.001
	G3	20	2.9 ± 1.0	
48	G1	20	2.0 ± 0.8	0.538
	G2	20	0.8 ± 0.3	0.001
	G3	20	2.2 ± 0.8	

RESULTS

The 60 study patients (42 women and 18 men) varied in age from 25 to 63 years (median, 41.2 years). The three groups did not differ in mean age, body weight, or ASA status. None of the patients had a history of jaundice or gallstone pancreatitis. Eleven patients (18.3%) had previously undergone lower abdominal surgery. There was no significant difference in the duration of surgery among the three groups ($P = 0.587$): 66.4 ± 20.1 min for group A, 62.8 ± 19.5 min for group B, 68.5 ± 18.3 min for group C (Table 1).

The VAS score decreased after surgery in all patients. Analysis of variance followed by multiple comparisons using the Dunnet procedure, with group C used as a control, suggested that the mean VAS score for group B was significantly less than that for group A and C. The mean VAS scores for group A were lower than Group C, but the difference was not significant (Table 2).

The overall incidence of visceral, parietal, and shoulder pain in our study were 81.7%, 50.0%, and 26.7%, respectively. However, the incidence of visceral pain in group B was less than that in the other groups ($P < 0.05$) (Table 3). The number of patients in group B experiencing visceral pain after surgery was also significantly lower

Table 3 Character of pain after laparoscopic cholecystectomy *n* (%)

Group	*n*	Visceral	Parietal	Shoulder
A	20	18 (90.0)	10 (50.0)	7 (35.0)
B	20	12 (60.0)	9 (45.0)	1 (5.0)
C	20	19 (95.0)	11 (55.0)	8 (40.0)
Total	60	49 (81.7)	30 (50.0)	16 (26.7)

than that in the other groups ($P < 0.05$). The overall incidence of parietal pain was 50.0% in group A, 45.0% in group B and 55.0% in group C ($P > 0.05$). There was no difference in the incidence of parietal pain between the three groups. Only one patient in group B reported shoulder pain, as compared with 16 (26.7%) of the 40 patients in groups A and C ($P < 0.01$).

Rescue analgesia (intramuscular pethidine hydrochloride 50 mg once) was administered if the VAS was higher than 10. The amount of pethidine hydrochloride used per capita in group B (2.5 ± 11.2 mg) was significantly lower than that in group A (30.0 ± 25.1 mg) and group C (25.0 ± 25.6 mg).

DISCUSSION

Even though postoperative pain after LC is markedly less than that after open cholecystectomy, pain is still the patient's first complaint after LC[9]. Although postoperative pain is reduced compared to laparotomic surgery[10], effective analgesic treatment still remains crucial for early patient discharge[11]. Usually, postoperative pain following LC peaks immediately after surgery, and decreases within 24 h, and then increases to a second or even a third peak later[12].

The incidence of pain after laparoscopy may be attributed to the carbon dioxide gas (CO_2) used to induce pneumoperitoneum[13,14]. CO_2 remains in the peritoneal cavity for several days after surgery and causes stretching of the phrenic nerve endings[15], local hypothermia, and diaphragmatic irritation *via* carbonic acid[16]. The benefit of using intraperitoneal local anesthetics for shoulder and abdominal pain control has been proven[7,17-19], however, several other studies did not confirm these findings[20-23].

Pain after LC includes three components, visceral, parietal, and shoulder pain[3]. In the early postoperative period, many studies report that visceral pain is predominant, especially during the first hours after surgery[3]. At the same time, parietal pain is less intense because of the small incisions and limited damage to the abdominal wall. Shoulder pain may occur later with visceral pain. The most common location of postoperative pain is in the right upper quadrant, followed by the trocar site and the shoulder[24].

In this study, all operations were progressed according to the line of least tissue damage. We took the gallbladder out of the peritoneal cavity *via* the umbilical incision which was less sensitive than the other incisions. Thus, we observed that parietal pain was mild in this study and did not contribute substantially to the VAS score.

Fibrin sealant has been an extremely effective and widely used adjunct to surgical procedures for the control of diffuse slow bleeding over large surfaces. In addition, fibrin sealant has been used as a carrier for other compounds. Thus, it has been used to release medicines slowly at a fixed site which are therefore effective for a long time.

We observed a significant reduction in pain after gallbladder bed implantation of fibrin sealant combined with ropivacaine. This effect was indirectly reflected in the progressive reduction in both the VAS score and visceral pain in this group of patients. This suggests that the progressive reduction in the VAS score in this group of patients was primarily attributable to the effective control of visceral pain.

The VAS score for the patients with fibrin sealant alone implanted in the gallbladder bed was less than that of the control group, although the differences were not statistically significant. This suggests that the gallbladder bed with implanted fibrin sealant alone may lead to a slight relief in postoperative pain.

Verma *et al*[19] reported that visceral pain is prominent after LC and can be effectively controlled by 0.5% bupivacaine-soaked Surgicel in the gallbladder bed alone. They used bupivacaine 0.5% (2 mg/kg) instilled over the oxidized regenerated cellulose strips (Surgicel) in the gallbladder bed, and found that the postoperative pain was significantly less in the these patients than in the control groups (bupivacaine infiltrated at the trocar sites and normal saline in the gallbladder bed and at the trocar sites).

These findings are in accordance with the anatomical characteristics of the phrenic nerve which supplies the gallbladder, porta hepatis, and liver, while sharing the root of nerves to the shoulder[25]. We used fibrin sealant carrying ropivacaine adhered to the gallbladder bed. Using this method, ropivacaine was released slowly and the stickiness of the fibrin sealant ensured that the drug remained in contact with the wound for a longer period of time. In our study, implanting fibrin sealant combined with ropivacaine in the gallbladder bed was effective in controlling shoulder pain, and only one of the patients in this treatment group experienced shoulder pain.

In conclusion, we conclude that implanting fibrin sealant combined with ropivacaine in the gallbladder bed is effective in controlling both visceral and shoulder pain after LC.

COMMENTS

Background

Even though postoperative pain after laparoscopic cholecystectomy (LC) is markedly less than that after open cholecystectomy, pain is still the patient's first complaint after LC.

Research frontiers

According to the anatomical characteristics of the nerve which supplies the gallbladder, the use of fibrin sealant carrying ropivacaine adhered to the gallbladder bed can relieve postoperative pain.

Innovations and breakthroughs

This study determined that implantation of fibrin sealant with sustained-release ropivacaine in the gallbladder bed could relieve the pain after LC.

Applications

The implantation of 5 mL fibrin sealant combined with ropivacaine (1 mg/kg

body weight) in the gallbladder bed provided significant postoperative pain relief compared with the implantation of fibrin sealant alone.

Terminology

Fibrin sealant can be used as a carrier for ropivacaine. With fibrin sealant, ropivacaine could be released slowly, and the stickiness of the fibrin sealant ensured that the drug remained in contact with the wound for a longer period of time.

Peer review

The authors have assessed the use of a fibrin sealant with local anaesthetic in the gallbladder bed on post-operative pain after LC. Fibrin sealant with local anaesthetic was associated with lower post-operative pain scores.

REFERENCES

1 **Soper NJ**, Stockmann PT, Dunnegan DL, Ashley SW. Laparoscopic cholecystectomy. The new 'gold standard'? *Arch Surg* 1992; **127**: 917-921; discussion 921-923

2 **Bisgaard T**, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. *Pain* 2001; **90**: 261-269

3 **Joris J**, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. *Anesth Analg* 1995; **81**: 379-384

4 **Lau H**, Brooks DC. Predictive factors for unanticipated admissions after ambulatory laparoscopic cholecystectomy. *Arch Surg* 2001; **136**: 1150-1153

5 **Edwards ND**, Barclay K, Catling SJ, Martin DG, Morgan RH. Day case laparoscopy: a survey of postoperative pain and an assessment of the value of diclofenac. *Anaesthesia* 1991; **46**: 1077-1080

6 **Akaraviputh** T, Leelouhapong C, Lohsiriwat V, Aroonpruksakul S. Efficacy of perioperative parecoxib injection on postoperative pain relief after laparoscopic cholecystectomy: a prospective, randomized study. *World J Gastroenterol* 2009; **15**: 2005-2008

7 **Feroci F**, Kröning KC, Scatizzi M. Effectiveness for pain after laparoscopic cholecystectomy of 0.5% bupivacaine-soaked Tabotamp placed in the gallbladder bed: a prospective, randomized, clinical trial. *Surg Endosc* 2009; **23**: 2214-2220

8 **Mentes O**, Harlak A, Yigit T, Balkan A, Balkan M, Cosar A, Savaser A, Kozak O, Tufan T. Effect of intraoperative magnesium sulphate infusion on pain relief after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2008; **52**: 1353-1359

9 **Bisgaard T**. [Treatment of pain after laparoscopic cholecystectomy] *Ugeskr Laeger* 2005; **167**: 2629-2632

10 **Black NA**, Downs SH. The effectiveness of surgery for stress incontinence in women: a systematic review. *Br J Urol* 1996; **78**: 497-510

11 **Salihoglu Z**, Yildirim M, Demiroluk S, Kaya G, Karatas A, Ertem M, Aytac E. Evaluation of intravenous paracetamol administration on postoperative pain and recovery characteristics in patients undergoing laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2009; **19**: 321-323

12 **Reuben SS**, Steinberg RB, Maciolek H, Joshi W. Preoperative administration of controlled-release oxycodone for the management of pain after ambulatory laparoscopic tubal ligation surgery. *J Clin Anesth* 2002; **14**: 223-227

13 **Dobbs FF**, Kumar V, Alexander JI, Hull MG. Pain after laparoscopy related to posture and ring versus clip sterilization. *Br J Obstet Gynaecol* 1987; **94**: 262-266

14 **Shantha TR**, Harden J. Laparoscopic cholecystectomy: anesthesia-related complications and guidelines. *Surg Laparosc Endosc* 1991; **1**: 173-178

15 **Korell M**, Schmaus F, Strowitzki T, Schneeweiss SG, Hepp H. Pain intensity following laparoscopy. *Surg Laparosc Endosc* 1996; **6**: 375-379

16 **Semm K**, Arp WD, Trappe M, Kube D. [Pain reduction after pelvi/-laparoscopic interventions by insufflation of CO2 gas at body temperature (Flow-Therme)] *Geburtshilfe Frauenheilkd* 1994; **54**: 300-304

17 **Elhakim M**, Amine H, Kamel S, Saad F. Effects of intraperitoneal lidocaine combined with intravenous or intraperitoneal tenoxicam on pain relief and bowel recovery after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2000; **44**: 929-933

18 **Tobias JD**. Postoperative analgesia and intraoperative inhalational anesthetic requirements during umbilical herniorrhaphy in children: postincisional local infiltration versus preincisional caudal epidural block. *J Clin Anesth* 1996; **8**: 634-638

19 **Verma GR**, Lyngdoh TS, Kaman L, Bala I. Placement of 0.5% bupivacaine-soaked Surgicel in the gallbladder bed is effective for pain after laparoscopic cholecystectomy. *Surg Endosc* 2006; **20**: 1560-1564

20 **Rademaker BM**, Kalkman CJ, Odoom JA, de Wit L, Ringers J. Intraperitoneal local anaesthetics after laparoscopic cholecystectomy: effects on postoperative pain, metabolic responses and lung function. *Br J Anaesth* 1994; **72**: 263-266

21 **Scheinin B**, Kellokumpu I, Lindgren L, Haglund C, Rosenberg PH. Effect of intraperitoneal bupivacaine on pain after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 1995; **39**: 195-198

22 **Paulson J**, Mellinger J, Baguley W. The use of intraperitoneal bupivacaine to decrease the length of stay in elective laparoscopic cholecystectomy patients. *Am Surg* 2003; **69**: 275-278; discussion 278-279

23 **Papaziogas B**, Argiriadou H, Papagiannopoulou P, Pavlidis T, Georgiou M, Sfyra E, Papaziogas T. Preincisional intravenous low-dose ketamine and local infiltration with ropivacaine reduces postoperative pain after laparoscopic cholecystectomy. *Surg Endosc* 2001; **15**: 1030-1033

24 **Mraović B**, Jurisić T, Kogler-Majeric V, Sustic A. Intraperitoneal bupivacaine for analgesia after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 1997; **41**: 193-196

25 **Peter LW**, Roger W, Mary D, Lawrence HB. Biliary duct and gallbladder. In: Gray's anatomy. 37th ed. London: Churchill Livingstone, 1989: 1394-1395

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