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A Placebo-Controlled Comparison of Bupivacaine and Ropivacaine Instillation for Preventing Postoperative Pain After Laparoscopic Cholecystectomy

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Abstract

Purpose. The aim of this study was to determine the effect of local anesthetic instillation, to compare bupivacaine and ropivacaine in patients undergoing a laparoscopic cholecystectomy.

Methods. A total of 80 patients were randomly assigned to four groups to receive the intraperitoneal instillation of 21 ml of either 100 mg bupivacaine (Group B), 100 mg ropivacaine (Group R1), 150 mg ropivacaine (Group R2) or saline with epinephrine 1/200 000 at the end of the surgery. The postoperative pain was evaluated and the analgesic requirement was also assessed.

Results. The intraperitoneal instillation of 100 mg bupivacaine, 100 mg ropivacaine, or 150 mg ropivacaine at the end of a laparoscopic cholecystectomy significantly reduced the morphine consumption during the first 24 h. For preventing postoperative pain 150 mg ropivacaine proved to be significantly more effective than either 100 mg bupivacaine or 100 mg ropivacaine.

Conclusion. We herein showed that the intraperitoneal instillation of local anesthetic during laparoscopic cholecystectomy is a noninvasive, rapid, safe and simple analgesic technique that reduces the total morphine consumption during first 24 h.

Key words Laparoscopic cholecystectomy · Postoperative pain · Bupivacaine · Ropivacaine

Introduction

Less pain and a better pulmonary function reported after laparoscopic surgery explain its increasing success and it has now become a standard technique for performing a cholecystectomy.[1,2] Although the pain following a laparoscopic cholecystectomy is less intense than open surgery, patients often suffer visceral pain with coughing, respiratory movements and mobilization during the first hours and shoulder pain secondary to peritoneal insufflation after the eighth postoperative hour, during the night after surgery.[3,4] This can delay the patient's autonomy, lengthen the hospital stay, and increase morbidity and costs. Multimodal analgesic techniques are therefore necessary to provide effective postoperative analgesia for several components of pain. Nonsteroidal anti-inflammatory drugs (NSAIDs), local anesthetic infiltration to incision site, intraperitoneal saline, intraperitoneal local anesthetics, gas drainage, heated gas, low-pressure gas, and nitric oxide pneumoperitoneum have been used to reduce pain after a laparoscopic cholecystectomy.[5] However, the pain after laparoscopy may be moderate or severe for some patients and such patients may thus require opioid treatment. The use of NSAIDs for peritoneal inflammation after CO_2 pneumoperitoneum is rational but the preoperative administration of NSAIDs is questionable because of the pathophysiologic changes of renal blood flow induced by pneumoperitoneum.[6] The treatment of postlaparoscopy pain with NSAIDs yields controversial results.[7–11] The clinical significance of pain control after laparoscopic surgery remains controversial.[5] Intraperitoneal local anesthetic has been shown to reduce pain after laparoscopic gynecologic surgery.[12–13] Nevertheless, this technique seems to be controversial for pain relief after a laparoscopic cholecystectomy, because not all studies report similar results.[5] The comparative data on bupivacaine and ropivacaine have so far been sufficient. The local anesthetic administration after laparoscopic cholecystectomy was effective in pain prevention but there is lack of consensus regarding the dose, concentration, site, and manner of administration, but some studies failed to show efficacy. Ropivacaine is less car-

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diotoxic than bupivacaine and can hence be administered in larger doses. Intraperitoneal instillation of 100 mg of bupivacaine provides effective analgesia with plasma concentrations below toxic levels. A dose of 150 mg of ropivacaine was selected to test whether this dose would increase the analgesic efficacy over that of bupivacaine. The aim of this study was to determine the effect of intraperitoneal local anesthetics, to compare bupivacaine and ropivacaine, and to understand the potency of these local anesthetics for preventing postoperative pain after a laparoscopic cholecystectomy.

Methods

After institutional approval, written informed consent was obtained from 80 ASA I and II patients aged 20–77 years, who were scheduled for a laparoscopic cholecystectomy. The patients were informed about the different components of postoperative pain they would experience. They were given an explanation of VAS (visual analogue scale) and were familiarized with use of the PCA (patient-controlled analgesia) device. The exclusion criteria were: morbid obesity, severe chronic disease, allergic reactions to NSAIDs and local anesthetics, and chronic opioid treatment. The patients were also excluded if they underwent surgery for acute cholecystitis or if the operation had been converted to an open procedure. All patients received the same anesthetic technique. They were premedicated with 0.07 mg kg^{-1} midazolam 30 min before surgery. Standard patient monitoring was used. General anesthesia was induced with fentanyl (1.5 μg kg^{-1}), thiopental (5–7 mg kg^{-1}), and vecuronium (0.1 mg kg^{-1}) for muscle relaxation and maintained with sevoflurane in 70% N_2O and 30% O_2 and supplemental doses of fentanyl (50–100 μg) if required. After intubation diclofenac Na (75 mg) was given intramuscularly. The mechanical ventilator was set to maintain $PaCO_2$ at between 32–40 mmHg depending on different stages of laparoscopy. The intra-abdominal pressure during laparoscopy was automatically maintained at 14 mmHg by a CO_2 insufflator and a slightly reversed Trendelenburg position was used when requested by the surgeon. Before the end of the surgery, metoclopramide (10 mg) was given intravenously to all patients to reduce the incidence of nausea and vomiting. No patients underwent the placement of intraperitoneal drain. The neuromuscular block was antagonized with neostigmine (0.04 mg kg^{-1}) and atropine (0.08 mg kg^{-1}).

At the end of the laparoscopic cholecystectomy, the patients were allocated randomly to one of four groups. Group S (n = 20) physiological (0.9%) sodium chloride 21 ml intraperitoneally; Group B (n = 20) bupivacaine 20 ml (100 mg) with epinephrine 1 ml (1/200 000) intraperitoneally; Group R_1 (n = 20) ropivacaine 10 ml (100 mg) plus 10 ml 0.9% NaCl with epinephrine 1 ml (1/200 000) intraperitoneally; Group R_2 (n = 20) ropivacaine 15 ml (150 mg) plus 5 ml 0.9% NaCl with epinephrine 1 ml (1/200 000) intraperitoneally. All patients underwent the instillation of 21 ml of blinded solution in a standardized manner by the operating surgeon, under visual control, at the end of the surgical procedure: 7 ml under each subdiaphragmatic area and 7 ml to the gallbladder bed. The surgical wounds were not infiltrated with local anesthetic.

In the postanesthesia care unit, a PCA pump (Pain Management Provider, Abbott, Wiesbaden, Germany) was programmed to deliver intravenous morphine bolus 1 mg and 5 min lock-out interval, with no background infusion. The intensity of the different postoperative pain components was recorded on a visual analogue scale (0–100 mm) at rest, during mobilization (patients were asked to move from supine to the sitting position) and on coughing. The patients were asked about the location of pain, whether at the shoulder, incision sites, and/or inside the abdomen. The pain intensity was measured 0, 1, 2, 4, 8, 12, 24 h after surgery. When the score according to the VAS was >40, a loading dose of 5 mg morphine had been administered as a rescue analgesic and it was repeated every 5 min until a pain score of <40 was obtained.

The sedation was assessed on a 5-point scale (0 = awake, 1 = sleepy but easily arousable, 2 = sleepy but arousable with verbal stimulus, 3 = very sleepy but arousable with physical stimulus, 4 = difficult to awaken). Postoperative nausea, vomiting, pruritus, respiratory rate, urinary retention, headache, and agitation were recorded throughout the study period. The age and weight were analyzed by one-way analysis of variance (ANOVA). The mean arterial pressure and heart rate were analyzed with repeated-measures analysis of variance. The gender, ASA, nausea, and vomiting were analyzed with the χ^2 test. The height, respiratory rate, sedation levels, duration of operation, pain scores, total morphine consumption, patient satisfaction, and effectiveness were analyzed by the Kruskal–Wallis test.

The statistical analysis was performed with the software program SPSS v. 10.1. $P < 0.05$ was considered statistically significant. The indicated differences between the mean ranks were compared using multiple comparisons after the Kruskal–Wallis test as calculated according to the Handbook of Parametric and Nonparametric Statistical Procedures.[14]

Results

The groups were similar in regard to gender, age, height, weight, ASA, and duration of operation (Table 1).

Table 1. Patient data (mean ± SD)

	Group S	Group B	Group R_1	Group R_2
Gender (M/F)	3/17	3/17	1/19	4/16
Age (years)	50 ± 11	49 ± 12	49 ± 16	50 ± 12
Height (cm)	163 ± 6	164 ± 7	161 ± 3	163 ± 7
Weight (kg)	78 ± 14	81 ± 13	73 ± 12	74 ± 9
ASA (I/II)	13/7	17/3	12/8	11/9
Duration of operation (min)	84 ± 10	80 ± 14	82 ± 14	87 ± 9

Table 2. Pain scores (mean ± SD)

	Time 0	1 h	2 h	4 h	8 h	12 h	24 h
Group S	33 (31.64)	22 (21.59)	14 (14.97)	10.5 (12.44)	8.5 (9.63)	12.5 (15.77)	4 (6.63)
Group M	14.5 (22.47)	15.5 (21.79)	6 (8.6)	6 (7.35)	7 (11.87)	4.5 (5.89)	2 (4)
Group R_1	26.5 (28.68)	16 (18.81)	6 (11.14)	2.5 (6.98)	5 (5.92)	3.5 (6.54)	3 (4.58)
Group R_2	11.5 (24.14)	4 (9.17)	4.5 (13.59)	5 (8.06)	4.5 (8.05)	1 (3)	0.5 (2.18)

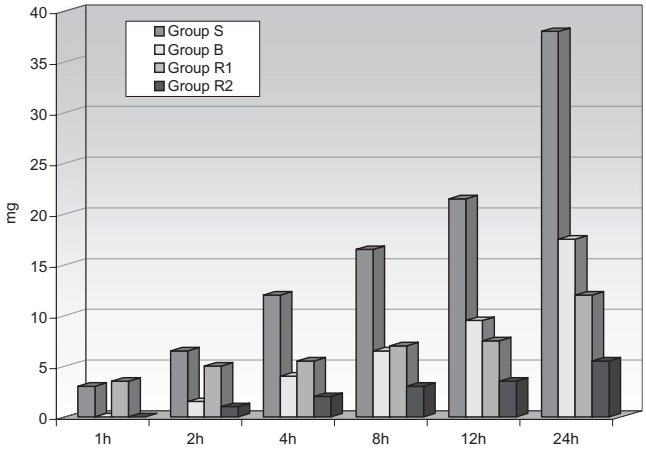

Fig. 1. Total morphine consumption (mg) in groups

There were no significant differences between the four groups in relation to mean arterial pressure, heart rate, respiratory rate, and sedation level. No significant difference was found between groups with respect to VAS at rest, during mobilization, and on coughing except in the first 1, 2, and 12 h. The pain scores in Group S were greater than Group R_2 and this difference was significant statistically for the first 1, 2, and 12 h (Table 2). Shoulder pain was reported by 15 patients (Group S = 5, Group M = 2, Group R_1 = 6, Group R_2 = 2) but this result was not statistically significant. The total morphine consumption in Group S was significantly more than in the other three groups at all time intervals (Fig. 1) (Kruskal–Wallis χ^2 and the *P* values of total morphine consumption between Group S and Group M, R_1, and R_2 for all time intervals (1, 2, 4, 8, 12, 24 h) were respectively 16.4 and 0.001, 19 and 0.001, 23.4 and 0.001, 27.4 and 0.001, 31.7 and 0.001, and 37.8 and 0.001). In the first 1 and 2 h, morphine consumption in Group R_1 was significantly more than Group M and Group R_2. After 4 h, morphine consumption in Group R_2 was significantly less than in Group M and Group R_1. Patient satisfaction and effectiveness were significantly better in Group M and Group R_2 than in Group S (Kruskal–Wallis χ^2 and *P* values of patient satisfaction and effectiveness between Group S and Group M, Group R_2; 10.6 and 0.014, 10.2 and 0.017). No differences in the incidence of nausea/vomiting were observed between the groups. None of the other above-mentioned side effects was reported by any of the groups.

Discussion

The results of this study demonstrated the intraperitoneal instillation of 100 mg bupivacaine, 100 mg ropivacaine, or 150 mg ropivacaine at the end of laparoscopic cholecystectomy to significantly reduce the morphine consumption during the first 24 h. In preventing postoperative pain 150 mg of ropivacaine was significantly more effective than 100 mg of bupivacaine and 100 mg of ropivacaine. There were no differences between the groups in the adequacy of analgesia as assessed by VAS scores at rest, during mobilization, and on coughing except for 1, 2, and 12 h. In a protocol where analgesia was available on a patient-controlled basis, it was anticipated there would be no differences between the groups regarding the pain scores, since each individual could adjust the dose of analgesic to his own requirements always within a security margin. The efficacy of local anesthetic infiltration has been demonstrated in numerous studies on a laparoscopic cholecystectomy. Chundrigar et al.[15] reported that 0.25% bupivacaine (50 mg) reduced the postoperative pain during first 24 h. On 60

patients Narchi et al.[16] also showed significant efficacy of bupivacaine 50 mg but Joris et al.[17] could not find any statistical significance. Szem et al.[18] showed reduced pain scores only for the first 6 h. Mraovic et al.[3] reported the efficacy of 150 mg bupivacaine. Scheinin et al.[19] failed to show any efficacy with the same dose of bupivacaine. All of these studies thus demonstrated local anesthetic administration to provide controversial results. The dose, concentration, site, and manner of administration were different and no consensus was apparent. Goldstein et al.[12] found the morphine-sparing effect of ropivacaine (150 mg) was significantly greater than that of bupivacaine (100 mg) after gynecologic surgery. On the other hand, in a recent study, the intraperitoneal instillation of ropivacaine during a laparoscopic cholecystectomy thus resulted in lower pain scores and in reduced morphine requirements in comparison to a placebo.[20]

Shoulder pain is a frequent complication in the postoperative period and it has been reported in from 35% to 63% of cases.[21] The intensity of shoulder pain reported after laparoscopic cholecystectomy is markedly lower than that reported after gynecologic laparoscopy.[21–24] We found a low incidence of shoulder pain in all treatment groups, because the residual intraperitoneal CO_2 was carefully removed by the surgeon and we injected local anesthetics into the subdiaphragmatic area.

We did not observe any side effects attributable to the local anesthetic. We could not measure the plasma concentration of bupivacaine and ropivacaine but several reports have shown the intraperitoneal instillation of 100 mg bupivacaine to not result in toxic concentrations.[16] Deans et al.[25] confirmed this after the instillation of 1.5 mg kg^{-1} bupivacaine during hernia repair. The range of the mean plasma concentration (0.92–1.14 μg ml^{-1}) after 100–150 mg bupivacaine instillation is below the toxic concentration of 3 μg ml^{-1}.[26] Ropivacaine has been infiltrated in doses of 300 and 375 mg for hernia repair without reaching toxic concentrations.[27] The range of the mean plasma concentration (0.08–0.3 μg ml^{-1}) after wound infiltration and drain lavage with 225 mg ropivacaine after major shoulder surgery was also below toxic concentrations of 0.6 μg ml^{-1}.[28] The doses of bupivacaine and ropivacaine used in our study were lower than those thought to cause systemic toxicity.

In summary, we herein demonstrated the intraperitoneal instillation of local anesthetic during a laparoscopic cholecystectomy to be a noninvasive, rapid, safe, and simple analgesic technique which reduces the total morphine consumption during the first 24 h. In particular, the 150 mg ropivacaine group had better results. Since laparoscopy is one of the most frequent outpatient procedures and since postoperative pain remains a major cause in delaying the discharge of patients, we encourage the use of local anesthetics via this route in daily outpatient practice.

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