

Evaluation of the effect of periportal infiltration of ropivacaine in laparoscopic cholecystectomy patients: a randomized double-blind, placebo-controlled study in a tertiary-care teaching hospital

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Received January 6, 2015. Accepted January 13, 2015

Abstract

Background: Pain after laparoscopic cholecystectomy (LC) is very common and has multifactorial origin. Traditionally, several methods including postoperative nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and opioid derivatives have been used to counter the earlier mentioned complications. However, procedures such as peritoneal infiltration and preincisional port-site infiltration of long-acting local anesthetics have reduced the requirement of postoperative analgesia and reduced the incidence of drug-induced nausea and vomiting.

Objective: To evaluate the effect of periportal infiltration of ropivacaine in patients who underwent LC.

Materials and Methods: A total of 100 patients undergoing LC were randomly divided into two groups: group I ($n = 50$) patients were infiltrated with port-site long-acting local anesthetic ropivacaine and group II ($n = 50$) patients were infiltrated with normal saline (matching placebo). In the postoperative period, both groups were compared with regard to severity of pain using visual analog scale (VAS), analgesic requirement, and incidence of nausea and vomiting.

Result: Male-to-female ratio, mean age, weight, duration of surgery, and duration between extubation and first analgesic dose in groups I and II were 1:9 and 1:6.16, 37.12 ± 7.80 and 39.82 ± 9.88 years ($p = >0.05$), 60.76 ± 3.94 and 61.88 ± 4.94 kg ($p > 0.05$), 60.10 ± 15.90 and 61.90 ± 18.94 min ($p = >0.05$), and 438.90 ± 190.80 and 184.40 ± 46.27 min ($p = <0.05$), respectively. Total number of injection diclofenac/tramadol administered in first 24 h after extubation in group I was $42 (0.84 \pm 0.40)/2 (0.04 \pm 0.20)$ and that in group II was $101 (2.02 \pm 0.42)/56 (0.92 \pm 0.38)$, respectively, and the difference was statistically significant ($p = 0.001$). Shoulder pain was noticed in four patients in ropivacaine group and in five patients in placebo group ($p = >0.05$).

Conclusion: Preincisional port-site infiltration of ropivacaine reduced the postoperative pain; no significant change in the incidence of shoulder pain was noticed. Significant reduction was observed in requirement of NSAIDs and opioids in ropivacaine group, which also reduced the drug-induced nausea and vomiting.

KEY WORDS: Laparoscopic cholecystectomy, ropivacaine, local anesthetics, periportal infiltration

Access this article online

Website: <http://www.ijmsph.com>

DOI: 10.5455/ijmsph.2015.06012015159

Quick Response Code:



Introduction

Laparoscopic cholecystectomy (LC), although the undisputed standard treatment for cholecystectomy, is plagued by postoperative visceral and shoulder pain, a result of stretching of diaphragmatic fibers by pneumoperitoneum and irritation by carbonic acid.^[1-4] Unresolved pain may cause increased morbidity and prolonged hospitalization besides physiologic

changes such as cardiac stress, delayed return of gastrointestinal motility, and decreased vital capacity with increased pulmonary morbidity.^[5] Many approaches for pain relief such as intramuscular nonsteroidal anti-inflammatory drugs (NSAIDs), intraperitoneal local anesthesia, local anesthetic infiltration of wound, and adequate removal of gas are in use. Peripheral use of local anesthetic after laparoscopic surgery provides clinically relevant postoperative pain relief.^[2] Ropivacaine is a long-acting local anesthetic agent. It produces effects similar to other local anesthetics via reversible inhibition of sodium ion influx in nerve fibers. It is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibers, resulting in a relatively reduced motor blockade. Thus, ropivacaine has a greater degree of motor sensory differentiation, which could be useful when motor blockade is undesirable. The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity. The drug displays linear and dose proportional pharmacokinetics. It is metabolized extensively in the liver and excreted in urine.^[6]

In this study, we have evaluated the effect of periportal infiltration of ropivacaine for postoperative pain, nausea, and vomiting in patients who underwent LC.

Materials and Methods

This double-blind, placebo-controlled study was conducted by the Department of Surgery at Shri Guru Ram Rai Institute of Medical and Health Sciences for a period of 6 months from June 2014 to December 2014. Before the commencement of the study, approval was taken from institutional ethics committee and written informed consent was obtained from all the participants.

A total of 100 patients undergoing LC were randomly selected for the study and were divided into two groups. Both groups comprised 50 patients each, matched in terms of age, body mass index, and comorbid conditions. Hypersensitivity test for ropivacaine was carried out one day before surgery in all the study patients. Patients with hypersensitivity to ropivacaine, less than 14 years or more than 70 years of age, pregnant females, those with previous upper abdominal operation or suspected bile duct stones, those on class III antiarrhythmic drugs, and those with all other contraindications to LC were excluded from study. Group I patients were subjected to port-site infiltration of 0.75% ropivacaine (20 mL) before making skin incisions, and Group II patients were infiltrated

on port site with 20-mL normal saline (placebo). The randomization as well as the preparation of an unmarked syringe containing 20 mL ropivacaine or saline was performed by an independent surgeon. The operating surgeon, the staff, and the patients were blinded to this procedure. Similar anesthetic, preanesthetic medications, and anesthetic techniques were applied in all patients.

Postoperative pain was assessed using the visual analog scale (VAS), consisting of 10 cm scale representing varying intensity of pain from 0 (no pain) to 10 cm (worst possible pain). Pain was interpreted as mild, moderate, and severe on the basis of VAS score. Score of 1–3 was taken as mild, 4–7 as moderate, and >7 as severe. Pain was assessed for first 24 h at 3, 6, 12, and 24 h after surgery. The pain was assessed at rest, on coughing, and on walking. The postoperative pain assessment included pain at port sites, shoulder pain, or pain at any other site. Pain was managed by deep intramuscular (im) diclofenac and intravenous (iv) tramadol. The nausea was assessed by the patient's complaint and the need for the use of an antiemetic drug.

The following parameters were evaluated in both groups of patients: Pain assessment using VAS at 3, 6, 12, and 24 h. The total number of injection diclofenac 75 mg given in first 24 h at VAS >3. The total number of injection tramadol 100 mg given in first 24 h at VAS >3.

The results were reported as mean and standard deviation for quantitative variables and percentages for qualitative variables. Difference in percentage among groups was assessed using χ^2 -test. Statistical significance among mean differences was evaluated using one-way analysis of variance. A *p*-value of <0.05 was considered statistically significant.

Results

In our study, mean age of patients in group I was 37.12 ± 7.80 years whereas that in group II was 39.82 ± 9.88 years. This difference was not found to be statistically significant ($p > 0.05$). Mean weight in group I was 60.76 ± 3.94 kg and that in group II was 61.88 ± 4.94 kg, and this difference was also not found to be statistically significant ($p > 0.05$). Group I comprised 5 males and 45 females whereas group II comprised 7 males and 43 females. Mean duration of surgery in group I was 60.10 ± 15.90 min whereas that in group II was 61.90 ± 18.94 min. Mean duration between extubation and first analgesic dose was 438.90 ± 190.80 min in group I and 184.40 ± 46.27 min in group II [Table 1].

Table 1: Baseline characteristics

	Group I	Group II
Total number of patients	50	50
Male-to-female ratio	5:45	7:43
Age in years (mean \pm SE)	37.12 ± 7.80	39.82 ± 9.98
Weight in kg (mean \pm SE)	60.76 ± 3.94	61.88 ± 4.94
Mean duration of surgery in minutes (mean \pm SE)	60.10 ± 15.90	61.90 ± 18.94
Duration of first dose of analgesic after extubation in minutes (mean \pm SE)	438.90 ± 190.80	184.40 ± 46.27

Table 2: Postoperative pain assessment at VAS at 3, 6, 12, and 24 h and use of analgesics

	Group I				Group II			
	3 h	6 h	12 h	24 h	3 h	6 h	12 h	24 h
Mild pain	40	37	40	40	5	20	23	35
Moderate pain	10	13	10	10	45	30	27	15
Severe pain	–	–	–	–	–	–	–	–
No. of injection diclofenac	10	12	10	10	45	30	11	15
No. of injection tramadol	–	1	1	–	–	25	16	5

VSA, visual analog scale

At 3 h, 10 patients from group I and 45 from group II had moderate pain; an im injection of diclofenac 75 mg was administered to the patients having moderate pain and no injection was administered to those with mild pain. Injection tramadol was not administered to any patient [Table 2].

At 6 h, 13 patients from group I and 30 from group II had moderate pain. Injection diclofenac was administered to 12 patients in group I and iv injection tramadol to 1 patient who previously had received injection diclofenac. Diclofenac injection was administered to 30 patients in group II; among them, 25 patients had persistent pain, who were later administered with tramadol injection [Table 2].

At 12 h, 10 patients from group I and 27 from group II had moderate pain. Injection diclofenac was administered to all patients with moderate pain in group I; among them, one patient had persistent pain, who later received injection tramadol. From group II, 11 patients were administered injection diclofenac and 16 were administered injection tramadol because they already had received diclofenac injection 6 h earlier [Table 2].

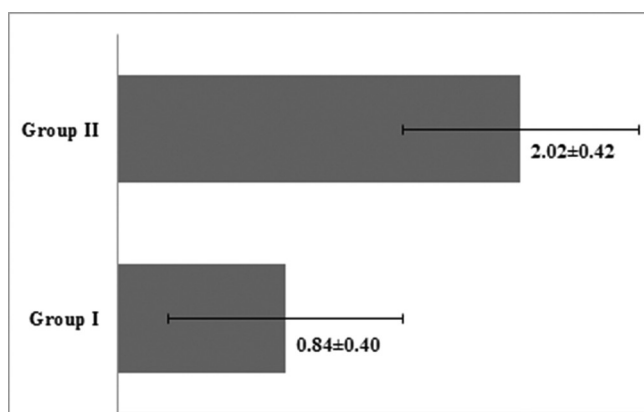
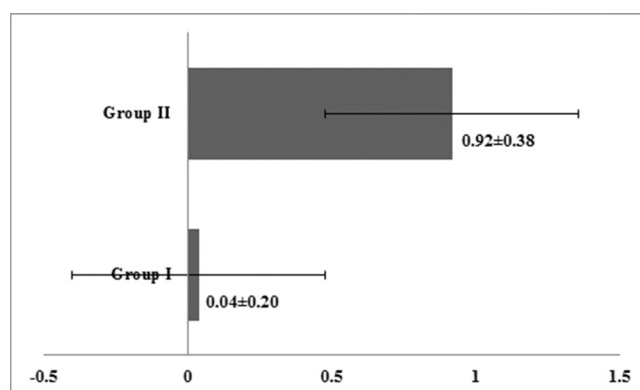
At 24 h, 10 patients from group I and 15 from group II had moderate pain, who received injection diclofenac. Patients in group II had adjuvant analgesia with injection tramadol on persistence of pain [Table 2].

Total number of injection diclofenac administered in first 24 h after extubation in group I was 42 and that in group II was 101. The mean number of im diclofenac injection in

24 h after extubation in group I was 0.84 ± 0.40 and in group II was 2.02 ± 0.42 ; this difference was statistically significant ($p = 0.001$) [Figure 1]. The total number of injection tramadol administered in first 24 h after extubation was 2 in group I and 46 in group II. The mean number of im tramadol injection in 24 h after extubation in group I was 0.04 ± 0.20 and in group II was 0.92 ± 0.38 ; the difference between the two groups was highly statistically significant ($p = 0.001$) [Figure 2]. Shoulder pain was noticed among four patients in ropivacaine group and five patients in placebo group; the difference between the two groups as per the shoulder pain was not significant ($p = >0.05$).

Discussion

LC with its advantages of smaller cosmetic incision, reduced blood loss, and shorter hospital stay has become standard treatment for symptomatic gallstones. However, there is still a significant degree of abdominal pain in the postoperative period, which peaks within the first few hours after the operation but diminishes with time.^[7] Pain may be somatic (incision site) or visceral (gallbladder bed) or a result of pneumoperitoneum.^[8] Studies have suggested that somatovisceral local anesthesia with long-acting local anesthetic agents relieves incisional, intra-abdominal, and shoulder pain in LC.^[7,9] These agents reduce pain by

**Figure 1:** Number of injection diclofenac/patient in first 24 h.**Figure 2:** Number of injection tramadol/patient in first 24 h.

reversibly decreasing the rate of depolarization and repolarization of excitable membranes.^[10] The effectiveness of local parietal anesthesia regarding postoperative pain and analgesic consumption was proved in other studies.^[11,12] Similar results were also shown by intraperitoneal administration of local anesthetics.^[13,14] It is important that the local infiltration of long-acting anesthetic be made before giving incision.^[15] Preincisional or preemptive analgesia with long-acting local-acting anesthesia theoretically achieves peripheral blockage of pain stimuli, which is more advantageous than treating pain after it occurs. It is postulated that preemptive analgesia blocks the nociceptive impulse conduction and subsequent central sensitization, consequently immediate postoperative pain may be reduced and the development of chronic pain may be prevented.^[16]

In this study, the mean number of im injection diclofenac 75mg given in 24 h after extubation in ropivacaine group was 0.84 ± 0.40 and that in placebo group was 2.02 ± 0.42 ($p < 0.001$). The mean number of iv injection tramadol 100 mg given in first 24 h after extubation in ropivacaine group was 0.04 ± 0.20 and that in placebo group was 0.92 ± 0.38 ; the difference between the two groups was highly statistically significant ($p = < 0.001$). It shows that port-site infiltration of ropivacaine reduces the requirement of analgesics, which is comparable to the previous studies.^[7-9,11-13,16-20] In our study, the consumption of opioids was 4% in ropivacaine group and 92% in placebo group, which is in accordance with other previous studies.^[17-20] These authorities used opioids whereas we used opioid derivative. In our study, incidence of nausea and vomiting was 6% in ropivacaine group and 16% in placebo group; the difference between two groups was statistically significant ($p = < 0.05$). The incidence of shoulder pain in ropivacaine group was 8% and that in placebo group was 10%, which was not statistically significant ($p > 0.05$) and not in accordance with the previous study, wherein incidence of shoulder pain was reported to be 28.5% by Theodoros *et al.*^[18] In our study, there was significantly lower VAS score in ropivacaine group than that in placebo group, which is in accordance with the previous studies.^[7-9,11-13,16-20]

Conclusion

Our study suggests the efficacy of preincisional port-site infiltration of ropivacaine in reducing postoperative pain, though no significant change in the incidence of shoulder pain was noticed. It achieves peripheral blockage of pain stimuli, which is more advantageous than treating pain after it occurs. It also results in significant reduction in requirement of NSAIDs and opioids, thus also reducing drug-induced nausea and vomiting.

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How to cite this article: Bijalwan A, Sharma JP, Dutta M, Sharma SC, Beg MA. Evaluation of the effect of periportal infiltration of ropivacaine in laparoscopic cholecystectomy patients: a randomized double-blind, placebo-controlled study in a tertiary-care teaching hospital. *Int J Med Sci Public Health* 2015;4:721-725

Source of Support: Nil, **Conflict of Interest:** None declared.