

## ORIGINAL ARTICLE

# A comparative study of intraperitoneal ropivacaine and bupivacaine for postoperative analgesia in laparoscopic cholecystectomy: a randomized controlled trial

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### ABSTRACT

**Introduction:** Laparoscopic cholecystectomy is now the gold standard for treatment of symptomatic gallstones. After this surgery patients suffer visceral and shoulder pain secondary to peritoneal insufflation. Use of intraperitoneal and port site instillation of local anaesthetics has been used to reduce postoperative pain and decreases the need for intravenous opioids. Studies regarding comparison of intraperitoneal use of ropivacaine and bupivacaine to reduce postoperative pain are few. This study compared the efficacy of ropivacaine and bupivacaine in reducing postoperative pain after laparoscopic cholecystectomy.

**Methodology:** After ethical committee's clearance and informed consent 100 patients with symptomatic cholelithiasis, aged 20-70 years, of either gender, ASA status I to III and within  $\pm$  20% of ideal body weight, scheduled for laparoscopic cholecystectomy were included. Patients were randomized into two groups with 50 patients in each group.

Group-B: Patients received 0.5% bupivacaine in a dose of 2 mg/kg diluted in normal saline to make a solution of 50 ml.

Group-R: Patients received 0.75% ropivacaine in a dose of 2 mg/kg diluted in normal saline to make a solution of 50 ml.

Drug was instilled intra-peritoneal through in situ placed infra-umbilical trocar before extubation. NIBP, HR, SpO<sub>2</sub>, VAS, verbal rating scale (VRS) and rescue analgesia were recorded immediately postoperatively and then regularly every hour for the next 12 hours.

**Results:** HR, SBP and DBP were comparatively lower in Group-R than in Group-B.

The VAS score was significantly lower in Group-R from postoperative 5th hr to 12th hr. Rescue analgesia was given when VAS was > 40. VRS score was significantly lower in Group-R from postoperative 7th hr, showing longer duration of analgesia in this group. The rescue analgesia requirement was also less in Group-R.

**Conclusion:** We conclude that the instillation of bupivacaine and ropivacaine intraperitoneally is an effective method of postoperative pain relief in laparoscopic cholecystectomy. It provides good analgesia in immediate postoperative period with ropivacaine providing longer duration of analgesia.

**Key words:** Laparoscopic cholecystectomy; Intraperitoneal; Ropivacaine; Bupivacaine

**Citation:** Meena RK, Meena K, Loha S, Prakash S. A comparative study of intraperitoneal ropivacaine and bupivacaine for postoperative analgesia in laparoscopic cholecystectomy: a randomized controlled trial. *Anaesth Pain & Intensive Care* 2016;20(3):295-302

**Received:** 10 April 2016; **Reviewed:** 6 May 2016; **Corrected:** 23 My 2016; **Accepted:** 16 June 2016

### INTRODUCTION

Laparoscopic cholecystectomy (LC) is now the gold standard treatment for symptomatic gallstones

and is the commonest operation performed laparoscopically world-wide. The indications for its use in the treatment of gallstone are the same

as open operation although the cholecystectomy rate has increased, since the introduction of laparoscopic technique.<sup>1</sup>

Although pain following LC is less intense than open surgery it can occur due to stretching of parietal peritoneum from insufflations of gas intraperitoneally, release of inflammatory mediators and irritation produced by blood. This can delay the patient's autonomy; lengthen the hospital stay, and increase morbidity and costs. Multi modal analgesic techniques are therefore necessary to provide effective postoperative analgesia.<sup>2</sup>

Administration of intraperitoneal local anesthetic (LA), either during or after surgery, is used by many surgeons as a method of reducing postoperative pain. This technique was first evaluated in patients undergoing gynaecological laparoscopic surgery by Narchi et al.<sup>3</sup> Its application in LC was initially examined in a randomized trial in 1993 by Chundrigar et al.<sup>4</sup> Since then, several trials evaluating the efficacy of intraperitoneal LA in LC have been published worldwide.<sup>5</sup>

The LA has been administered in different doses and at different sites with varying success.<sup>6</sup> intraperitoneal administration of local anesthetic has not only proven to be effective in the relief of postoperative pain, but also reduces nausea and vomiting.<sup>7</sup>

Intraperitoneal use of local anesthetics decreases incidence of postoperative pain and the need for intravenous opioids. There have been encouraging results in recent studies using bupivacaine with NSAIDS and opioids.<sup>8</sup>

The objective of our study was to compare the efficacy of intraperitoneal bupivacaine and ropivacaine for postoperative pain relief and to observe for side effects.

## METHODOLOGY

This randomized, blinded study included 100 patients with uncomplicated, symptomatic cholelithiasis admitted to general surgery department of IMS, BHU. Informed consent was obtained. All the investigated patients were managed by experienced surgeons. The study was approved by the institutional ethics committee of the institute. Patients were randomly divided into two groups. Inclusion criteria were age between 20-70 years, either gender, ASA physical status I to III, scheduled for LC. Patients with following underlying co-morbidities were excluded; coagulopathy, infection at local site, congestive heart failure,

uncontrolled diabetes mellitus, respiratory distress, systemic infection, allergy to drugs used, emergency operation, history of malignancy, regular use of NSAIDS or any other analgesic, history of alcohol or drug abuse, confirmed local anesthetic toxicity, chronic pain syndrome, neurological disease and treatment with steroids prior to surgery.

At the time of pre-anesthetic check-up patient's age, gender, height, weight, and relevant history were recorded. Patients were examined for airway assessment, blood pressure (systolic, diastolic and mean), heart rate, and other relevant systems. Patients were also instructed on the use of VSA.

Investigations included haemoglobin, urea, creatinine, total leucocytes count, fasting blood sugar, ECG, and chest X-Ray. In the operating room, baseline heart rate, non-invasive arterial blood pressure, pulse oximetry and respiratory rate were recorded. 18G peripheral venous cannula was inserted on the dorsal side of the patient's left hand, and 5ml/kg Ringer lactate was preloaded. Patients were randomized into one of the two groups using a computer generated table of random numbers. Drug solution was prepared by a doctor who was not directly participating in the study. Drug was filled in pre coded 50 ml syringe. Blinded solution was prepared in perioperative period procedure. Blinding was continued in postoperative period. Dose was chosen on bases of previous studies.

Group-B: Patients received 0.5% bupivacaine in a dose of 2 mg/kg diluted in normal saline to make a solution of 50 ml.

Group-R: Patients received 0.75% ropivacaine in a dose of 2 mg/kg diluted in normal saline to make a solution of 50 ml.<sup>13</sup>

All patients received ondansetron (0.1 mg/kg) intravenously half an hour prior to induction of anesthesia and fentanyl (2 µg/kg) intravenously just before induction. Surgery was carried out under general anesthesia with propofol (1-2.5 mg/kg) and vecuronium (0.12 mg/kg) to facilitate tracheal intubation. Anesthesia was maintained on 60% N<sub>2</sub>O in oxygen with 0.5 to 1% Isoflurane. Adequate muscle relaxation was achieved with intermittent doses of vecuronium bromide (0.01 mg/kg). Ventilation (tidal volume 6-8 ml/kg) was adjusted to maintain end tidal carbon dioxide between 35 and 40 mmHg. Patients were placed in 15-20° reverse Trendelenberg position during surgery. During laparoscopy, intra-abdominal pressure was maintained at 12 mmHg. All surgeries were performed by the same experienced surgeon. The

CO<sub>2</sub> was carefully evacuated at the end of surgery by manual compression of the abdomen with open trocars. The drug was instilled intra-peritoneally through the infra-umbilical incision before removal of trocar at end of the surgery, by an experienced surgeon. Trendelenberg position was used to facilitate dispersion of drug solution in sub hepatic region. Patients were shifted to recovery room only after complete recovery from anesthesia. All patients were monitored for next 12 hours in post anesthesia care unit.

Non-invasive blood pressure, heart rate and peripheral oxygen saturation were recorded immediately postoperatively and then regularly every hour till next 12 hours. The following verbal rating pain scale was used

#### Verbal Rating Pain Scale (VRS)

Score 0: no pain and patient sedated

Score 1: patient awake and no pain on coughing

Score 2: pain on coughing but not on deep breathing

Score 3: pain on deep breathing but not at rest

Score 4: slight pain at rest

Score 5: severe pain at rest.

The degree of postoperative pain was assessed using both visual analogue scale (VAS) and VRS on arrival in the recovery room, immediately after surgery and thereafter one hourly till 12 hours postoperatively. Patients having VAS > 40 mm after surgery were administered a bolus of diclofenac aqueous (75 mg) IV as rescue analgesia. Ondansetron (0.1 mg/kg IV) was administered on complaint of nausea. Time to first analgesic requirement, total analgesic consumption in the first 12 hours postoperatively and occurrence of adverse events were also recorded. Patients were regularly asked about pruritus and shoulder pain, and blood pressure was monitored for episodes of hypotension (MAP < 60 mmHg), heart rate (H.R) was monitored for episodes of bradycardia (HR < 60). Total duration of surgery was recorded in all

the cases. All peri-operative complications like biliary spillage, hemorrhage, intra-operative bradycardia, hypotension and hypertension were recorded.

Statistical analysis was done using SPSS for Windows version 16.0 software. For non-continuous data Chi-square test was used. The mean and standard deviation of the parameters studied during observation period were calculated for two treatment groups and compared using Student's t-test. The critical value of 'p' indicating the probability of significant difference was taken as < 0.05.

## RESULTS

Table 1 shows that mean age, height, weight and duration of surgery in the two groups which was comparable

Table 2 shows the comparison of mean heart rate in two groups at different intervals which showed that they were statistically significant ( $p < 0.05$ ) from post-operative 1st hr to 9th hr. Afterwards they were comparable and statistically non-significant. Heart rate was comparatively lower in Group-R than in Group-B in postoperative period.

Table 3 shows the comparison of mean systolic blood pressure in two groups at different intervals which showed that they were comparable and statistically non-significant ( $p < 0.05$ ) except in the immediate post-operative period. Systolic blood pressure was comparatively lower in Group-R than in Group-B in postoperative period.

Table 4 shows the comparison of mean diastolic blood pressure in two groups at different intervals which showed that they were comparable and statistically non-significant ( $p < 0.05$ ). Diastolic blood pressure was comparatively lower in Group-R than in Group-B in postoperative period

Table 5 shows that there was significant difference between the VAS score from 5th postoperative hr to 12th hr except in the 6th hr. This statistical difference was due to lower VAS score in Group-R.

Table 1: Demographic distribution

Variables	Group-B (Mean $\pm$ SD)	Group-R (Mean $\pm$ SD)	p-value
Age( yr)	41.58 $\pm$ 14.574	43.64 $\pm$ 13.815	0.470
Height( cm)	162.76 $\pm$ 9.428	164.36 $\pm$ 8.647	0.379
Weight( kg)	65.24 $\pm$ 11.698	67.28 $\pm$ 10.581	0.363
Duration of surgery( min)	33.74 $\pm$ 10.766	30.30 $\pm$ 6.011	0.051
Sex (M/F)	16/34	21/39	0.300

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Table 2: Comparison of heart rate in two groups (per min)

Variables	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
HR - baseline	81.58 ± 7.659	83.64 ± 9.501	-1.194	0.236
HR - Immediate postoperative period	85.92 ± 7.174	81.64 ± 14.470	1.874	0.064
HR - 1	80.94 ± 7.797	73.76 ± 13.602	3.238	0.002
HR - 2	84 ± 9.640	76.30 ± 14.305	3.189	0.002
HR - 3	88.34 ± 12.047	75.04 ± 15.712	4.750	<0.001
HR - 4	79.02 ± 6.906	72.74 ± 13.585	2.914	0.004
HR - 5	79.36 ± 6.404	74.50 ± 12.500	2.447	0.016
HR - 6	79.70 ± 7.560	73.00 ± 11.350	3.474	0.001
HR - 7	81.06 ± 7.327	74.32 ± 11.133	3.576	0.001
HR - 8	81.14 ± 7.467	75.32 ± 9.584	3.387	0.001
HR - 9	81.20 ± 8.010	77.02 ± 11.188	2.148	0.034
HR - 10	79.30 ± 5.219	76.38 ± 10.721	1.732	0.086
HR - 11	79.88 ± 5.731	77.26 ± 10.762	1.519	0.132
HR - 12	79.80 ± 6.752	78.82 ± 8.324	0.647	0.519

Table 3: Systolic blood pressure distribution (mmHg)

Variables	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
SBP - baseline	123.00 ± 8.778	120.64 ± 14.787	0.970	0.334
SBP - Immediate postoperative period	132.00 ± 8.330	125.08 ± 12.873	3.191	0.002
SBP - 1	126.10 ± 9.679	124.28 ± 12.749	0.804	0.423
SBP - 2	121.36 ± 8.223	120.36 ± 12.753	466	0.642
SBP - 3	121.80 ± 9.100	118.46 ± 10.979	1.656	0.101
SBP - 4	120.24 ± 9.011	117.78 ± 0.332	1.269	0.208
SBP - 5	120.32 ± 8.163	117.54 ± 11.022	1.433	0.155
SBP - 6	119.74 ± 6.223	118.18 ± 9.983	0.938	0.351
SBP - 7	120.34 ± 7.345	119.54 ± 7.702	0.532	0.596
SBP - 8	120.06 ± 7.924	118.50 ± 9.511	0.891	0.375
SBP - 9	121.50 ± 11.603	119.20 ± 9.315	1.093	0.277
SBP - 10	117.88 ± 11.349	119.64 ± 10.129	-0.818	0.415
SBP - 11	119.82 ± 9.220	118.58 ± 9.498	0.662	0.509
SBP - 12	117.88 ± 9.410	121.00 ± 10.844	-1.537	0.128

Table 4: Diastolic blood pressure (mmHg) distribution

Variables	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
DBP - baseline	79.62 ± 5.739	78.84 ± 5.508	0.693	0.490
DBP - Immediate postoperative period	85.42 ± 5.507	83.76 ± 7.397	1.273	0.206
DBP - 1	80.04 ± 5.653	78.66 ± 10.481	0.819	0.415
DBP - 2	81.28 ± 7.778	79.96 ± 10.292	0.724	0.471
DBP - 3	82.42 ± 7.877	78.70 ± 10.066	2.058	0.042
DBP - 4	78.04 ± 6.509	78.26 ± 8.238	-0.148	0.883
DBP - 5	77.26 ± 7.376	77.52 ± 8.190	-0.167	0.868
DBP - 6	77.10 ± 5.068	77.54 ± 6.575	-0.375	0.709
DBP - 7	76.04 ± 6.803	78.02 ± 6.832	-1.452	0.150
DBP - 8	77.04 ± 6.518	76.60 ± 8.236	0.296	0.768
DBP - 9	77.00 ± 8.303	76.74 ± 7.491	0.164	0.870
DBP - 10	76.80 ± 6.007	76.96 ± 7.295	-0.120	0.905
DBP - 11	76.72 ± 5.782	76.16 ± 7.875	0.405	0.686
DBP - 12	76.30 ± 7.080	76.16 ± 7.427	0.096	0.923

Table 5: VAS distribution in two groups

Variables	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
VAS - Immediate postoperative period	22.20 ± 5.067	23.20 ± 8.676	-.704	0.483
VAS - 1	29.20 ± 4.445	27.40 ± 5.997	1.705	0.091
VAS - 2	30.96 ± 8.002	28.80 ± 8.722	1.290	0.200
VAS - 3	28.60 ± 9.260	26.60 ± 7.174	1.207	0.230
VAS - 4	28.60 ± 4.953	27.40 ± 4.870	1.222	0.225
VAS - 5	31.00 ± 4.629	27.80 ± 4.647	3.450	0.001
VAS - 6	29.40 ± 4.243	27.80 ± 5.067	1.712	0.090
VAS - 7	30.00 ± 2.020	27.40 ± 4.870	3.487	0.001
VAS - 8	30.40 ± 3.476	26.80 ± 4.712	4.347	<0.001
VAS - 9	30.80 ± 3.959	25.40 ± 5.789	5.445	<0.001
VAS - 10	28.20 ± 3.881	23.40 ± 5.573	4.998	<0.001
VAS - 11	23.60 ± 4.849	20.60 ± 4.243	3.293	0.001
VAS - 12	21.40 ± 4.522	16.20 ± 4.903	5.513	<0.001

Table 6: Verbal rating scale distribution

VRS time	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
VRS - Immediate postoperative period	1.92 ± .340	1.62 ± .567	3.205	0.002
VRS - 1	2.04 ± .283	1.74 ± .565	3.359	0.001
VRS - 2	2.08 ± .665	1.84 ± .817	1.611	0.110
VRS - 3	1.88 ± .799	1.52 ± .646	2.477	0.015
VRS - 4	1.82 ± .438	1.68 ± .471	1.540	0.127
VRS - 5	2.06 ± .424	1.96 ± .283	1.387	0.169
VRS - 6	1.94 ± .424	1.80 ± .495	1.519	0.132
VRS - 7	2.02 ± .247	1.78 ± .465	3.226	0.002
VRS - 8	1.90 ± .416	1.64 ± .485	2.876	0.005
VRS - 9	2.06 ± .373	1.56 ± .501	5.657	<0.001
VRS - 10	1.58 ± .499	1.32 ± .471	2.680	0.009
VRS - 11	1.26 ± .443	1.00 ± .000	4.149	<0.001
VRS - 12	1.10 ± .303	1.00 ± .000	2.333	0.022

Table 7: Number of patients requiring rescue analgesics

Postoperative time interval	Group-B (n=50)		Group-R (n=50)		χ <sup>2</sup>	p-value
	No.	%	No.	%		
Immediate period	1	2	0	0	1.010	0.315
1st hour	5	10	3	6	0.543	0.461
2nd hour	17	34	16	32	0.045	0.832
3rd hour	22	44	13	26	3.560	0.059
4th hour	3	6	2	4	0.211	0.646
5th hour	4	8	1	2	1.895	0.169
6th hour	1	2	2	4	0.344	0.558
7th hour	1	2	1	2	0.000	1.000
8th hour	1	2	0	0	1.010	0.315
9th hour	7	14	0	0	7.527	0.006
Total doses of rescue analgesia required	60		38		-	-

**Table 8: Time to 1st analgesic requirement**

Variables	Group-B (Mean ± SD)	Group-R (Mean ± SD)	t-value	p-value
Time to 1st Analgesic Requirement	117.55 ± 46.856	131.03 ± 33.795	-1.429	0.157
Total Analgesia Consumption (mg)	97.34 ± 46.693	83.82 ± 24.528	1.540	0.128

Table 6 shows that there was significant difference between these two groups in VRS score in immediate post-operative period, 1st hr, 3rd hr and then from 7th hr to 12th hr. This difference is due to the lower VRS score in Group-R.

The number of patients requiring rescue analgesia was comparable in both groups and was non-significant. There was a statistical difference between the groups at the 9th hour. Rescue analgesia was given when VAS score was > 40 (Table 7).

The time required for rescue analgesia was less in bupivacaine group than with ropivacaine, which means Group-R has a longer action for relief of pain. Also the total analgesia required is with ropivacaine less but was statistically insignificant (Table 8).

## DISCUSSION

In comparisons to open cholecystectomy, LC is associated with less intense pain.<sup>9, 10, 11</sup>

In the present study, heart rates were lower in Group-R than in Group-B and that too for a longer time probably due to more dense and prolonged analgesia. Incidence of bradycardia was significantly higher with ropivacaine compared to bupivacaine, which was statistically significant. Gupta et al did same study with fentanyl and bupivacaine but the incidence of bradycardia was not increased.<sup>8</sup> The reason for this difference in incidence between the two studies could not be ascertained.

Blood pressures (systolic, diastolic, and mean) were comparable and statistically insignificant in both the study groups, the reason being the rescue analgesia given on demand whenever VAS scores reached 40. Studies done by Gupta et al, Tae Han Kim et al, Goldstein et al also revealed the same findings, moreover none of the agents used intraperitoneally were described as causing rise in blood pressure.<sup>8, 13, 14</sup>

Our study (Table 5) showed that the analgesic effect was more pronounced with ropivacaine in the 7th hr. The difference in VAS score increased from 7th hr similarly, VRS scores in Group-B and in Group-R were significantly reduced in the immediate postoperative period and at first hr respectively. At 3rd hour VRS scores showed significantly less pain

in patients receiving ropivacaine. VRS scores at the end of 7th hour showed a significant difference with ropivacaine ( $2.02 \pm .247$  in Group-B and  $1.78 \pm .465$  in Group-R). Therefore, VAS and VRS were more in Group-B than in Group-R at all-time intervals.

Refaie et al<sup>12</sup> and Scheinin et al<sup>15</sup> also concluded that intensity of pain is reduced with bupivacaine compared to normal saline. Pain scores were  $1.7 \pm 0.2$ ,  $1.2 \pm 0.1$  and  $0.9 \pm 0.2$  with bupivacaine at one, two and three hrs respectively vs.  $1.9 \pm 0.2$ ,  $3.2 \pm 0.2$  and  $1.3 \pm 0.3$  in group with saline.<sup>12</sup>

Kim TH et al also concluded that intraperitoneal instillation of ropivacaine at the beginning of LC combined with normal saline infusion is an effective method for reducing pain after LC.<sup>13</sup> Newcomb et al conducted a study to compare the efficacy of local anesthetic infiltration with or without preoperative non-steroidal anti-inflammatory drugs.<sup>16</sup> They concluded that the use of preoperative rofecoxib, 0.5% bupivacaine infiltration, or both for postoperative analgesia did not decrease post-operative pain or decrease length of stay after LC compared with placebo. However, in our study intraperitoneal instillation of both bupivacaine and ropivacaine reduced the pain.

In 2007, Kucuk et al determined the effect of local anesthetic instillation and compared bupivacaine and ropivacaine in patients undergoing LC. The study showed that intraperitoneal instillation of 100 mg bupivacaine, 100 mg ropivacaine, or 150 mg ropivacaine at the end of a LC significantly reduced the morphine consumption during the first 24 h. For preventing postoperative pain. 150mg ropivacaine proved to be significantly more effective than either 100 mg bupivacaine or 100 mg ropivacaine.<sup>2</sup> Ropivacaine proved more useful than bupivacaine in reducing the intensity of pain up to 12 hrs.

The number of patient requiring analgesia was not significantly different between the two groups up to 8th hr, which implies the pain relief was comparable between the two groups. In the 9th hr there was a significant difference between the two groups and from 10th hr onwards no patient required analgesia in either group. The no of patients receiving bupivacaine required more frequent dosing of

analgesics and up to later periods of monitoring in postoperative hours, whereas requirement of second dose of analgesia got decreased and interval between two doses got increased considerably in patient receiving ropivacaine. A study done by Ashraf et al showed that the total analgesia requirement for patients with bupivacaine was lesser than with patients given normal saline<sup>17</sup>, whereas Kang H et al compared ropivacaine with normal saline and showed better analgesia with ropivacaine.<sup>13</sup>

Time to first analgesic requirement was shorter with bupivacaine. The total analgesic dose consumption was also higher in this group. The differences in time to first analgesic requirement and total analgesic consumption were statistically non significant ( $p < 0.05$ ). This implies that the analgesia provided by ropivacaine is of longer duration and denser than bupivacaine. Total dose of analgesic consumption was higher in our study groups as compared to Gupta et al; this was probably due to tramadol given in premedication and longer duration of surgery in their study. Multiple doses of fentanyl and denser analgesia and sedation could have further lead to subsequent lesser dosing. In 2007, a similar study was conducted by Kucuk et al which showed that the intraperitoneal instillation of 100 mg bupivacaine, 100 mg ropivacaine, or 150 mg ropivacaine at the end of a LC significantly reduced the morphine consumption during the first 24 hrs.<sup>2</sup> The instillation of ropivacaine 150 mg was more effective than bupivacaine 100 mg or ropivacaine 100 mg. Trikoupis et al also recorded the time of the first analgesic demand; the total amount of morphine received through PCA in the first 24 hours, and revealed similar results to us.<sup>18</sup>

Goldstein et al recorded that morphine consumption at wake-up and over the first 24 hr was significantly lower with bupivacaine and ropivacaine when compared with normal saline.<sup>14</sup> A study done by Rafaei et al revealed that the number of patients who needed postoperative analgesia in with bupivacaine was significantly lower than control.<sup>12</sup> The morphine sparing effect of ropivacaine was significantly greater than that of bupivacaine. Park et al used fentanyl as rescue analgesia and concluded that fentanyl dose consumption was less in ropivacaine than normal saline.<sup>20</sup> Sarvestani et al conducted a study using hydrocortisone which resulted in decreased pain and analgesic requirement.<sup>19</sup>

### Complications

Ten percent of patients in the bupivacaine group

had intra-operative complications. Incidence of bradycardia was more in Group-R (18%) than in Group-B (2%), and difference was statistically significant ( $p = 0.008$ ).

Incidence of hypotension was more in patients receiving ropivacaine (6%) than bupivacaine (0%) but the results were not statistically significant ( $p = 0.079$ ).

Incidence of emesis was equal in both the groups.

Incidence of pruritus was more with ropivacaine (12%) than with bupivacaine (4%), but difference was statistically non-significant ( $p = 0.140$ ). Pruritus was self-limited.

The incidence of shoulder pain was less in our study perhaps because postoperative follow up was of shorter duration.

### Limitations of the study

Patients were followed for 12 hour postoperatively which might have led us to overestimate rescue analgesic dose, as after 12 hours intensity of pain is decreased and less number of analgesic doses are required. Duration of analgesia provided could have been ascertained more precisely if study would have been longer.

We compared 2  $\mu\text{g}/\text{kg}$  of bupivacaine and 2  $\mu\text{g}/\text{kg}$  of ropivacaine. Cardiotoxicity and central nervous side effects of ropivacaine are less compared to bupivacaine in same plasma concentration.<sup>5,21,22</sup> but, absorption after intraperitoneal instillation may be rapid, leading to plasma concentrations above the central nervous system toxicity threshold. We did not measure the plasma concentration of either drug. During general anesthesia, signs of neurological toxicity are masked, which calls for caution in dosing.

### CONCLUSION

The results of our study show that intraperitoneal instillation of local anesthetic solution in laparoscopic cholecystectomy provides effective postoperative analgesia. Analgesia provided by ropivacaine was of longer duration as compared to bupivacaine.

**Conflict of interest:** None declared by the authors

**Authors' contribution:** RKM – concept of study and manuscript editing

KM – conduction of study and data collection

SL – statistical analysis and literature search

SP – manuscript editing

## REFERENCES

1. Cuschieri A. Laparoscopic cholecystectomy. *J R Coll Surg Edinb.* 1999 Jun;44(3):187-92. [PubMed]
2. Kucuk C, Kadiogullari N, Canoler O, Savli S. A placebo-controlled comparison of bupivacaine and ropivacaine instillation for preventing postoperative pain after laparoscopic cholecystectomy. *Surg Today.* 2007;37(5):396-400. [PubMed]
3. Narchi P, Benhamou D, Fernandez H. Intraperitoneal local anaesthetic for shoulder pain after day-case laparoscopy. *Lancet.* 1991 Dec 21-28;338(8782-8783):1569-70. [PubMed]
4. Chundrigar T, Hedges AR, Morris R, Stamatakis JD. Intraperitoneal bupivacaine for effective pain relief after laparoscopic cholecystectomy. *Ann R Coll Surg Engl.* 1993 Nov;75(6):437-9. [PubMed] [Free full text]
5. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anesthesia in laparoscopic cholecystectomy: a systematic review and meta-analysis. *Anesth Analg.* 2006 Sep;103(3):682-8. [PubMed]
6. Gupta A, Thorn SE, Axelsson K, Larsson LG, Agren G, Holmström B, et al. Postoperative pain relief using intermittent injections of 0.5% ropivacaine through a catheter after laparoscopic cholecystectomy. *Anesth Analg.* 2002 Aug;95(2):450-6. [PubMed]
7. Trikoupi A, Papavramidis T, Kyurdzhieva E, Kesisoglou I, Vasilakos D. Intraperitoneal administration of ropivacaine during laparoscopic cholecystectomy: 14AP12-5. *Eur J Anaesth.* 2010;27 (47) :222. [Free full text]
8. Gupta R, Bogra J, Kothari N, Kohli M. Postoperative analgesia with intraperitoneal fentanyl and bupivacaine: A randomized control trial. *Can J Med.* 2010;1(Suppl 1):1-9.
9. Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-regional local anaesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multimodal analgesia: a randomized, double-blinded, placebo-controlled study. *Anesth Analg.* 1999 Oct;89(4):1017-24. [PubMed]
10. Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: characteristics and effect of intraperitoneal bupivacaine. *Anaesth Analg.* 1995 Aug;81(2):379-84. [PubMed]
11. Hendolin HI, Pääkkönen ME, Alhava EM, Tarvainen R, Kempainen T, Lahtinen P. Laparoscopic or open cholecystectomy: a prospective randomised trial to compare postoperative pain, pulmonary function, and stress response. *Eur J Surg.* 2000 May;166(5):394-9. DOI: 10.1080/110241500750008961. [PubMed]
12. Rafaie AMN, Khatab MM. Reduction of early postoperative pain after diagnostic laparoscopy with local bupivacaine: a randomized placebo controlled study. *J Middle East Fertility Society.* 2005;10(3):244-49.
13. Kim TH, Kang H, Park JS, Chang IT, Park SG. Intraperitoneal Ropivacaine Instillation for Postoperative Pain Relief after Laparoscopic Cholecystectomy. *J Korean Surg Soc.* 2010;79:130-136. [Free full text]
14. Goldstein A, Grimault P, Henique A, Keller M, Fortin A, Darai E. Preventing postoperative pain by local anesthetic instillation after laparoscopic gynecologic surgery: a placebo-controlled comparison of bupivacaine and ropivacaine. *Anesth Analg.* 2000 Aug;91(2):403-7. [PubMed]
15. Scheinin B, Kellokumpu I, Lindgren L, Haglund C, Rosenberg PH. Effect of intraperitoneal bupivacaine on pain after laparoscopic cholecystectomy. *Acta Anaesthesiol Stand.* 1995 Feb;39(2):195-8. [PubMed]
16. Newcomb W, Lincourt A, Hope W, Schmelzer T, Sing R, Kercher K, et al. Prospective, double-blinded, randomized, placebo-controlled comparison of local anesthetic and nonsteroidal anti-inflammatory drugs for postoperative pain management after laparoscopic surgery. *Am Surg.* 2007 Jun;73(6):618-24; discussion 624-5. [PubMed]
17. Readman E, Maher PJ, Ugoni AM, Gordon S. Intraperitoneal ropivacaine and a gas drain: Effects on postoperative pain in laparoscopic surgery. *J Am Assoc Gynecol Laparosc.* 2004;11:486-91. [PubMed]
18. Louizos AA, Hadzilia SJ, Leandros E, Kouroukli IK, Georgiou LG, Bramis JP. Postoperative pain relief after laparoscopic cholecystectomy: A placebo-controlled double-blind randomized trial of preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25% *Surg Endosc.* 2005;19:1503-6. [PubMed]
19. Sarvestani AS, Amini S, Kalhor M, Roshanravan R, Mohammadi M, Lebaschi AH. Intraperitoneal hydrocortisone for pain relief after laparoscopic cholecystectomy. *Saudi J Anaesth.* 2013 Jan;7(1):14-7. doi: 10.4103/1658-354X...[PubMed] [Free full text]
20. Park YH, Kang H, Woo YC, Park SG, Baek CW, Jung YH, et al. The effect of intraperitoneal ropivacaine on pain after laparoscopic colectomy: a prospective randomized controlled trial. *J Surg Res.* 2011 Nov;171(1):94-100. doi:10.1016/j.jss.2010.03.024. [PubMed]
21. Barczynski M, Konturek A, Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of pneumoperitoneum for laparoscopic cholecystectomy: a randomized, double-blind, placebo controlled study. *Surg Endosc.* 2006 Jul;20(7):1088-93. [PubMed]
22. Labaille T, Mazoit JX, Paqueron X, Franco D, Benhamou D. The clinical efficacy and pharmacokinetics of intraperitoneal ropivacaine for laparoscopic cholecystectomy. *Anesth Analg.* 2002 Jan;94(1):100-5. [PubMed]
23. Knudsen K, Beckman Suurkula M, Blomberg S, Sjøvall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. *Br J Anaesth.* 1997 May;78(5):507-14. [PubMed] [Free full text]

