

# A Study on Efficacy of Levo Bupivacaine Over Ropivacaine for Postoperative Analgesia After Laparoscopic Cholecystectomy: A Placebo Controlled Comparative Study

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## ABSTRACT

**Introduction:** Various drugs have been used to reduce postoperative shoulder tip pain like nonsteroidal anti-inflammatory drugs (NSAIDs), opioids and local anaesthetics (LAs), both at surgical site and intraperitoneally, with varying success. Laparoscopic procedures are associated with smaller incisions, lower morbidity, shorter hospitalizations, earlier return to normal activity, and less postoperative pain, the leading hypothesis is that carbon dioxide (CO<sub>2</sub>) induced phrenic nerve irritation. The incidence of shoulder pain varies from 35% to 80% and ranges from mild to severe. In some cases it has been reported to last more than 5 weeks after surgery. Pain intensity peaks during the first postoperative hours and usually declines over the following 2–3 days. The present study is designed to compare the effects of intraperitoneal sub diaphragmatic instillation of ropivacaine and levobupivacaine for the relief of shoulder tip pain after laparoscopic cholecystectomy.

**Material and Methods:** The present prospective, randomized, controlled, double blind study was conducted in the Department of Anaesthesiology and Critical care, Rama Medical College & Hospital, Pilkhuwa, Hapur. Ninety patients of either sex belonging to American Society of Anesthesiologists (ASA) physical status class I or II, between 20-60 years of age, scheduled to undergo laparoscopic cholecystectomy were included in the study. Shoulder tip pain and abdominal pain was assessed by using the visual analogue scale (VAS) at 0, 2, 4, 8 and 24 hours after the completion of the procedure.

**Results:** Intraperitoneal sub diaphragmatic instillation of LA was used as it provided numerous benefits including being a

cost effective method associated with minimal side effects due to less systemic absorption and no chance of increased infection due to catheter Group L, Group R and Group S. Patients received 10ml of 0.25% levobupivacaine, ropivacaine and Saline respectively, under each dome of diaphragm. Both levobupivacaine (0.25%) and ropivacaine (0.25%) are effective for this purpose, though levobupivacaine relieved pain for a longer duration, without increasing any other complication or side effects.

**Conclusion:** Intraperitoneal sub diaphragmatic instillation of local anaesthetics is an effective means of pain control for shoulder tip pain in patients undergoing laparoscopic cholecystectomy in the postoperative period.

**Keywords:** Levobupivacaine, Ropivacaine, Laparoscopic Surgeries, Postoperative Shoulder Pain.

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## INTRODUCTION

Laparoscopic procedures are being increasingly accepted for surgeries as these are associated with smaller incisions, lower morbidity, shorter hospitalizations, earlier return to normal activity, and less postoperative pain.<sup>1-3</sup> The origin of pain after laparoscopic cholecystectomy is multifactorial. The incidence of shoulder pain varies from 35% to 80% and ranges from mild to severe.<sup>4-6</sup> In some cases; it has been reported to last more than 5 weeks after surgery.<sup>7</sup> The precise mechanism of shoulder pain after laparoscopy remains unclear, the leading hypothesis is that

carbon dioxide (CO<sub>2</sub>) induced phrenic nerve irritation causes referred pain to fourth cervical root (C4) dermatome which is further projected to shoulder.<sup>8</sup> Pain intensity peaks during the first postoperative hours and usually declines over the following 2–3 days.<sup>9-10</sup> The irritation might be caused by local acidosis, distension of the diaphragm, or irritation secondary to CO<sub>2</sub> remaining in the abdomen. Significant correlation has been found between the size of gas bubble under the diaphragm and post operative pain.<sup>11</sup>

Various drugs have been used to reduce postoperative shoulder tip pain like nonsteroidal anti-inflammatory drugs (NSAIDs), opioids and local anaesthetics (LAs), both at surgical site and intraperitoneally, with varying success. Levobupivacaine Racemic mixture (50:50) have a safer pharmacological profile with less cardiac and neurotoxic adverse effects. The pure S (-) enantiomers of bupivacaine, i.e., ropivacaine and levobupivacaine were thus introduced into the clinical anaesthesia practice.

The present study is designed to compare the effects of intraperitoneal sub diaphragmatic instillation of ropivacaine and levobupivacaine for the relief of shoulder tip pain after laparoscopic cholecystectomy.

**MATERIAL AND METHODS**

The present prospective, randomized, controlled, double blind study was conducted in the Department of Anaesthesiology and Critical care, Rama Medical College & Hospital, Pilkhuwa, Hapur. Ninety patients of either sex belonging to American Society of Anesthesiologists (ASA) physical status class I or II, between 20-60 years of age, scheduled to undergo laparoscopic cholecystectomy were included in the study. The patients with history of previous open surgery in the upper abdomen, acute cholecystitis posted for laparoscopic cholecystectomy, inability to understand VAS, history of allergy to Local anaesthetic agents (LA), BMI>35 and need for more invasive procedure (for e.g. insertion of T-Drain, or conversion to open cholecystectomy) were not included in the study

All the patients were examined during the preoperative visit a day prior to surgery. After approval from the institutional ethical committee and informed written consent from the patients, patients were explained about the details of anaesthesia plans and the procedure during the preoperative visit. They were also explained about scoring on the visual analogue scale for pain (VAS; 0: no pain and 10: worst possible pain). Each patient received oral tablet alprazolam 0.25 mg, tablet ranitidine 150 mg at bedtime and in morning and tablet metoclopramide 10 mg in the morning at 6 am on the day of surgery. The patients were randomly allocated using sealed envelopes to one of the three groups as follows:

**Group L (n=30)** Patients received 10ml of 0.25% levobupivacaine under each dome of diaphragm.

**Group R (n=30)** Patients received 10ml of 0.25% ropivacaine under each dome of diaphragm.

**Group S (n=30)** Patients received 10 ml of normal saline under each dome of diaphragm.

On patient's arrival in the operating room, after establishing non-invasive monitoring (electrocardiogram, heart rate, blood pressure, respiratory rate, pulse oximetry), an intravenous line was secured. Injection glycopyrrolate 0.2 mg i.v. was given to all patients. After recording the baseline vital signs, general anaesthesia was induced with injection propofol 2 mgkg-1, injection morphine 0.1 mgkg-1 and injection vecuronium bromide 0.1 mgkg-1 intravenously. Anaesthesia was maintained with isoflurane (1%) in nitrous oxide and oxygen in ratio of 67/33. Endotracheal tube was used to secure the airway. Ventilation was controlled with a tidal volume of 8 to 10 mlkg-1 and the respiratory rate adjusted to maintain EtCO2 value of 30 to 35 mmHg. Nasogastric tube was then placed. Laparoscopic surgery was performed by using the same technical principles for all the patients. Pneumoperitoneum was established with CO2 insufflation at pressure of up to 12mm of Hg. All the patients were monitored continuously for ECG, HR, RR, SpO2 and EtCO2 throughout the surgery. Before deflation of pneumoperitoneum, each patient received the drugs under each hemi diaphragm as allotted to them in the group by direct instillation through the laparoscopic port using a 10 ml syringe. The surgeons were asked to infiltrate 2 ml of 0.25% bupivacaine at all the port sites in all the patients. At the end of surgery injection ondansetron 4 mg i.v. was given to all patients and residual neuromuscular block was antagonized with 2.5 mg of neostigmine methylsulfate and 0.4 mg glycopyrrolate.

Patients were observed for up to 24 hrs. Rescue analgesia, was given with paracetamol infusion 1g intravenously (over 15mins) in post-operative period if VAS score >4 or if the patient demanded analgesia. After instillation of the drug hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic Blood Pressure (DBP) and mean arterial pressure (MAP) were recorded every 5 minutes for the first half hour and at 1, 2, 4, 8 and 24 hrs. EtCO2 was monitored from the time of instillation of the drug for every 5 mins till extubation. Shoulder tip pain and abdominal pain was assessed by using the visual analogue scale (VAS) at 0, 2, 4, 8 and 24 hours after the completion of the procedure at rest. Other informations such as first request for analgesia by the patient, total consumption of analgesic in 24 hours, nausea and/or vomiting, any other complaint were also noted.

**Table 1: Age and weight distribution**

	Group R (n=30)	Group L (n=30)	Group S (n=30)	P Value
Age (in year)	40.23 ± 13.17	42.70 ± 11.40	41.17 ± 10.56	0.715
Weight (in Kg)	59.53 ± 11.80	59.00 ± 11.84	61.90 ± 10.19	0.574

**Table 2: VAS pain score for abdominal pain at rest**

Abdominal pain -at rest	Group R (n=30)		Group L (n=30)		Group S (n=30)	
	Median	IQR	Median	IQR	Median	IQR
0hr	1	0 - 2	0.5	0 - 2	1	0 - 2
2 hr	2	1 - 3	1	1 - 2	2	1 - 3
4 hr	2	1 - 2.25	1	1 - 3	2	1.75 - 3
8 hr	1	0 - 2	2	1 - 2	2	1 - 2
24 hr	1	1 - 1	1	1 - 1	1	1 - 1

Table 3: VAS pain score for STP at rest

Pain at shoulder tip at rest	Group R (n=30)		Group L (n=30)		Group S (n=30)		P Value	Group R vs. Group L	Group R vs. Group S
	Median	IQR	Median	IQR	Median	IQR			
0 hr	0	0 - 0	0	0 - 0	0	0 - 0	0.152	1.000	<b>0.111</b>
2 hr	0	0 - 1	0	0 - 0	0	0 - 1	0.132	<b>0.098</b>	0.720
4 hr	0	0 - 1	0	0 - 1	0	0 - 1	0.540	0.296	0.892
8 hr	0	0 - 1	1	0 - 1	1	0 - 1	<b>0.059</b>	0.253	<b>0.023</b>
24 hr	0	0 - 1	0	0 - 1	0.5	0 - 1	<b>0.066</b>	0.576	<b>0.031</b>

## OBSERVATIONS & RESULTS

The mean age in ropivacaine Group R, Group L, Group S was 40.23±13.17 yrs, 42.70±11.40yrs, 41.17±10.56 yrs respectively. Thus the mean age group in all the three groups are comparable (p>0.05).

The mean weight in Group R, Group L, Group S was 59.53±11.80 Kg, 59.00±11.84 Kg, 61.90±10.19Kg respectively. There was no statistical difference between the groups, thus weight in all the three groups was comparable (p>0.05). (Table 1)

On comparing the pain intensity on VAS pain score it was observed that the pain scores in all the three groups were comparable except at 4hr wherein the patients in Group S had more pain than Group L and Group R but this difference was not statistically significant (p value 0.099). (Table 2)

On comparing Pain intensity on VAS pain score for shoulder tip pain at rest it was observed that patients in Group S experienced more pain than patients in Group R and Group L. This difference was found to be at 8 and 24 hrs postoperatively (p value 0.059 and 0.066 respectively) but was not statistically significant.

On comparing Group R with Group S, the pain intensity score were higher in Group S at 0,8 and 24hrs, being statistically

significant at 8 and 24hrs (p value 0.023 and 0.031 respectively). On comparing Group L with Group S, the pain intensity scores were found to be higher in saline group at 0,2 and 24hrs, the difference being statistically significant at 2hrs (p value 0.051). Although the pain intensity scores were higher for Group S at 0 and 24 hrs it was not found to be statistically significant.

On comparing Group R with Group L it was observed that VAS scores were lower in Group L at 2hr but this was not statistically significant (p value 0.098). (Table 3)

The mean time for first request for analgesia by the patients was 2hrs in Group S which was considerably earlier when compared with Group R (9hrs) and Group L (11hrs). This difference was found to be statistically significant (p value <0.05). No significant difference was found in the time for first request of analgesia between Group L and Group R, though the duration was longer for Group L. (Table 4)

There was no significant difference found in the incidence of nausea and vomiting between the three groups. One patient in levobupivacaine group complained of shivering in the post-operative period. (Table 5)

Table 4: First request for analgesia

	Group R (n=30)	Group L (n=30)	Group S (n=30)	P Value	Group R vs. Group L	Group R vs. Group S	Group L vs. Group S
First request for Analgesia (in Hrs)	9 (2.75 - 16.5)	11 (4 - 20)	2 (1.75 - 5.5)	<b>0.001</b>	0.348	<b>0.008</b>	<b>0.001</b>

Table 5: Nausea, Vomiting and other side effects

	Group R (n=30)		Group L (n=30)		Group S (n=30)	
	Frequency	%	Frequency	%	Frequency	%
Nausea	16	53.3%	16	53.3%	19	63.3%
Vomiting	9	30.0%	3	30.0%	13	43.3%
Shivering	0	0%	1	3.3%	0	0%

## DISCUSSION

Local anaesthetics have been used in a numerous ways to relieve post-operative pain after laparoscopic surgeries. Sub diaphragmatic catheters with repeated intraperitoneal instillation, nebulization with LA, these maybe with or without periportal infiltration. Thus intraperitoneal sub diaphragmatic instillation of LA was used as it provided numerous benefits including being a cost effective method associated with minimal side effects due to less systemic absorption and no chance of increased infection due to catheter.12-17

Group L, Group R and Group S Patients received 10ml of 0.25% levobupivacaine, ropivacaine and Saline respectively, under each dome of diaphragm. Both levobupivacaine (0.25%) and ropivacaine (0.25%) are effective for this purpose, though levobupivacaine relieved pain for a longer duration, without increasing any other complication or side effects.

Laparoscopic procedures are associated with smaller incisions, lower morbidity, shorter hospitalizations, earlier return to normal activity, and less postoperative pain. Other benefits of

laparoscopic surgery include reduced bleeding, improved cosmetic results and patient satisfaction. However, pain after laparoscopy may be moderate or severe for some patients, and may require extensive analgesic treatment.

Local anaesthetics have been used in a numerous ways to relieve post-operative pain after laparoscopic surgeries. Various techniques discussed in literature include instillation of LA in the gall bladder bed, placement of surgical soaked LA in gall bladder bed, sub diaphragmatic catheters with repeated intraperitoneal instillation, nebulization with LA, these maybe with or without periportal infiltration with LA with varying success. In the present study intraperitoneal instillation was used as the proposed mechanism of STP is CO<sub>2</sub> induced phrenic nerve irritation leading to referred pain to fourth cervical root (C4) dermatome which is further projected to shoulder. Sub diaphragmatic instillation was used as direct action of LA on the phrenic nerve between the liver and diaphragm could be achieved with minimal dose. Thus intraperitoneal sub diaphragmatic instillation of LA was used as it provided numerous benefits including being a cost effective method associated with minimal side effects due to less systemic absorption and no chance of increased infection due to catheter.

The patients were randomly allocated, using sealed envelopes, to one of the three groups - Group L, Group R and Group S Patients received 10ml of 0.25% levobupivacaine, ropivacaine and Saline respectively, under each dome of diaphragm. In the post-operative period abdominal and STP were compared between the three groups in terms of intensity on a VAS scale of 10, total analgesia required in the first 24hrs and the time before first request of analgesia by the patient. Both levobupivacaine (0.25%) and ropivacaine (0.25%) are effective for this purpose, though levobupivacaine relieved pain for a longer duration, without increasing any other complication or side effects.

## CONCLUSION

Thus it can be concluded that intraperitoneal sub diaphragmatic instillation of local anaesthetics is an effective means of pain control for shoulder tip pain in patients undergoing laparoscopic cholecystectomy in the postoperative period. Both levo bupivacaine (0.25%) and ropivacaine (0.25%) are effective for this purpose, though levobupivacaine relieved pain for a longer duration, without increasing any other complication or side effects.

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