RESEARCH PAPER

Comparative Study on Efficacy of Intraperitoneal Instillation of Levo Bupivacaine versus Ropivacaine for Post-Operative Analgesia after Laparoscopic Cholecystectomy – A Randomized Controlled Trial

Malepati Chandana[1], Samson David[1], Krishna Prabhu[1], Arthi Asokan[1*]

[1]Department of Anaesthesiology,*

Sri Venkateshwaraa Medical College Hospital and Research Centre, Ariyur, Puducherry.

Email: drarthimd@gmail.com

ABSTRACT

Background: Postoperative pain control remains an important part of laparoscopic cholecystectomy. This study compares the efficacy of intraperitoneal instillation of Levobupivacaine to Ropivacaine for postoperative analgesia, evaluating hemodynamic stability, pain scores and analgesic demand.

Aim: To compare the efficacy of intraperitoneal instillation of Levobupivacaine and Ropivacaine for postoperative analgesia after laparoscopic cholecystectomy.

Methods: A randomized controlled trial was done on sixty individuals who underwent elective laparoscopic cholecystectomy. Patients were randomly divided into two groups: Group R (Ropivacaine) and Group L (Levobupivacaine). Baseline features, hemodynamic parameters, Visual Analogue Scale (VAS) pain levels, duration of analgesia and rescue analgesic requirements were all documented and studied.

Results: The average age was similar between groups ($p = 0.316$), while the gender distribution was significantly different ($p = 0.012$). There were no significant variations in weight ($p = 0.629$), height ($p = 0.478$), BMI ($p > 0.05$), or ASA classification. Group R and Group L are equivalent in duration of surgery ($p>0.05$). Heart rate changes showed quicker analgesic decline in Group L (4-12 hours, $p < 0.05$), whereas systolic and diastolic blood pressure were equivalent between groups ($p > 0.05$). Group L showed a temporary increase in mean arterial pressure (MAP) (1-4 hours, $p < 0.05$), which then stabilized. Group R showed significantly lower VAS values at repeated postoperative intervals ($p < 0.05$), indicating better analgesic efficacy. Ropivacaine resulted in prolonged analgesia (9.13 ± 0.86 vs. 7.57 ± 0.50 hours, $p <0.001$). Group R had considerably fewer patients who needed rescue analgesia ($p < 0.01$), with 93.3% requiring no extra analgesia compared to 66.7% in Group L.

Conclusion: In laparoscopic cholecystectomy, Ropivacaine administered intraperitoneally gives better postoperative analgesia than Levobupivacaine. Ropivacaine improves pain control, extends analgesic duration and reduces the need for rescue analgesia, making it a better choice for postoperative pain management.

Keywords: Laparoscopic cholecystectomy, Levobupivacaine, Pain management, Postoperative analgesia, Ropivacaine.

How to cite this article: Chandana M, David S, Prabhu K, Asokan A. Comparative Study on Efficacy of Intraperitoneal Instillation of Levo Bupivacaine versus Ropivacaine for Post-Operative Analgesia after Laparoscopic Cholecystectomy – A Randomized Controlled Trial. Int J Drug Deliv Technol. 2026;16(33s):640-645. DOI: 10.25258/ijddt.16.33s.76

INTRODUCTION

LC is currently regarded as the gold standard for gallbladder removal [1,2]. Furthermore, compared to open cholecystectomy, LC has benefits such as fewer analgesic needs, quicker recovery, and shorter hospital stays [3,4]. Nonetheless, diaphragmatic, and peritoneal straining, irritation from CO2 insufflation, intra-abdominal pH changes and the release of inflammatory mediators are the main causes of visceral and shoulder discomfort which are frequent postoperative complaints [5].

However, opioid medications may have adverse effects such itching, nausea, vomiting, and respiratory depression in the initial days after surgery. Non-opioid analgesics are strongly recommended as part of a multimodal pain management strategy because they offer effective pain relief with fewer adverse effects [6,7]. Investigating non-opioid alternatives for the management of LC postoperative pain is therefore essential. Many analgesic techniques, including intraperitoneal administration of local anesthetics, regional anesthesia (transversus abdominis plane block), and systemic analgesia (opioids, NSAIDs), have been studied to enhance pain management after LC [8]. A local anaesthetic administered directly into the peritoneal cavity known as intraperitoneal instillation has drawn attention since it may help lower visceral pain and opioid use without having serious systemic adverse effects. The effectiveness of various intraperitoneal local anaesthetics including bupivacaine, Ropivacaine and lidocaine has been assessed in a number of clinical trials [9,10].

Our standard preparation of bupivacaine is a racemic mixture of levo and dextro isomers. Levobupivacaine, an amide local anesthetic that is the S (-) enantiomer of racemic bupivacaine, can be used in place of bupivacaine.

Compared to bupivacaine, levobupivacaine had a lower frequency of cardiac and neurotoxicity [11]. Because levobupivacaine has a lower affinity for cardiac sodium channels than the dextroisomer and a higher affinity for binding plasma proteins, it reduces the risk of cardiotoxicity [12]. The FDA has authorized the use of ropivacaine for both surgical anesthesia and acute pain management.

MATERIALS AND METHODS

After receiving approval from the Institutional Scientific and Ethics committee and obtaining a CTRI (Clinical Trials Registry-India) registration number (REF/2023/07/069658), the trial was carried out. A comprehensive pre-anesthetic evaluation was performed on all patients who satisfied our inclusion criteria and provided their consent for this study. Using the sealed envelope procedure, the patients were randomly assigned to two groups (blind to the investigator). Every case that was enrolled in the trial was operated on by a single, skilled laparoscopic surgeon.

Sample Size

The sample size was calculated based on Ratain kumar Choudhary et al. with confidence Interval-95%, power-80%, Ratio between Groups-1 and Mean difference-4, we calculated total sample size of 60 in which 30 is allocated in each group using Open Epi Sofware version 3.0 [13].

Group R: Patients received Intraperitoneal instillation of 0.25% Ropivacaine 20ml on each side for postoperative analgesia following Laparoscopic Cholecystectomy (n=30).

Group L: Patients received Intraperitoneal instillation of 0.25% Levobupivacaine 20 ml on each side for post-operative analgesia following Laparoscopic Cholecystectomy (n=30).

Patients were shifted to the operation room, after getting consent and an intravenous access with large bore cannula was secured in the non-dominant hand. Standard monitoring ECG, NIBP, SPO2 and ETCO2 was monitored and recorded. Intravenously (IV) ondansetron 4 mg, glycopyrolate 0.2 mg, and fentanyl 2 mcg/kg were given to each patient, and they were preoxygenated with 100% O2 for three minutes. Propofol 2 mg/kg (IV) was used for induction, vecuronium 0.1 mg/kg (IV) was used to ease endotracheal intubation, and an appropriate-sized endotracheal tube was used to secure the airway.

Intermittent doses of 66% N2O in 33% O2 + isoflurane (1.2%) + 0.01 mg/kg vecuronium were used to maintain anesthesia. Following the procedure, the operating surgeon administered 10 milliliters of 0.25% levobupivacaine intraperitoneally under each diaphragm dome to patients in group L. The operative surgeon gave the patients in group R 10 milliliters of 0.25% ropivacaine intraperitoneally under each diaphragm dome. The residual neuromuscular blockade was reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.005mg/kg at the end of the surgery.

Patients in both the groups were extubated once they are awake, active, hemodynamically stable and breathing adequately. Further assessment was done in the postoperative room by the anaesthesiologist blinded to the study groups. The intensity of the pain was assessed in the post-operative room using visual analogue scale (VAS) at 30 mints, 1 hr, 2hr, 6hr, 12hr and 24hr, where zero score corresponds to no pain and 10 corresponds to maximum or worst pain. For analgesic supplements, a VAS value of 4 or above is considered the cutoff. For post-operative analgesia, patients received a gradual intravenous injection of 1 gm of paracetamol on demand. The demand time was recorded in hours following operation. In a similar vein, any need for repeated analgesic doses was recognized and documented.

RESULTS AND DISCUSSION

The data collected were subjected to Statistical Analysis using SPSS version 16. Frequency analysis, Cross Tabulation, Chi Square test and Independent Sample ‘t’ test were performed for appropriate variables. For every significance test, the probability value, or p, was set at 0.05. A ‘p’ value less than 0.05 is considered significant and a value less than 0.01 is considered as highly significant. The results of the Statistical analysis are presented in the tables and figures given below (Table 1-3, figures 1-3).

The goal of providing effective analgesia after Laparoscopic cholecystectomy had been challenging to accomplish. The primary objective of the present study was to compare two drugs Ropivacaine and Levobupivacaine in intraperitoneal instillation after Laparoscopic cholecystectomy and determine which medication provided the most analgesia during the post-operative phase.

The comparison of heart rate between the two study groups revealed significant changes in hemodynamic parameters at 6 hours and 12 hours. At 4 hours, Group L had a significantly higher HR (98.47 ± 12.70 bpm vs. 89.70 ± 11.49 bpm, $p = 0.007$), which persisted at 6 hours (98.87 ± 4.11 bpm vs. 93.30 ± 14.38 bpm, $p = 0.046$) and 12 hours (90.97 ± 6.11 bpm vs. 85.43 ± 11.75 bpm, $p = 0.026$), indicating an earlier decline in analgesic efficacy or increased sympathetic response in Group L. By 24 hours, the HR differences were no longer significant (80.03 ± 9.32 bpm vs. 78.87 ± 16.09 bpm, $p = 0.732$), indicating that pain control in both groups had stabilized. These data indicate that intraperitoneal Ropivacaine may give greater hemodynamic stability in the early postoperative period than Levobupivacaine between 4 and 12 hours after surgery. This finding aligns with the study by Hasnain and Lakshmi Priya and Sharan et al. where heart rates were significantly lower in Group R compared to Group L for a prolonged period [14,15].

The comparison of systolic blood pressure (SBP) between the Ropivacaine (Group R) and Levobupivacaine (Group L) groups at various postoperative time intervals reveals no statistically significant differences. At 1 hour postoperatively, Group R had slightly higher SBP (129.33

± 15.30 mmHg vs. 125.33 ± 12.79 mmHg, p = 0.276),when compared to Group L which remained comparable at 2 hours (123.67 ± 13.26 mmHg vs. 123.00 ± 9.88 mmHg, p = 0.826), at 4 hours (122.67 ± 11.12 mmHg vs. 121.67 ± 12.34 mmHg, p = 0.743),6 hours (117.67 ± 13.05 mmHg vs. 119.67 ± 12.99 mmHg, p = 0.554), 12 hours (115.33 ± 12.52 mmHg vs. 112.33 ± 8.98 mmHg, p = 0.291) and 24 hours (112.67 ± 12.58 mmHg vs. 109 mmhg). These data indicate that Ropivacaine and Levobupivacaine have equivalent efficacy in sustaining hemodynamic stability after laparoscopic cholecystectomy.

Comparing three groups—Group L (levobupivacaine plus dexmedetomidine), Group R (ropivacaine plus dexmeditomidine), and Group C (normal saline)—Joginder et al.'s study found no discernible difference in systolic blood pressure before or after surgery [16].

MAP levels were similar in both groups at baseline (89.23 ± 11.82 mmHg in Group L and 88.10 ± 9.25 mmHg in Group R, p = 0.681). Group L's MAP was significantly higher after one hour after surgery (97.23 ± 8.39 mmHg) than Group R's (90.53 ± 7.17 mmHg, p = 0.002). By 6 hours, the MAP values of the two groups became comparable (87.57 ± 6.56 mmHg vs. 87.97 ± 8.40 mmHg, p = 0.838), and this trend remained at 12 hours (87.00 ± 7.70 mmHg vs. 85.20 ± 8.24 mmHg, p = 0.386) and 24 hours (85.77 ± 8.28 mmHg vs. 83.53 ± 5.78 mmHg, p = 0.231). These findings indicate that Levobupivacaine initially causes a considerably higher MAP than Ropivacaine in the early postoperative period (1-4 hours), but this effect fades over time with both groups displaying equivalent MAP values by 6 hours and beyond. But in the study by Joginder et al, there was no significant difference in MAP both at pre-operative and post-operative stages in all the three groups compared [levobupivacaine plus dexmedetomidine, Ropivacaine plus dexmedetomidine and Control] [16].

A comparison of Visual Analogue Scale (VAS) pain scores between the Ropivacaine (Group R) and Levobupivacaine (Group L) groups at different postoperative time intervals reveals significant variations in pain perception with time. At baseline, both groups had similar mean VAS scores (4.40 ± 1.19 in Group R vs. 4.80 ± 0.81 in Group L, p = 0.133), indicating similar starting pain levels. However, after 1 hour postoperatively Group R reported considerably lower pain scores (2.70 ± 1.02) than Group L (3.80 ± 0.81, p < 0.001) indicating greater early pain control with Ropivacaine. After 2 hours (2.57 ± 0.97 in Group R vs. 3.77 ± 0.97 in Group L, p < 0.001) and 4 hours (2.60 ± 0.77 in Group R vs. 4.40 ± 0.50 in Group L, p < 0.001) Group R experienced considerably reduced pain levels.

At 6 hours, Group R pain scores increased to 4.00 ± 0.00, whereas Group L had somewhat higher scores (4.33 ± 0.61, p = 0.004) indicating some degradation of the initial analgesic effect. At 12 hours, the difference remained statistically significant with Group R displaying a lower VAS score (3.37 ± 0.56) than Group L (4.17 ± 0.53, p < 0.001) indicating sustained but somewhat decreasing efficacy. At 24 hours, Group R had lower pain scores (4.33 ± 0.61 vs. 4.63 ± 0.49 in Group L, p = 0.039) and the difference was significant.

In the first four hours following surgery, ropivacaine generally provided greater pain relief than levobupivacaine, with significantly lower VAS scores. Ropivacaine maintained a slight analgesic benefit for up to 24 hours, despite the fact that both groups reported very little rising pain after 6 hours. According to these findings, ropivacaine might be the most effective treatment for early postoperative pain following laparoscopic cholecystectomy. Similarly, ropivacaine significantly reduced postoperative pain levels at rest when compared to bupivacaine, particularly in the early postoperative phase, according to a study by Hasnain and Lakshmi Priya [14].

The study found that Ropivacaine considerably reduced pain scores from the first to the 24th hour after surgery. This finding is consistent with previous research which has demonstrated that Ropivacaine provides long lasting analgesia due to its pharmacological features, such as reduced lipophilicity and greater selectivity for sensory nerve fibres than bupivacaine [17]. These properties contribute to the lower pain scores by Ropivacaine in the study, as Ropivacaine is lesser propensity for motor blocking promotes improved patient comfort and early mobilization [18]. In a similar vein, Meena RK's study compared two groups that received intraperitoneal 0.5% bupivacaine in a dose of 2 mg/kg diluted in normal saline (Group B) and 0.75% ropivacaine in a dose of 2 mg/kg diluted in normal saline (Group R) for post-operative analgesia in laparoscopic cholecystectomy [19]. Group R had a significantly lower VAS score from the fifth to the twelfth hour. These results are in line with those of a number of other research [20-22].

In the first 24 hours following surgery, the Ropivacaine group (Group R) needed significantly fewer rescue analgesics than the Levobupivacaine group (Group L) (p < 0.01). 93.3% of patients in Group R did not need more analgesics, 6.7% needed just one dose, and none needed a second. In contrast, Group L had a larger percentage of patients who needed rescue analgesics with 66.7% not needing any, 23.3% requiring one dosage and 10% requiring two doses. Similarly, in a study by Hasnain and Lakshmi Priya has compared Ropivacaine (Group R) with Bupivacaine (Group B) in Laparoscopic cholecystectomy and has revealed that Ropivacaine group required less rescue analgesia in comparison to Bupivacaine group and the difference was statistically significant [14].

The Ropivacaine group (Group R) experienced considerably longer pain alleviation than the Levobupivacaine group (Group L) (p = 0.000). The average duration of analgesia in Group R was 9.13 ± 0.86 hours, while in Group L it was 7.57 ± 0.50 p-value (<0.001) demonstrates that Ropivacaine provided longer pain relief compared to Levobupivacaine during laparoscopic cholecystectomy Ropivacaine may be a better option for intraperitoneal instillation to improve postoperative pain control. In contrast, in a study by Hasnain and Lakshmi Priya time to the first dose of rescue analgesia was similar between the Bupivacaine and Ropivacaine groups [14].

Hence from the present study, we conclude that intraperitoneal instillation of 0.25% Ropivacaine was effective in post-operative analgesia after laparoscopic cholecystectomy.

REFERENCES

1. Arabzadeh A, Seyedsadeghi M, Sadeghi N, Nejati K, Erdi AM. Comparison of intraperitoneal bupivacaine and intravenous ketorolac for postoperative pain management following laparoscopic cholecystectomy. Anesth Pain Med. 2021; 11(6): e114623.
2. Abaid RA, Cecconello I, Zilberstein B. Simplified laparoscopic cholecystectomy with two incisions. ABCD. 2014; 27:154–156.
3. Luo Z, Wang H, Huang D. The impact of parecoxib on pain management for laparoscopic cholecystectomy: a meta-analysis of randomized controlled trials. Surg Laparosc Endosc Percutan Tech. 2019; 29(2):69–74.
4. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anaesthesia in laparoscopic cholecystectomy: a systematic review and meta-analysis. Anesth Analg.2006; 103(3):682–688.
5. Wei X, Yao X. The impact of intraperitoneal levobupivacaine on pain relief after laparoscopic cholecystectomy: a meta-analysis of randomized controlled studies. Surg Laparosc Endosc Percutan Tech.2020; 30(1):1–6.
6. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg. 2013; 26(3):191–196.
7. Bisgaard T, Warltier DC. Analgesic treatment after laparoscopic cholecystectomy. Anesthesiology.2006; 104(4):835–846.
8. Sarkar D, Srivastava R. & Gupta A. Intraperitoneal instillation of local anaesthetics: A novel approach for pain management in laparoscopic surgeries. Anaesthesia: Essays and Researches. 2019; 13(2):245-250.
9. Chundrigar T, Pathak D & Shinde R. Efficacy of intraperitoneal Ropivacaine for postoperative pain relief in laparoscopic cholecystectomy: A randomized controlled trial. Journal of Clinical Anaesthesia.2018; 46: 56-61.
10. Gurkan Y, Aksu C & Solak M. Intraperitoneal local anaesthesia in laparoscopic surgery: An updated review. Current Anaesthesia Reports. 2022;12(2): 78-88.
11. Goyal A, Singi Y, Mallya P, Bhat G and Shankaranarayana P. A comparison between intrathecal levobupivacaine and bupivacaine for quality and safety during infraumbilical surgeries. Cureus.2022;14(10):e30590.
12. Singh A, Gupta A, Datta PK and Pandey M. Intrathecal levobupivacaine versus bupivacaine for inguinal hernia surgery: A randomized controlled trial. Korean J Anesthesiol. 2018;71(3):220-225.
13. Ratan Kumar Choudhary, Praveen Kumar, S.K.S Puri, Shailja Sharma. A Study on Efficacy of Levo Bupivacaine Over Ropivacaine for Postoperative Analgesia After Laparoscopic Cholecystectomy: A Placebo Controlled Comparative Study, Int J Med Res Prof.2017; 3(5):388-91.
14. Hasnain S, Lakshmi Priya RS. Comparison of Ropivacaine and Bupivacaine in Intraperitoneal Instillation for Postoperative Analgesia in Laparoscopic Cholecystectomy: A Randomized Controlled Trial. Cureus. 2024;16(11):e73167.
15. Sharan R, Singh M, Kataria AP, Jyoti K, Jarewal V, Kadian R. Intraperitoneal instillation of bupivacaine and Ropivacaine for postoperative analgesia in laparoscopic cholecystectomy. Anesth Essays Res. 2018; 12:377–380.
16. Joginder Pal Attri, Harjinder Kaur, Ravipaul Singh, Harjeet Singh, Kulwinder Pal Singh. Comparative Study of Intraperitoneal Instillation of Levobupivacaine (0.25%) Plus Dexmedetomidine Versus Ropivacaine (0.25%) Plus Dexmedetomidine for Post-operative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy, International Journal of Scientific Study.2020;8:(3).
17. Markham A, Faulds D. Ropivacaine: a review of its pharmacology and therapeutic use in regional anaesthesia. Drugs. 1996; 52:429–449.
18. McClure JH. Ropivacaine. Br J Anaesth. 1996; 76:300–307.
19. 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; 20:295–300.
20. Rapolu S, Kumar KA, Aasim SA. A comparative study on intraperitoneal bupivacaine alone or with dexmedetomidine for post-operative analgesia following laparoscopic cholecystectomy. IAIM. 2016; 3:33–40.
21. Shivhare P, Dugg P, Singh H, Mittal S, Kumar A, Munghate A. A prospective randomized trial to study the effect of intraperitoneal instillation of Ropivacaine in postoperative pain reduction in laparoscopic cholecystectomy. J Minim Invasive Surg Sci. 2014; 3:18009.
22. 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; 37:396–400.

TABLES AND FIGURES

Table 1: Comparison of VAS between two groups at different time Intervals

Time	Group R (n=30)		Group L (n=30)		't' value	'p' value
	Mean	Std. Deviation	Mean	Std. Deviation		
Baseline	4.40	1.192	4.80	0.805	-1.523	0.133
1hr	2.70	1.022	3.80	0.805	-4.630	0.000**
2 hr	2.57	0.971	3.77	0.971	-4.784	0.000**
4 hr	2.60	0.770	4.40	0.498	-10.748	0.000**
6 hr	4.00	0.000	4.33	0.606	-3.010	0.004**
12hrs	3.37	0.556	4.17	0.531	-5.701	0.000**
24 hrs	4.33	0.606	4.63	0.490	-2.107	0.039*

Figure 1: Comparison of VAS between two groups at different time Intervals

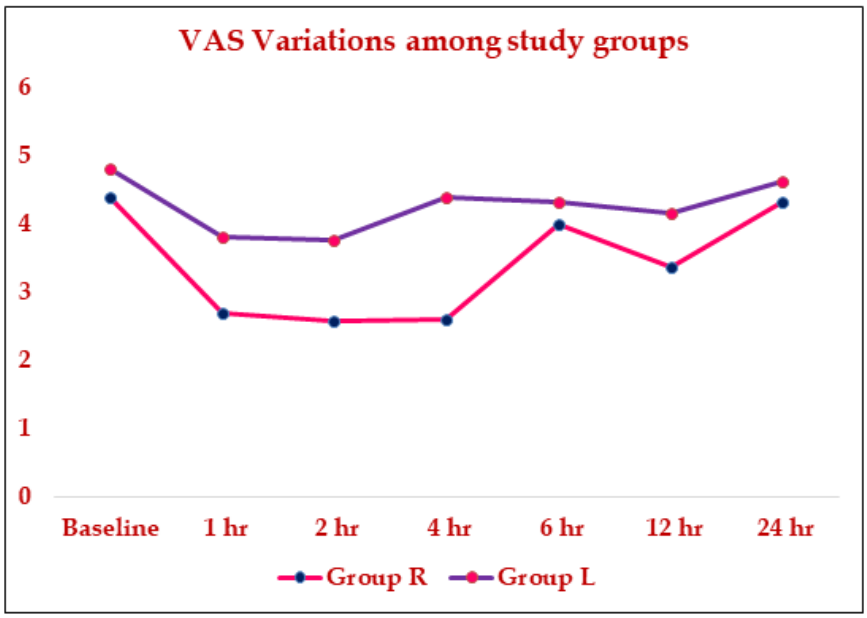

Table 2: Comparison of mean duration of Pain relief among two study groups

Duration of Pain relief (hrs)				't' test value	p value
Group R(n=30)		Group L(n=30)			
Mean	Std. Deviation	Mean	Std. Deviation		
9.13	0.860	7.57	0.504	8.606	p<0.01 Highly Significant

Figure 2: Comparison of mean duration of Pain relief among two study groups

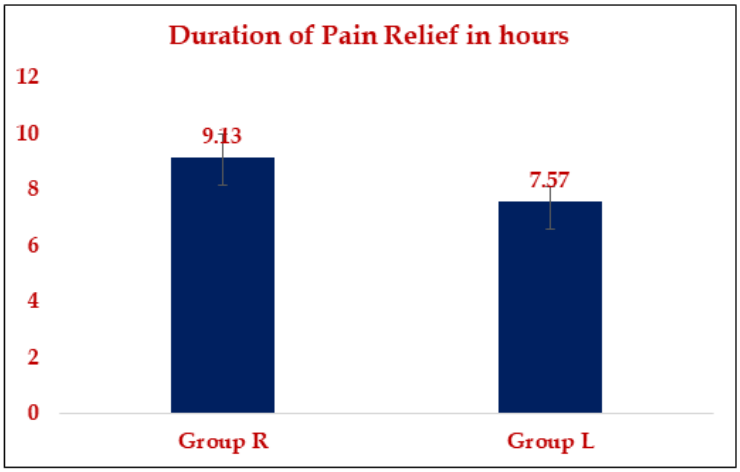

Table 3: Distribution of study subject based on number of rescue analgesics requirement in 24 hours

No. of Rescue analgesics in post-operative 24hrs		Group R (n=30)	Group L (n=30)	Total	Chi Square
0	Frequency	28	20	48	7.111 p<0.01 Highly Significant
	%	93.3%	66.7%	80.0%	
1	Frequency	2	7	9	
	%	6.7%	23.3%	15.0%	
2	Frequency	0	3	3	
	%	0.0%	10.0%	5.0%	
Total	Frequency	30	30	60	
	%	100.0%	100.0%	100.0%	

Figure 3: Distribution of study subjects based on number of rescue analgesics requirement in 24 hours