Original Article

Comparison of the Mean Duration of Analgesia of Intraperitoneal Bupivacaine and Ropivacaine Versus Placebo After Laparoscopic Cholecystectomy

Muhammad Waqid Bin Abdullah[1], Roshan Butt[1], Afzaal Baig[1], Syed Muhammad Talha Bukhari[2] and Zubair Ahmad[1] and Haseeb Ahmad[1]

ABSTRACT

Objective: To compare the mean duration of analgesia of intraperitoneal bupivacaine, ropivacaine and placebo after laparoscopic cholecystectomy.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the department of Surgery, Services Hospital, Lahore from 27th of July 2021 to 26th of January 2022.

Methods: A total of 90 patients above the age of 18 years, undergoing laparoscopic cholecystectomy were included in this study and divided in to 3 equal groups, Group R (Ropivacaine group), Group B (Bupivacaine group) and Group S (Normal saline group) using computer generated randomization. Patients in Group R were administrated 35 ml of 0.375% ropivacaine (131.25 mg), patients in Group B were administrated 35 ml of 0.25% bupivacaine (87.5 mg) while patients in Group S were administrated 35 ml of 0.9% normal saline. The primary outcome was set as the significance of difference in mean duration of analgesia between the groups in the post-operative period.

Results: The Mean±SD of age in this study was 40.71±12.23 years with an age range of 20 to 62 years. The ratio of male gender was higher (71.11%) compared to female gender (28.88%) in overall study population. The overall mean duration of surgery was 31.83±6.13 hours. The results of primary outcome of the study show that mean duration of analgesia in post-operative period was significantly longer in Group R compared to Group B and Group S (13.43±2.04, 7.56±1.81 and 4.13±1.1 respectively, p=0.000).

Conclusion: Intraperitoneal ropivacaine provides longer duration of analgesia compared to bupivacaine and placebo after laparoscopic cholecystectomy.

Key Words: Bupivacaine, Duration of analgesia, Laparoscopic cholecystectomy, Ropivacaine.

Citation of article: Abdullah MW, Butt R, Baig A, Bukhari SMT, Ahmad Z, Ahmad H. Comparison of the Mean Duration of Analgesia of Intraperitoneal Bupivacaine and Ropivacaine Versus Placebo After Laparoscopic Cholecystectomy. Med Forum 2024;35(4):46-50. doi:10.60110/medforum.350410.

INTRODUCTION

Gallstones are the leading cause of gastrointestinal surgeries globally, which cost the healthcare system a lot. Gallstone disease (GD) requires hospitalisation in 11–36% of patients. Genetic and environmental factors include obesity, metabolic disorders, dyslipidemia, fatty liver, lifestyle, gender, drinking, and family history are linked to gallstones.

[1.] Department of Surgery, Services Hospital, Lahore.
[2.] Department of Surgery, PKLI, Lahore.

Correspondence: Muhammad Waqid Bin Abdullah, Consultant Surgeon, Department of Surgery Services Hospital, Lahore.
Contact No: 03338002606
Email: waqidabdullah@gmail.com

Received: January, 2023
Accepted: April, 2023
Printed: April, 2024

Di Ciaula A detailed how cholesterol forms 80% of gallstones.[1] The liver uses laminated lipoproteins to release bile. Micelles are soluble molecules formed by gallbladder vesicle disintegration with bile salts. Their role in fat digestion and absorption is comparable to detergents. Mixed micelles carry cholesterol less efficiently than vesicles, creating supersaturation. Excess cholesterol in bile may crystallise cholesterol monohydrate. Gallstones are caused by hepatic cholesterol production in the form of lecithin and bile salts, gallbladder stasis, and bile concentration.[2] Note that liver fluke outbreaks may explain why brown pigment gallstones are more prevalent in Southeast Asia than in the US.[3]

Physical examinations may distinguish acute cholecystitis from mild biliary colic. Acute cholecystitis produces localised right upper quadrant discomfort, inflammation, and peritoneal abscess.[4]

Laparoscopic (LC) surgery has been the primary GD treatment since 1987. However, rising morbidity made it dubious in the early years. This was owing to severe post-operative discomfort, particularly immediately

after surgery. Neuropathy, inflammation, and incision trauma may accompany laparoscopic surgery. Stretching of the abdominal wall, peritoneal traction, and tissue injury are also related. This minimally invasive method is currently the worldwide gold standard for gall bladder removal and is utilised in over 90% of cholecystectomies. Modern LC offers less post-op discomfort, early healing, shorter hospital stays, and better cosmetic results.

As pain management following surgery is the most critical element of LC, opioids, NSAIDS, N2O, and intraperitoneal local anaesthetics have been suggested to treat it.[5] Common opioid methods are effective analgesics. This effectiveness is dose-dependent and connected to nausea, vomiting, and respiratory depression.Studies indicate that infiltrating local anaesthetics such as lignocaine, bupivacaine, ropivacaine, and levobupivacaine with multimodal analgesics has more analgesic benefits than other approaches for post-op pain reduction.[5,7,8] This strong analgesic speeds healing and reduces hospital stays.[9]

However, studies demonstrate that intraperitoneal spray of local anaesthetics does not reduce post-op discomfort or adverse outcomes in LC surgical operations as well as other methods.[10]

Long-acting amide group local anaesthetic ropivacaine prevents the splanchnic nerve from delivering pain signals to the central nervous system, lowering visceral discomfort during surgery. Ropivacaine is safe and effective for abdominal spraying after laparoscopic surgery and infiltration of local incisions. Infiltration with ropivacaine has been shown to reduce post-op discomfort in recent studies. Adjuvants prolong anaesthesia and enhance analgesia.[11]

As mentioned above, LC surgery is the most recommended technique for GD, and post-op pain relief is crucial to reducing morbidity and ensuring success. Our local health care facilities utilise various medications and procedures to reduce post-op discomfort. International literature compares ropivacaine to other local anaesthetics, but local data is few. Thus, we aimed to examine the mean duration of intraperitoneal bupivacaine, ropivacaine, and placebo following LC cholecystectomy in our local population. This research will contribute to local data and assist surgeons choose better post-op pain treatment choices for LC cholecystectomy patients.

METHODS

The Department of Surgery, Services Hospital, Lahore conducted this 6-month randomised control trial from July 27, 2021 to January 26, 2022. The sample size was calculated using these assumptions: The ropivacaine group had a post-op analgesic duration of 13.47±1.38 hours, whereas the placebo group had 4.47±0.86 hours (confidence interval=95%, Power=90%).[12] The sample size was 90 patients, 30 per group. This research randomly assigned 90 patients over 18 years old having LC cholecystectomy to three equal groups, Group R (Ropivacaine), Group B (Bupivacaine), and Group S (Normal saline).Patients with VAS pain >3, right hypochondrium discomfort, and pericholecystic edoema underwent LC cholecystectomy. The diagnosis was radiologically confirmed.Group R got 35 ml of 0.375% ropivacaine (131.25 mg), Group B 0.25% bupivacaine (87.5 mg), and Group S 0.9% normal saline.

Patients with common bile duct (CBD) stones, dilated CBD, acute cholecystitis, bile duct exploration, T-drain insertion, or surgical complications were excluded. The research also excluded gall bladder cancer and amide local anaesthetic sensitivity individuals. After gall bladder removal, hemostasis was performed and all fluids, blood, and CO2 were sucked. It was then time for intraperitoneal instillation onto subdiaphragmatic suprahepatic and gallbladder fossa surfaces. The liver surface (20 ml) and gallbladder fossa (5 ml) received the drug. The patient remained in the right lateral trendelenberg position for 10–15 minutes. The remaining 10 ml of medication solution was infiltrated at the port.Each patient received 1.5 mg/kg diclofenac and 15 mg/kg paracetamol intravenously before extubation. The surgeon performed the operations with at least five years of expertise. Each patient's demographics and medical history were collected.Each patient in all 3 groups had analgesia duration determined.

Visual Analogue Scale measured pain. From patient transfer to rescue analgesia for post-op discomfort (VAS >3), analgesia duration was documented. The main result was the significance of mean analgesic duration in intraperitoneal bupivacaine, ropivacaine, and placebo groups following LC cholecystectomy. Before starting the trial, the hospital's ethics committee approved it. Patients were informed of the research purpose and gave signed permission. Data was analysed using SPSS 25. Quantitative factors were reported as Mean±SD, whereas qualitative variables were presented as frequency and percentage. A one-way ANOVA test was used to determine the significance of differences between study groups, with p-value < 0.05 being significant.

RESULTS

The Mean±SD of age in this study was 40.71±12.23 years with an age range of 20 to 62 years. The number of male gender was 64 (71.11%) while female gender was 26 (28.88%) in overall study population. The overall mean duration of surgery was 31.83±6.13 hours. The group wise details of demographics and clinical history is shown in Table-I.

Table No. 1: Demographic and clinical history n=90

Demographic and clinical history		Group R n=30	Group B n=30	Group S n=30
Age (Mean±SD) years		41.6±13.03	40.8±11.62	39.73±12.35
Gender	Male n (%)	21 (70)	20 (66.66)	23 (76.66)
	Female n (%)	9 (30)	10 (33.33)	7 (23.33)
BMI≥30 n (%)		13 (43.33)	12 (40	14 (46.66)
Diabetes mellitus n (%)		14 (46.66)	12 (40)	11 (36.66)
History of cholelithiasis (Mean±SD) months		6.2±2.41	5.73 ±2.27	6.93±1.89
Duration of surgery (Mean±SD) min		32.53±6.71	31.36±5.81	30.93±7.63

The results of primary outcome of the study show that mean duration of analgesia (time needed for the first dose of rescue analgesia) was significantly higher in Group R compared to Group B and Group S as shown in Table-2.

Table No. 2: Mean duration of analgesia in the post-op period

n=90

Primary outcomes	Group R n=30	Group B n=30	Group S n=30	p-value
Duration of analgesia (Mean±SD) hours	13.43± 2.04	7.56± 1.81	4.13± 1.1	0.000

DISCUSSION

Less invasive surgical techniques like LC are being employed more frequently in recent years with positive results. Nonetheless, some patients experience complaints of shoulder and abdominal pain after laparoscopic surgery, which delay their recovery and hospital departure. Furthermore, postoperative discomfort may develop into chronic pain if it is not appropriately managed. Opioids are used to treat pain, but they have specific adverse effects that can impede healing. Therefore, to reduce postoperative pain during laparoscopic surgery, laparoscopic surgeons are now interested in exploring intraperitoneal administration of local anesthetic.[13]

In a study conducted by Ahmed A and Ahmed M in health care centers of Pakistan where health facilities were at lower levels, the post-op analgesic efficacy of intraperitoneal administration of ropivacaine 0.5% (dosage of 2 mg/kg) was compared with the standard procedure of analgesia routinely used in open cholecystectomy in that hospital. The results of this study showed significantly lesser pain in ropivacaine group compared to the control group at 1, 6 and 24 hours post operatively (p-value<0.05). There were also significantly lesser rate of adverse events in the study group compared to controlled group (38% Vs 62%, p-value<0.05).[14]

Mannan A et al planned a randomized controlled trial to determine the analgesic efficacy of intraperitoneal bupivacaine use in patients undergoing LC cholecystectomy. The results favored the intraperitoneal use of bupivacaine due to its prolonged analgesic effect in shape of both longer time to need rescue analgesic (16.53 ±2.65 Vs 0.99 ±0.51 hours, p<0.001) and amount of rescue analgesic used (31.00±14.98 mg Vs 124.80 ±26.68 mg tramadol, p<0.001) in the bupivacaine group compared to placebo group.[15]

Das NT compared intraperitoneal infiltration of ropivacaine (0.375%), bupivacaine (0.25%) and placebo in terms of relieving the post-op pain in LC cholecystectomy. This study showed a mean duration of analgesia with ropivacaine as 13.47+1.38 hours, with bupivacaine as 7.93+1.44 hours and with placebo as 4.47+0.86 hours. The study therefore concluded that ropivacaine is significantly more effective than bupivacaine and placebo in providing long term analgesia in post-op period.[12]

Shan R conducted a randomized controlled study to determine the decrease in post-op pain and time to need for rescue analgesia with intraperitoneal induction of ropivacaine (0.5%) compared to bupivacaine (0.5%) while carrying out LC cholecystectomy. The results showed that the pain score on VAS was lesser in the ropivacaine group compared to bupivacaine group. Similarly time to need for rescue analgesic was also longer in patients where ropivacaine was used. The study concluded that intraperitoneal administration of ropivacaine is more efficient mean of managing postoperative pain and it offers a prolonged analgesia.[15]

Shrey S compared the intraperitoneal administration of ropivacaine (0.75%) and bupivacaine (0.5%) for their post-op analgesic efficacy after LC cholecystectomy. The pain score in these two study groups was calculated on VAS which showed that the patients in the ropivacaine group had significantly longer period to need the rescue analgesia compared to patients in bupivacaine group (295.38 ± 74.15 Vs 148.04 ± 53.47, p= 0.0001). The study also reported that in ropivacaine group, 56.6% patients didn't need the rescue analgesia during the study while this was true for 26.6% of the patients in the bupivacaine group (p=0.019). There was lesser score assessed on VAS in ropivacaine compared to bupivacaine group at the post-op follow up time for pain assessment at 8 hours (p= 0.032). The researcher concluded that ropivacaine is a better intraperitoneal option than bupivacaine for managing postoperative

pain because it lasts longer, offers better quality analgesia up to 8 hours postoperatively, requires less rescue analgesic during the postoperative period, and has fewer adverse effects.[16]

The Mean±SD of age in our study was 40.71±12.23 years with an age range of 20 to 62 years. The number of male gender was 64 (71.11%) while female gender was 26 (28.88%) in overall study population. The overall mean duration of surgery was 31.83±6.13 hours. The results of primary outcome of the study show that mean duration of analgesia (time needed for the first dose of rescue analgesia) in post-op period was significantly longer in Group R compared to Group B and Group S (13.43±2.04, 7.56±1.81 and 4.13±1.1 respectively, p=0.000). Hence these results prove that intraperitoneal use of amide local anesthetics is useful in lowering the post-op pain in patients undergoing laparoscopic cholecystectomy. Moreover, these results also show that intraperitoneal ropivacaine is significantly more effective in providing prolonged analgesic effects in these patients as compared to bupivacaine and placebo. These results are in line with the studies discussed earlier and therefore adds useful data on this subject.[12-17]

The major limitation of our study is the small sample size. Moreover, we worked only on one parameter of post-op outcomes. Future studies with larger sample size and more parameters contributing in the successful surgical procedure will add up to this useful data for laparoscopic surgeons working in our local health care set ups.

CONCLUSION

The study concludes that intraperitoneal ropivacaine provides longer duration of analgesia compared to bupivacaine and placebo after laparoscopic cholecystectomy. The use of ropivacaine will be helpful in our local surgical practices in improving the outcomes thereby contributing to successful surgical procedures.

Acknowledgments: The assistance of paramedic staff during procedures and helping in maintaining the patient's data is acknowledged.

Author's Contribution:

Concept & Design of Study:	Muhammad Waqid Bin Abdullah
Drafting:	Roshan Butt, Afzaal Baig
Data Analysis:	Syed Muhammad Talha Bukhari, Zubair Ahmad, Haseeb Ahmad
Revisiting Critically:	Muhammad Waqid Bin Abdullah, Roshan Butt
Final Approval of version:	Muhammad Waqid Bin Abdullah

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None

Ethical Approval: No. ERB/430/1023/SIM dated 05.03.2021

REFERENCES

1. Di Ciaula A, Portincasa P. Recent advances in understanding and managing cholesterol gallstones. F1000 Res 2018;7:F1000 Faculty Rev-1529.
2. Macierzanka A, Torcello-Gómez A, Jungnickel C, Maldonado-Valderrama J. Bile salts in digestion and transport of lipids. Adv Colloid Interface Sci 2019;274:102045.
3. Saijuntha W, Sithithaworn P, Kiatsopit N, Andrews RH, Petney TN. Liver Flukes: Clonorchis and Opisthorchis. Adv Exp Med Biol 2019;1154:139-180.
4. Nguyen CL, van Dijk A, Smith G, Leibman S, Mittal A, Albania M, et al. Acute cholecystitis or simple biliary colic after an emergency presentation: why it matters. ANZ J Surg 2020;90(3):295-9.
5. Akhtar MS, Khan N, Qayyum A, Khan SZ. Cost difference of enhanced recovery after surgery pathway vs. Conventional care In Elective Laparoscopic Cholecystectomy. J Ayub Med Coll Abbottabad 2020;32(4):470-475.
6. Wennmacker SZ, Dijkgraaf MGW, Westert GP, Drenth JPH, van Laarhoven CJHM, de Reuver PR. Persistent abdominal pain after laparoscopic cholecystectomy is associated with increased healthcare consumption and sick leave. Surg 2018;163(4):661-666.
7. Bougie O, Blom J, Zhou G, Murji A, Thurston J. Use and misuse of opioid after gynecologic surgery. Best Pract Res Clin Obstet Gynaecol 2022;85(Pt B):23-34.
8. Siriwardana RC, Kumarage SK, Gunathilake BM, Thilakarathne SB, Wijesinghe JS. Local infiltration versus laparoscopic-guided transverse abdominis plane block in laparoscopic cholecystectomy: double-blinded randomized control trial. Surg Endosc 2019;33(1):179-183.
9. Ergin A, Aydin MT, Çiyiltepe H, Karip AB, Fersahoğlu MM, Özcabi Y, et al. Effectiveness of local anesthetic application methods in postoperative pain control in laparoscopic cholecystectomies; a randomised controlled trial. Int J Surg 2021;95:106134.
10. Yong L, Guang B. Intraperitoneal ropivacaine instillation versus no intraperitoneal ropivacaine instillation for laparoscopic cholecystectomy: A systematic review and meta-analysis. Int J Surg 2017;44:229-243.

11. Athanasiou S, Hadzillia S, Pitsouni E, Kastanias S, Douskos A, Valsamidis D, et al. Intraoperative local infiltration with ropivacaine 0.5% in women undergoing vaginal hysterectomy and pelvic floor repair: Randomized double-blind placebo-controlled trial. Eur J Obstet Gynecol Reprod Biol 2019;236:154-159.
12. Das NT, Deshpande C. Effects of Intraperitoneal Local Anaesthetics Bupivacaine and Ropivacaine versus Placebo on Postoperative Pain after Laparoscopic Cholecystectomy: A Randomised Double Blind Study. J Clin Diagn Res 2017; 11(7):UC08-UC12.
13. Govil N, Kumar P. Intraperitoneal Levobupivacaine with or without Clonidine for Pain Relief after Laparoscopic Cholecystectomy: A Randomized, Double-blind, Placebo-controlled Trial. Anesth Essays Res 2017;11(1):125-128.
14. Ahmed A, Ahmed M. Intraperitoneal infiltration of ropivacaine for post-operative analgesia in open cholecystectomy. Pak Armed Forces Med J 2017;67(6):1038-43.
15. Manan A, Khan AA, Ahmad I, Usman M, Jamil T, Sajid MA. Intraperitoneal bupivacaine as post-laparoscopic cholecystectomy analgesia. J Coll Physicians Surg Pak 2020;30(1):9-12.
16. 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(2):377-380.
17. Shrey S, Singam A, Latwal BS, et al. A comparative study of intraperitoneal ropivacaine and bupivacaine for postoperative analgesia in laparoscopic cholecystectomy. J Evolution Med Dent Sci 2020;9(04):200-205.