

Assessment of Low Concentration and High Volume Intraperitoneal Bupivacaine in Producing Analgesia Following Laparoscopic Cholecystectomy

Assessment of
Intraperitoneal
Bupivacaine in
Analgesia
Following
Laparoscopic
Cholecystectomy

Shabbir Ahmed, Muhammad Fazal ur Rehman and Movahid Anwer

ABSTRACT

Objective: To assess low-concentration and high volume intraperitoneal bupivacaine in producing analgesia following laparoscopic cholecystectomy.

Study Design: A prospective randomized controlled trial.

Place and Duration of Study: This study was conducted at the Department of General Surgery at Bakhtawar Amin Hospital and Medical College, Multan from March 2018 to July 2018.

Materials and Methods: All 110 patients were distributed into two equal groups. Peritoneal cavity was irrigated with a mixture of 480ml normal saline and 20ml of 0.5% bupivacaine in group-B and with 500ml normal saline in group-S. Analgesia duration, total analgesic requirement in first 24 hours and NRS score recorded at extubation, 30 minutes, 1, 3, 6, 12 and 24 hour postoperatively, were compared. Data was put in SPSS v.23 and compared with independent t-test and Chi square test, as applicable. $P \leq 0.05$ was considered statistically significant.

Results: Age, weight, gender distribution, surgery duration, propofol requirement and MAC of isoflurane were not significantly different ($p > 0.05$). The duration of analgesia was 17.64 ± 3.54 hours in group-B and 0.83 ± 0.49 hours in group-S ($p < 0.001$). Total tramadol requirement within postoperative 24 hours was significantly more in group-S ($p < 0.001$). The NRS score was significantly better in group-B at extubation, 30 minutes, 1, 3, 6 hours ($p < 0.05$) while at 12 and 24 hours, the difference was not statistically significant ($p > 0.05$).

Conclusion: Bupivacaine in low concentration and high volumes is significantly effective in prolonging analgesia duration and improving NRS score after LC.

Key Words: bupivacaine, postoperative analgesia, laparoscopic cholecystectomy (LC).

Citation of article: Ahmed S, Rehman MF, Anwer M. Assessment of Low Concentration and High Volume Intraperitoneal Bupivacaine in Producing Analgesia Following Laparoscopic Cholecystectomy. Med Forum 2019;30(3):100-104.

INTRODUCTION

For the treatment of benign diseases of gall bladder, laparoscopic cholecystectomy has become an ideal procedure. This procedure is associated with shorter hospital stay and reduced postoperative pain as compared to the conventional method¹⁻³. However, pain is still a major complaint after LC with first 24 hours postoperatively^{4, 5}. Variety of analgesics and opioids have been tried to decrease the pain following LC. The success rate of these drugs have been variable so far.

Department of Surgery, Bakhtawar Amin Hospital and Medical College, Multan.

Correspondence: Dr. Shabbir Ahmed, Assistant Professor of Surgery, Bakhtawar Amin Hospital and Medical College, Multan.

Contact No: 0333-6058036

Email: shabbirahmad2011@hotmail.com

Received: September, 2018

Accepted: February, 2019

Printed: March, 2019

In conventional approach, the pain is parietal in origin while in LC, the pain is of variety of origins such as incisional pain (somatic pain), shoulder pain (visceral pain due to irritation of phrenic nerve) and deep intra-abdominal pain (visceral pain)^{6,7}. Pain is the chief cause in 17-41% of the patients undergoing laparoscopic cholecystectomy for overnight stay at the hospital and the major reason for prolonged rehabilitation in these patients⁸.

As the postoperative pain for laparoscopic cholecystectomy is very complex, multi modal treatment approach is suggested by the specialists. Empathy building with the patients, explanation of the procedure and its complications to the patients, making the patients feel confident and administration of NSAIDs before the procedure are the modalities included in the comprehensive treatment approach for the treatment of post laparoscopic cholecystectomy approach. Administration of peri operative opioids, infiltration of local anesthetics and irrigation of the peritoneal cavity with the local anesthetics are some other modes of action for the treatment of pain. However, provision of effective analgesia following laparoscopic cholecystectomy still remains a challenge.

For postoperative analgesia after laparoscopic cholecystectomy, instillation of various local anesthetic agents in peritoneal cavity has become popular recently. Low volume (20 cc in 100 cc normal saline) and high concentration (0.5% - 0.125%) of bupivacaine has been used in some studies but the duration of their analgesia lasted only for few hours postoperatively⁹⁻¹². In another study, high volume (20 cc in 500 cc normal saline) and low concentration (0.02%) of bupivacaine was used for irrigating the peritoneal cavity after laparoscopic cholecystectomy and their results were promising in producing prolonged and more effective analgesia¹³. The reason behind that might be that larger volumes are able to irrigate large sub hepatic areas and can produce more effective analgesia.

Data regarding the efficacy of low concentration and high volume of bupivacaine for irrigating the peritoneal cavity after laparoscopic cholecystectomy and producing effective analgesia is not sufficient. We planned to conduct this study on a relatively larger population to get better and more precise results about the efficacy of irrigation of peritoneal cavity with large volumes of diluted bupivacaine following laparoscopic cholecystectomy in producing postoperative analgesia..

MATERIALS AND METHODS

After getting approved from the hospital ethics committee, this prospective randomized controlled trial was carried out in the Department of General Surgery at Bakhtawar Amin Hospital and Medical College, Multan, from March 2018 to July 2018. The study by Jain S et al.¹³ was taken as reference and sample size was calculated. With non-probability consecutive sampling technique, we selected 110 patients of American Society of Anesthesiologists physical status I or II and age being between 18 – 60 years. All these patients were planned for elective cholecystectomy under general anesthesia. All the patients who were pregnant, diagnosed cases of acute pancreatitis or choledocholithiasis, currently using opioids, had chronic pain or allergy to local anesthetics, and required conversion of laparoscopic cholecystectomy to open cholecystectomy were not involved in our study.

All the patients were randomly assigned into two groups with equal number of patients, after taking written informed consent. Numeric pain rating scale (0 = no pain and 10 = extremely severe pain) was explained to all the patients. All the patients were kept nil per oral for minimum eight hours prior to surgery. Premedication was done 0.025 mg /kg midazolam, 2 µg /kg fentanyl and 0.1 mg /kg ondansetron and all these drugs were given intravenously. Propofol 2 mg/kg was given intravenously to induce general anesthesia. Vecuronium 0.1 mg/kg was given by intravenous route to achieve muscle relaxation and endotracheal intubation was done. Isoflurane 0.8 to 1% in a mixture of air and nitrous oxide was used to sustain anesthesia.

During surgery, intra-abdominal pressure was maintained below 12mmHg. Heart rate and mean arterial pressure were logged at 5 minutes interval. During surgery, analgesia was achieved with 1.5 mg/kg intravenous diclofenac sodium and no further analgesics were administered during the procedure. Post operatively, 1.5 mg/kg intravenous diclofenac sodium was given at 8 hours and then at 16 hours. All the patient were randomly distributed into two groups. Each group consisted of 55 patients. In Group B, a mixture of 480 ml normal saline and 20 ml of 0.5% bupivacaine was used for irrigation of peritoneal cavity, while in group S, we used 500 cc of normal saline to irrigate the peritoneal cavity. The irrigation fluids were used during the dissection of gall bladder and were then aspirated after the completion of dissection. Some of the irrigation fluid was used to irrigate the surgical bed and the peritoneal cavity after the extraction of the gall bladder. For facilitation of dispersing the drugs to the sub hepatic area, patients were placed in Trendelenburg's position with right lateral tilt for a minimum of five minutes. Irrigation was performed with the help of subcostal trocar under direct laparoscopic control. After this, irrigation fluid was aspirated. All the surgical ports were closed after placing the drain in sub hepatic area. The inhalational anesthetics i.e. nitrous oxide and isoflurane were stopped and 0.04 mg/kg neostigmine along with 0.01 mg/kg glycopyrrolate was given intravenously for the reversal of neuromuscular blockade. Patients were extubated when the sufficient muscle power had returned. After awakening of the patient and observing the verbal response, patients were moved to PACU. Rescue analgesia was provided with intravenous injection mg 2 mg/kg tramadol according to the patients' requirement. The time for first rescue analgesic administration was noted and was noted as duration of analgesia. Numeric rating scale score was recorded by postoperative nursing staff at 30 minutes, 1 hour, 3 hour, 6 hour, 12 hour and 24 hour postoperatively. NRS ≥ 4 was the criteria for administering the analgesics.

The primary objective of the study to compare the analgesia duration between the groups. Secondary objective included the comparison of total analgesic requirement in first 24 postoperative hours and NRS score recorded at various intervals. All the data was collected on a performa by the researchers themselves. The data was put in SPSS version 23 and compared. Continuous data was compared with independent t-test and Chi square test was applied on nominal data. $P \leq 0.05$ was considered to be significant, statistically.

RESULTS

Mean age of the patients was 42.96 ± 10.85 years and 43.61 ± 10.06 years in group B and S, respectively ($p = 0.750$). Mean weight of the patients was 58.01 ± 8.29

kg and 54.62 ± 9.64 kg in group B and S, respectively ($p = 0.051$). Out of 55 patients, 17 were males in group B and 26 were males in group S ($p = 0.079$). The duration of surgery was 60.76 ± 5.29 minutes in group S and 59.45 ± 5.57 minutes in group B ($p = 0.209$). Propofol requirement and MAC of isoflurane were 107.53 ± 2.32 mg and 0.91 ± 0.03 in group B; and 107.09 ± 1.89 mg and 0.92 ± 0.02 in group S (p -value 0.283 and 0.204), respectively. Table-I

Table No.I: Baseline and operative data.

Variable	Group B (n=55)	Group S (n=55)	P value
Age, years	42.96 ± 10.85	43.61 ± 10.06	0.750
Weight, kg	58.01 ± 8.29	54.62 ± 9.64	0.051
Gender (male / female)	17 / 38	26 / 29	0.079
Surgery duration, min	59.45 ± 5.57	60.76 ± 5.29	0.209
Propofol requirement, mg	107.53 ± 2.32	107.09 ± 1.89	0.283
MAC of isoflurane	0.91 ± 0.03	0.92 ± 0.02	0.204

Data is mentioned as mean $\pm$ standard deviation or Ratio.

Table No.2: Outcome Data

Variable	Group B (n=55)	Group S (n=55)	P value
Analgesia duration, hours	17.64 ± 3.54	0.83 ± 0.49	<0.001
Total tramadol requirement within 24 hours, mg	29.82 ± 14.33	122.38 ± 23.54	<0.001
Numeric Pain Rating Scale Score			
At extubation	0.73 ± 0.33	4.86 ± 0.71	<0.001
30 min	1.06 ± 0.49	2.39 ± 0.98	<0.001
1 hour	1.34 ± 0.41	1.67 ± 0.75	0.005
3 hour	2.12 ± 0.68	2.53 ± 1.13	0.023
6 hour	1.77 ± 0.41	2.08 ± 0.76	0.011
12 hour	2.14 ± 0.92	2.36 ± 1.08	0.254
24 hour	2.03 ± 0.71	2.10 ± 0.74	0.624

Data is mentioned as mean $\pm$ standard deviation.

The duration of analgesia was 17.64 ± 3.54 hours in group B and 0.83 ± 0.49 hours in group S ($p < 0.001$). Total tramadol requirement in the first 24 hours was 29.82 ± 14.33 mg and 122.38 ± 23.54 mg in group B

and S, respectively ($p < 0.001$). The NRS score in group B and S was 0.73 ± 0.33 and 4.86 ± 0.71 at extubation ($p < 0.001$); 1.06 ± 0.49 and 2.39 ± 0.98 at 30 minutes ($p < 0.001$); 1.34 ± 0.41 and 1.67 ± 0.75 at 1 hour ($p = 0.005$); 2.12 ± 0.68 and 2.53 ± 1.13 at 3 hours ($p = 0.023$); 1.77 ± 0.41 and 2.08 ± 0.76 at 6 hours ($p = 0.011$); 2.14 ± 0.92 and 2.36 ± 1.08 at 12 hours ($p = 0.254$); and 2.03 ± 0.71 and 2.10 ± 0.74 at 24 hours ($p = 0.624$). Table-2

DISCUSSION

We observed in our study that irrigation of peritoneal cavity with low concentration high volume bupivacaine is effective in reducing postoperative pain, decreasing postoperative opioid analgesic need and prolonging the duration of analgesia. Postoperative pain a complex and can be managed with multimodal approach in which opioids consumption is less and recovery is fast^{14,15}. We gave diclofenac sodium and fentanyl to the patients in perioperative period along with irrigation of peritoneal cavity with bupivacaine in group B. Parietal pain can be treated with diclofenac sodium while bupivacaine is effective in visceral pain. Bupivacaine belongs to amide group of local anesthetics and is known for prolongation of analgesia¹⁶. The researchers who instilled highly concentrated low volume bupivacaine in the bed of gall bladder found it to be ineffective in producing sufficient analgesia¹⁷⁻¹⁹ as compared to short acting analgesics⁹⁻¹².

Cochrane review concluded that instillation of local anesthetics into the peritoneal can is not an effective method in producing post LC analgesia²⁰. This could be due to the use of small volumes of the local anesthetics which was unable to cover most of the intraperitoneal area. We used large volumes of diluted bupivacaine in our research which was effective in prolonging the time of analgesia and similar results were observed by Gupta PK et al.²¹ and Jain S et al.¹³. Nunez et al.²² observed large volumes of diluted levobupivacaine to be more effective than small volume of highly concentrated levobupivacaine in producing brachial plexus block. NRS score was found to be significantly better in group B, in our study. Tramadol requirement in postoperative period was considerably greater in group S than in group B.

Boddy et al.²³ and Gupta A et al.²⁴ did not find any substantial difference in analgesics requirement even after irrigating the peritoneal cavity with bupivacaine. However, the volumes of bupivacaine used in various studies included in above mentioned reviews were 10 ml to 200 ml with 0.1% to 0.5% concentration in contrast to our study where we used 500 ml with low concentrations. According to some studies, shoulder pain is reduced after irrigating the peritoneal cavity with bupivacaine²⁵ while some did not observe any promising results²⁶. We maintained intraperitoneal pressure below 12 mmHg and it is known to

significantly reduce postoperative shoulder pain following laparoscopic cholecystectomy²⁷. As far as the frequency of nausea and vomiting is concerned, we found no significant difference. Preoperative administration of ondansetron can be a noteworthy cause of similar occurrence of nausea and vomiting²⁸. Yari M et al²⁹ demonstrated in their study that there is no effect of instilling bupivacaine in peritoneal cavity on the frequency of nausea and vomiting.

CONCLUSION

Bupivacaine in low concentration and high volumes is significantly effective in prolonging the analgesia duration and improving NRS score in the patients who underwent laparoscopic cholecystectomy.

Author's Contribution:

Concept & Design of Study: Shabbir Ahmed
 Drafting: Muhammad Fazal ur Rehman
 Data Analysis: Movahid Anwer
 Revisiting Critically: Shabbir Ahmed, Muhammad Fazal ur Rehman
 Final Approval of version: Shabbir Ahmed

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

REFERENCES

- Gurusamy K, Junnarkar S, Farouk M, Davidson BR. Meta-analysis of randomized controlled trials on the safety and effectiveness of day-case laparoscopic cholecystectomy. *Brit J Surg* 2008;95(2):161-8.
- Xu B, Xu B, Zheng WY, Ge HY, Wang LW, Song ZS, He B. Transvaginal cholecystectomy vs conventional laparoscopic cholecystectomy for gallbladder disease: A meta-analysis. *World J Gastroenterol* 2015;21(17):5393.
- Buglass H. Open and laparoscopic cholecystectomy. *Handbook of Clinical Anaesthesia* E 2011;3:451.
- Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. *Eur J Surg* 2001;167(2):84-96.
- Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Factors determining convalescence after uncomplicated laparoscopic cholecystectomy. *Arch Surg* 2001;136(8):917-21.
- Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. *Pain* 2001;90(3):261-9.
- Bisgaard T. Analgesic Treatment after Laparoscopic Cholecystectomy A Critical Assessment of the Evidence. *Anesthesiol* 2006;104(4):835-46.
- 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%. *Surgical Endosc* 2005;19(11):1503-6.
- Yeh CN, Tsai CY, Cheng CT, Wang SY, Liu YY, Chiang KC, Hsieh FJ, Lin CC, Jan YY, Chen MF. Pain relief from combined wound and intraperitoneal local anesthesia for patients who undergo laparoscopic cholecystectomy. *BMC Surg* 2014;14(1):28.
- Yang SY, Kang H, Choi GJ, Shin HY, Baek CW, Jung YH, Choi YS. Efficacy of intraperitoneal and intravenous lidocaine on pain relief after laparoscopic cholecystectomy. *J Int Med Res* 2014;42(2):307-19.
- Choi GJ, Kang H, Baek CW, Jung YH, Kim DR. Effect of intraperitoneal local anesthetic on pain characteristics after laparoscopic cholecystectomy. *World J Gastroenterol* 2015;21(47):13386.
- Castillo-Garza G, Díaz-Elizondo JA, Cuello-García CA, Villegas-Cabello O. Irrigation with bupivacaine at the surgical bed for postoperative pain relief after laparoscopic cholecystectomy. *JSLs* 2012;16(1):105.
- Jain S, Nazir N, Singh S, Sharma S. A prospective randomised controlled study for evaluation of high-volume low-concentration intraperitoneal bupivacaine for post-laparoscopic cholecystectomy analgesia. *Ind J Anaesth* 2018;62(2):109.
- Kehlet H. Postoperative Opioid sparing to hasten RecoveryWhat are the issues? *Anesthesiol* 2005;102(6):1083-5.
- Marret E, Kurdi O, Zufferey P, Bonnet F. Effects of Nonsteroidal Antiinflammatory Drugs on Patient-controlled Analgesia Morphine Side EffectsMeta-analysis of Randomized Controlled Trials. *Anesthesiol* 2005;102(6):1249-60.
- Gencer ZK, Özkiriş M, Gencer M, Saydam L. Comparison of ropivacaine, bupivacaine, prilocaine, and lidocaine in the management of pain and hemorrhage during nasal pack removal. *Am J Rhinol Allerg* 2013;27(5):423-5.
- Elfberg BÅ, Sjövall-Mjöberg S. Intraperitoneal bupivacaine does not effectively reduce pain after laparoscopic cholecystectomy: a randomized, placebo-controlled and double-blind study. *Surg Laparo Endo Per* 2000;10(6):357-9.
- Zmora O, Stolik-Dollberg O, Bar-Zakai B, Rosin D, Kuriansky J, Shabtai M, et al. Intraperitoneal bupivacaine does not attenuate pain following laparoscopic cholecystectomy. *JSLs* 2000;4(4):301.

19. Jiranantar V, Rushatamukayanunt W, Lert-Akyamane N, Sirijearanai R, Piromrat I, Suwannanonda P, Muangkasem J. Analgesic effect of intraperitoneal instillation of bupivacaine for postoperative laparoscopic cholecystectomy. *J Med Assoc Thai* 2002;85:S897-903.
20. Gurusamy KS, Vaughan J, Toon CD, Davidson BR. Pharmacological interventions for prevention or treatment of postoperative pain in people undergoing laparoscopic cholecystectomy. *Cochrane DB Syst Rev* 2014(3).
21. Gupta PK, Hopkins PM. Effect of concentration of local anaesthetic solution on the ED50 of bupivacaine for supraclavicular brachial plexus block. *Brit J Anaesth* 2013;111(2):293-6.
22. Nuñez DA, López SA, Salamanca MM, Janeiro MA, Fernandez RF, Cobian JL. Brachial plexus block with levobupivacaine at the humeral canal: comparison of a small volume at high concentration with a large volume at low concentration. *Rev Esp Anesthesiol Reanim* 2005;52(9):529-35.
23. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anesthesia in laparoscopic cholecystectomy: a systematic review and meta-analysis. *Anesth Analg* 2006;103(3):682-8.
24. Gupta A. Local anaesthesia for pain relief after laparoscopic cholecystectomy-a systematic review. *Best Pract Res Clin Anaesthesiol* 2005;19(2):275-92.
25. Elhakim M, Elkott M, Ali NM, Tahoun HM. Intraperitoneal lidocaine for postoperative pain after laparoscopy. *Acta Anaesthesiol Scand* 2000;44(3):280-4.
26. Alam MS, Hoque HW, Saifullah M, Ali MO. Port site and intraperitoneal infiltration of local anesthetics in reduction of postoperative pain after laparoscopic cholecystectomy. *Medicine Today* 2009;22(1):24-8.
27. Barczyński M, Herman RM. A prospective randomized trial on comparison of low-pressure (LP) and standard-pressure (SP) pneumoperitoneum for laparoscopic cholecystectomy. *Surg Endosc* 2003;17(4):533-8.
28. Paventi S, Santevecchi A, Ranieri R. Efficacy of a single-dose ondansetron for preventing postoperative nausea and vomiting after laparoscopic cholecystectomy with sevoflurane and remifentanyl infusion anaesthesia. *Eur Rev Med Pharmacol Sci* 2001;5:59-64.
29. Yari M, Rooshani B, Golfam P, Nazari N. Intraperitoneal bupivacaine effect on postoperative nausea and vomiting following laparoscopic cholecystectomy. *Anesthesiol Pain Med* 2014;4(3).