Original Article

COMPARISON OF INTRAPERITONEAL BUPIVACAINE WITH INTRAVENOUS TRAMADOL HYDROCHLORIDE FOR POSTOPERATIVE PAIN RELIEF AFTER LAPAROSCOPIC CHOLECYSTECTOMY

Gohar latif Kalas[a], Fahad Hafeez Khan[b], Kamran Hakeem Khan[c], Nadeem Malik[d], Ishtiaq Anwar[e]
[a]Senior Registrar (SR), DHQ Teaching Hospital Mirpur, Azad Jamu Kashmir
[b]Medical Officer, DHQ Hospital Timergara
[c]Junior Registrar, General surgery, Nowshehra Medical College, Nowshehra
[d]CMO, Holy Family Hospital, Rawalpindi
[e]Research officer , Edo Eye Hospital

ABSTRACT:

OBJECTIVE: To determine the efficacy of intraperitoneal bupivacaine in post operative pain relief following cholecystectomy in comparison with intravenous tramadol.
STUDY DESIGN: Randomized Controlled Trial (RCT)
PLACE & DURATION OF STUDY: Study was conducted at surgery department in PIMS, Islamabad for duration of 8 months (June 2015 to January 2016).
PATIENTS AND METHODS: A sample size of 272 patients was calculated. Non probability consecutive sampling is used for patient selection. Patients were divided into two equal groups. Group A (IV tramadol group) was a control group while Group B (intraperitoneal bupivacaine group) was studied group. Study outcome was measured in terms of pain relief one hour after surgery, time of first rescue analgesic injection, number of rescue analgesic injections and time of mobilization.
RESULTS: Demographic characteristics were not significantly different between both groups. Mean VAS for pain relief at 1 hour following surgery was found to be 4.4 ±1.7 SD in control group A while 3.5 ±1.71 SD ($P<0.05$) in study group. Statistically significant ($P<0.05$) difference was found among both groups in mean time of first rescue injection (2.3 hours ±0.86SD VS 3.6 hours ±1.33SD), mean number of rescue injections (1.5 ±0.7SD VS 0.9 ±0.57 SD) and mean mobilization time (3.5 hours ±1.3SD VS 2.2 hours ±0.85SD).
CONCLUSIONS: Intraperitoneal bupivacaine is an effective treatment option for controlling postoperative pain and other associated morbidities following LC.
KEY WORDS: Laparoscopic cholecystectomy, Cholelithiasis, Gallstones, Bupivacaine

INTRODUCTION:

Laparoscopic cholesystectomy is the treatment of choice for gallstone disease[1]. It has numerous advantages over open cholesystectomy including less duration of hospital stay, less postoperative pain and earlier return of bowel function[2]. The common reason for delayed mobilization of patients in hospital and prolonged bed occupancy is the postoperative pain[3]. Although, pain following LC is less intense than open cholesystectomy but it is usually acute and sharp in character that starts with the surgical trauma and ends with healing of tissue[4]. Effective pain relief leads to early mobilization of patients after major surgery and helps to avoid risks of deep venous thromboembolism and other entities associated with delayed ambulation of patients. Different treatment choices have been proposed to reduce the postoperative pain after LC including the use of systemic opioids, regional anesthesia with intrathecal or epidural

Corresponding Author:
Ishtiaq Anwar
Research officer, Edo Eye Hospital
Email: Sulehrionline99@hotmail.com

opioids and local anesthesia[5]. Tramadol is a synthetic opioid which belongs to aminocyclohexanol group[6]. It is considered as a safe analgesic and its effect stays longer than that of other analgesics for relief of postoperative pain[7]. It acts as a weak agonist for all types of opioids receptors, inhibits noradrenalin uptake and stimulation of serotonin release[8,9,10]. Further, less respiratory depression is reported with tramadol in comparison with other opioids[11,12]. Few authors suggest that the intraperitoneal administration of local anesthetics like lidocaine and bupivacaine found to be effective in postoperative pain reduction following laparoscopic cholecystectomy[13]. In contrast, some other researchers found that intraperitoneal administration of bupivacaine or morphine is not an effective method[14]. Pain relief caused by local spillage of Bupivacaine can help to avoid adverse side effects associated with other drugs used intravenously[15,16]. We intend to compare beneficial effects of Bupivacaine with that of Tramadol in terms of postoperative pain relief, better of the two may be offered for such patients in our clinical environment.

MATERIAL AND METHODS:

This randomized control trial was carried out at the surgery department of PIMS, Islamabad. Duration of the study was seven months, from June 2015 to January 2016. A total of two hundred and seventy two (n=272) patients of ASA physical status I-II that underwent LC for symptomatic gall stones were enrolled after taking a thorough clinical history and fully informed written consents. Non Probability consecutive sampling is used for patient selection. Pregnant females and patient with coexisting CBD stones were excluded from the study. Two groups of the patients were made and randomly assigned by lottery method. Group A (Control group) received intravenous tramadol while Group B (Study group) received intraperitoneal instillation of 20 ml, 0.25% of bupivacaine through the laparoscopic cannula. Laparoscopic surgery was performed with standard four port cholecystectomy with 10mm ports (in umbilical and epigastric location) and two 5 mm ports in (right subcostal and lumber regions). Grasper were used for fundal traction. Dissector was used for dissecting fine calot's triangle. Chopstick method was used for crossing instrument ports and telescope port. Postoperative pain defined as a feeling of subjective discomfort after surgery. It was determined using visual analogue scale (VAS) graded from 0 to10, where 0 shows no pain and 10 shows maximum bearable pain. Main outcome measures to be observed during the study included: Maximum pain score at regular time interval, based upon VAS score; the time of first injection of analgesic drug; number of injections required (when patient complaint of pain) and time of mobilization of patients after surgery. Data was entered and analyzed through SPSS version 23.0 Quantitative variables were calculated as Mean ± Standard deviation while frequency and percentages were calculated for qualitative variables. The independent t-test was applied to compare mean VAS score between two groups. P-value less than 0.05 considered as significant.

RESULTS:

Out of total 272 patients, 28% (n=76) were male with mean age of 54.54 years ±7.15 SD and 72% (n=196) were female with mean age of 56.06 years ±6.59SD. Mean age of the Group A patient found to be 55.89 years ±6.85 and 55.37 year ±6.72 of Group B patient. No significant difference in Male to female ratio and their age was found among both groups. Mean pain score and mean VAS at one hour, 2 hours, 4 hours and 8 hours after surgery was calculated and compared by applying t-test to assess the significance of difference between two means. P-value was found to be 0.003 (<0.05) implying significant difference between two groups with patients in group B (IP-Bupivacaine) showed better control in pain intensity (table 1). Mean number of rescue injections following surgery were relatively less required in patient who were treated with IP-Bupivacaine (0.9 ±0.57 VS 1.5 ±0.74; p<0.034). Similar findings were noted in other outcomes like mean mobilization time and mean time of first rescue injection after surgery where group B showed significantly (P <0.05) better outcome than group A (table 2).

Table 1: Mean pain score at one, two, four and eight hours in both groups

	Group A (IV-Tramadol)	**Group B** (IP-Bupivacaine)	**P-Value**
VAS at one hour	4.4 ±1.7	3.5 ±1.7	0.003
VAS at 2 hour	4.2 ±1.6	3.6 ±1.6	0.009
VAS at 4 hour	4.3 ±1.5	3.4 ±1.5	0.007
VAS at 8 hour	4.4 ±1.7	3.9 ±1.9	0.03

Table 2: Mean time of mobilization and first rescue injection following surgery in both groups

	GROUP A (IV TRAMADOL)	**GROUP B (IP BUPIVACAINE)**	***P*- value (*t*-test)**
First injection time in hours (Mean ± SD)	2.3 ±0.86	3.6 ±1.33	0.006
Mobilization time in hours (Mean ± SD)	3.5 ±1.3	2.2 ±0.85	0.001

DISCUSSION:

Laparoscopic cholecystectomy has become the procedure of choice for surgical management of biliary lithiasis during the last few years[17]. Despite, short incision, reduced blood loss and rapid postoperative recovery, the procedure is not completely risk-free[18]. Postoperative pain is more frequent and an important factor that can delay the patients' postoperative function and discharge from the hospital following laparoscopic cholecystestomy[19]. Postoperative pain is variable in intensity, character and time course[20]. Various modalities have been assessed to ameliorate the pain associated with laparoscopic cholecystestomy including the use of local anesthetics to the site of surgery, and usage of appropriate NSAIDS[21,22]. Present study was planned to assess the efficacy of intraperitoneal instillation of bupivacaine during laparoscopic cholecystectomy in comparison with intravenous tramadol, which is widely used as a standard of care in our settings. Our results reflected that intraperitoneal instillation of bupivacaine during laparoscopic cholecystectomy is an effective treatment option for controlling postoperative pain. These rescue analgesic injections are required significantly less in numbers by these patients and can be mobilized at an earlier time. The data on head to head comparison between IV-tramadol and IP-bupivacaine is scarce. In one study, Shabir SA, et al[23] tried to find the better choice of analgesia for postoperative pain reduction after laparoscopic cholecystectomy and they found that Tramadol group was significantly better (p value<0.05) as compared to Bupivacaine group. These results are contrary to our results as Bupivicaine showed better outcomes in our study. The difference may be attributed to different selection criteria and higher doses of tramadol used. In another study, A. A. Louizos and S. J. Hadzilia[24] aimed to test the use of different combinations of analgesia for postoperative pain reduction. As per their study results, the pain score was significantly lower in patients who were treated with combination of pre-incisional local infiltration and intraperitoneal instillation of bupivacaine 0.25% than other groups. These results were comparable to our study where mean VAS in bupivacaine group found to be significantly lower than other analgesia. Moreover, Rescue analgesic treatment was significantly lower in patients of group D (35%) as compared with that of group A (84%) ($p < 0.05$); that is also similar to our study results where IP-Bupivacaine group needed rescue

injection at later time. Gouda M El-Labban & Emad N Hokkam in their randomized controlled study[25] compared the effectiveness of intraperitoneal instillation of levobupivacaine 0.25% versus intraincisional levobupivacaine 0.25% of postoperative pain reduction following laparoscopic cholecystectomy. The intraincisional infiltration of levobupivacaine 0.25% significantly reduces the post-operative abdominal pain (comparable to our study results; mean VAS 3.4 at 4 hours and 3.9 at 8 hours in our stuy). They concluded that intraincisional infiltration of levobupivacaine control the postoperative abdominal pain more effectively than intraperitoneal route. the need of rescue analgesia reduces by this approach. Hilvering B, Draaisma WA[26] aimed to evaluate the effect of combined subcutaneous infiltration and intraperitoneal instillation of levobupivacaine before the start of LC on post-operative abdominal pain following surgery. The abdominal pain estimated by VAS at half, 2, 4, 8 and 24 hours after surgery and found no significant reduction in postoperative abdominal pain with levobupivacaine in comparison with placebo during the 24-h follow-up; the overall difference in pain score was 2·2 (95 per cent confidence interval - 4·9 to 9·3; P = 0·540). While, our study results showed a mean VAS 3.4 at 4 hours and 3.9 at 8 hours in our study, significantly better. Their study results showed that there was no significant difference in other study outcomes like the duration of operation, use of anaesthesia, use of rescue analgesia, shoulder pain, duration of hospital stay and time to resumption of normal daily activities between the two groups. However, our results showed that Intraperitoneal administration of bupivacaine is effective for better postoperative pain control. These patients needed significantly lesser number of rescue analgesic injections and can be mobilized at an earlier time. This low response in their study might be to the use of 0.125% levobupivacaine in their study as compared to 0.25% we used in our study.

CONCLUSION:

Intraperitoneal administration of bupivacaine during laparoscopic cholecystectomy is an effective and better treatment option for postoperative pain control. These patients needed significantly lesser number of rescue analgesic injections and can be mobilized at an earlier time.

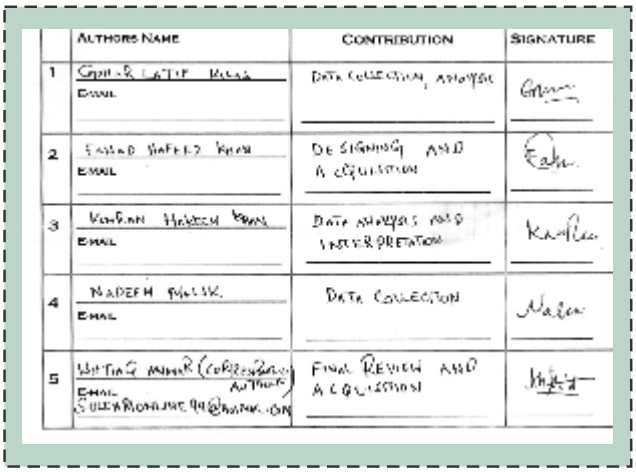
REFERENCES:

1. Lammert F, Miquel J. Gallstone disease: From genes to evidence-based therapy. J Hepatol. 2008;48:S124-S135.
2. Pulate PA, Narkhede T, Chandak SS. Laparoscopic Cholecystectomy - A Cross Sectional Study. MVP J Med Sci. 2015;2 (3):53-6.
3. Siddiqui NA, Azami R, Murtaza G, Nasim S. Postoperative port-site pain after gall bladder retrieval from epigastric vs. umbilical port in laparoscopic cholecystectomy: A randomized controlled trial. Int J Surg. 2012;10(2):213-6.
4. Upadya M, Pushpavathi SH, Seetharam KR. Comparison of intra-peritoneal bupivacaine and intravenous paracetamol for postoperative pain relief after laparoscopic cholecystectomy. Anesthesia, Essays and Researches. 2015;9(2):39-43.
5. Sandhu T, Paiboonworachat S, Ko-iam W. Effects of preemptive analgesia in laparoscopic cholesystectomy: a double-blind randomized controlled trial. Surg Endosc. 2011;25(1):23-7.
6. Chandanwale AS, Sundar S, Latchoumibady K, Biswas S, Gabhane M, Naik M, et al. Efficacy and safety profile of combination of tramadol-diclofenac versus tramadol-paracetamol in patients with acute musculoskeletal conditions, postoperative pain, and acute flare of osteoarthritis and rheumatoid arthritis: a Phase III, 5-day open-label study. J Pain Res. 2014;7(3):455–63.
7. Behdad S, Sekhavat L, Ayatollahi V, Meshkat F, Mortazavi A. Comparison of postoperative analgesic effect of tramadol and bupivacaine subcutaneous infiltration in patients undergoing cesarean section. Acta Clin Croat. 2013;52(5):93-7.

8. Ali M, Khan FA. Comparison of analgesic effect of tramadol alone and a combination of tramadol and paracetamol in day-care laparoscopic surgery. Eur J Anaesthesiol. 2009;26(2):475-9.
9. Akinci SB, Ayhan B, Aycan IO, Tirnaksiz B, Basgul E. the postoperative analgesic efficacy of intraperitoneal tramadol compared to normal saline or intravenous tramadol in laparoscopic cholesystectomy. Eur J Anaesthesiol. 2008;25(1):375-81.
10. Arjunan V, Santhanam R, Marchewka MK, Mohan S. Comprehensive quantum chemical and spectroscopic (FTIR, FT-Raman, 1H, 13C NMR) investigations of O-desmethyltramadol hydrochloride an active metabolite in tramadol - An analgesic drug. Spectrochim Acta A Mol Biomol Spectrosc. 2014;122(3):315-30.
11. Emir E, Serin S, Erbay H, Sungurtekin H, Tomatir E. Tramadol versus low dose tramadol-paracetamol for patient controlled analgesia during spinal vertebral surgery. Kaohsiung J Med Sci. 2010;26(2):308-15.
12. Covino BG. Clinical pharmacology of local anesthetic agents. In: Neural blockade in clinical anaesthesia and management of pain. Philadelphia: JB Lippincott Co.; 1988. P. 111-44.
13. Benhamou D, Narchi P, Mazoit JX. Postoperative pain after local anesthetics for laparoscopic sterilization. Obstet Gynecol. 2015;84(3):877-80.
14. Goldstein A, Grimault P, Henique A. Preventing postoperative pain by local anesthetic instillation after laparoscopic gynecologic surgery: A placebo-controlled comparison of bupivacaine and ropivacaine. Anesth Analg. 2014;91(2): 403-7.
15. Abdulla S, Eckhart R, Netter U, Abdulla W. A randomized, double-blind, controlled trial on non-opioid analgesics and opioids consumption for postoperative pain relief after laparoscopic cholesystectomy. Acta Anaesthesiol Belg. 2015;63(1):43-50.
16. Darwish AM, Hassan ZEAZ. Intraperitoneal bupivacaine vs. tramadol for pain relief following day case laparoscopic surgery. Gynecological Endoscopy. 2015;8(3):169-73.
17. Schirmer BD, Edge SB, Dix J. Laparoscopic cholecystectomy. Treatment of choice for symptomatic cholelithiasis. Ann Surg. 2016;213(3):665-9.
18. Duca S, Bălă O, Al-Hajjar N. Laparoscopic cholecystectomy: incidents and complications. A retrospective analysis of 9542 consecutive laparoscopic operations. HPB (Oxford). 2014;5(1):152-8.
18. Paulson J, Mellinger J, Baguley W. The use of intraperitoneal bupivacaine to decrease the length stay in elective laparoscopic cholecystestomy patients. Am Surg. 2015;69(3):275–8.
19. Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: Characteristics and effect of intraperitoneal bupivacaine. Anesth Analg. 2015;81(4):379-84.
20. Vadivelu N, Mitra S, Narayan D. Recent Advances in Postoperative Pain Management. Yale J Biol Med. 2016;83(3):11–25.
21. Khurana S, Garg K, Grewal A, Kaul TK, Bose A. A comparative study on postoperative pain relief in laparoscopic cholecystectomy: Intraperitoneal bupivacaine versus combination of bupivacaine and buprenorphine. Anesth Essays Res. 2016;10(2):23–8.
22. Shabir SA, Saleem B, Hakim A, A.M H. Postoperative Analgesia in Laparoscopic Cholecystectomy: A Comparative Study Using Bupivacaine Instillation And Infiltration Versus Parenteral Analgesia (Tramadol). The Internet Journal of Anesthesiology. 2015;29(4):1-4.
23. Louizos A A, Hadzilia S J, Leandros E, Georgiou L G, Bramis J P. Postoperative pain relief after Laparoscopic Cholecystectomy. A placebo-controlled double-blind randomized trial of preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25%. Surg Endo. 2017;19(3):1503-6.
24. Gouda M El-labban, Emad N Hokkam,

Mohamed A El-labban and Khaled Morsy. Intraincisional vs intraperitoneal infiltration of local anaesthetic for controlling early post-laparoscopic cholecystectomy pain. J Minim Access Surg. 2015;7(4):173–7.

25. Hilvering B, Draaisma WA, van der Bilt JD, Valk RM, Kofman KE. Randomized clinical trial of combined preincisional infiltration and intraperitoneal instillation of levobupivacaine for postoperative pain after laparoscopic cholecystectomy. Br J Surg. 2014;98(3):784-9.



	AUTHORS NAME	CONTRIBUTION	SIGNATURE
1	Email	DATA COLLECTION, ANALYSIS	
2	Email	DESIGNING AND ACQUISITION	
3	Email	DATA ANALYSIS AND INTERPRETATION	
4	Email	DATA COLLECTION	
5	Email	FINAL REVIEW AND ACQUISITION	

Submitted for publication: 10.05.2018

Accepted for publication: 23.01.2019
After Revision

Value of a man depends upon his courage; his veracity depends upon his self-respect and his chastity depends upon his sense of honor.

Hazrat Ali (Karmulha Wajhay)