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Evaluation of Postoperative Analgesia in Patients Undergoing Laparoscopic Cholecystectomy under General Anaesthesia: With or Without Bupivacaine Instillation in Gall Bladder Fossa

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ABSTRACT

Introduction: Laparoscopic Cholecystectomy is now the gold standard treatment of symptomatic gallstones. Post-surgery, patients suffer visceral and shoulder pain secondary to peritoneal insufflation. This study evaluates the analgesic effectiveness of 0.25% bupivacaine instillation in gall bladder fossa after laparoscopic cholecystectomy.

Methods: A prospective, double-blind study was conducted in 60 patients aged 20-60 years, ASA I and II, weighing 40-80 kgs, undergoing laparoscopic cholecystectomy under general anaesthesia. Patients were divided into two groups: Group A (30 patients) received 10 ml of 0.25% Bupivacaine, and Group B (30 patients) received 10ml Normal Saline in gall bladder fossa post-surgery. Postoperative pain was accessed using the visual analogue scale at 6, 12 and 24 hours postoperatively. Data were applied with appropriate statistical tests, results with p value <0.05 were considered significant.

Results: Demographic data were comparable in both groups (p>0.05). VAS score was significantly lower in group A(1.10± 0.76) compared to group B(2.73± 1.62)(p=0.00) at 6 hours postoperatively. VAS scores were comparable at 12 and 24 hours postoperatively. Rescue analgesic use was significantly less in group A (0%) compared to group B (20%) in the first 6 hours postoperatively (p=0.01). Rescue analgesia requirements were comparable and statistically insignificant for the rest of the study duration (p=0.79; p=0.64).

Conclusions: Postoperative pain was lower in patients receiving bupivacaine instillation in gall bladder fossa compared to those receiving normal saline during first six postoperative hours. VAS scores and rescue analgesic requirements were comparable on rest of the study duration.

Keywords: *Bupivacaine; Intraperitoneal; Laparoscopic Cholecystectomy; Post-operative pain.*

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INTRODUCTION

Laparoscopic Cholecystectomy (LC) is a widely performed procedure in general surgery, favoured for treating symptomatic cholelithiasis due to quicker recovery, less pain, and lower morbidity.[1] LC is a minimally invasive technique, reduces surgical trauma, blood loss, postoperative complications, and hospital stay. However, LC can result in significant postoperative shoulder and abdominal pain, increasing hospital stays, morbidity, and costs.

Uncontrolled postoperative pain can delay normal pulmonary function resumption, restrict mobility, and contribute to thromboembolic complications, nausea, vomiting, increase in cardiac workload owing to stress-induced catecholamine release.

Various methods for effective postoperative pain control methods include NSAIDs [2], local anesthetic wound infiltration, and intermittent intramuscular narcotics.[2,3] Intraperitoneal local anaesthetic instillation has shown promising beneficial effect in reducing postoperative pain with variable results.[4–12] In view of variable results obtained, the present study was conducted to evaluate the analgesic effectiveness and analgesia demand with gall bladder fossa instillation of 0.25% bupivacaine.

METHODS

A hospital based, prospective, analytical study was conducted in the Department of Anaesthesiology, Manipal College of Medical Sciences (MCOMS) after obtaining approval from Institutional Review Committee (MEMG/IRC/280/GA) from February 2021 to January 2022.

The calculation of sample size was based on findings of past study which documented the mean postoperative Visual Analogue Scale(VAS) Scores in the saline group and the bupivacaine group as 4.27±0.78 and 3.52±1.22 respectively.[11]

The sample size was calculated at level of significance 5% and power of 80% by using the following formula.

$$n = \frac{2[(a+b)^2 J^2]}{(\mu_1 - \mu_2)^2}$$

where, n = sample size in each of the groups
μ_1 = population mean in control group
μ_2 = population mean in bupivacaine group
J = population variance (SD)
a = conventional multiplier for alpha = 0.05
b = conventional multiplier for power = 0.80

Value of a = 1.96, b = 0.842

Putting the values in above formula, the ideally required minimum sample size for the study comes out to be 27.91 in each group. However, we took total sample size of 60 (30 in each group) to compensate for non-responders.

Non-Probability (Convenience) sampling technique was used for undertaking the study. Patient belonging to American Society of Anesthesiologists physical status (ASA-PS) grade I and II, aged 20 to 60 years and weighing 40-80kgs giving consent scheduled for elective LC were included in the study. Patients belonging to ASA Grade III, IV and V, history of drug allergy to any of the study drugs, a history of severe cardiovascular, respiratory, metabolic, endocrine, renal, hepatic or neurologic disease were excluded from the study. Also, patients converted to open cholecystectomy, having choledocholithiasis, acute pancreatitis, acute cholecystitis, history of previous abdominal surgery or were unable

to understand or respond to VAS or having chronic pain disease other than gall stone disease were not included in our study.

The patient was examined one day prior to surgery and standard institutional preoperative advice was offered. Enrolled patients were explained about the use of VAS score. All laparoscopic surgeries were carried out under general anesthesia by anesthesiologist being unaware of the drug instilled at the gall bladder fossa. All cases were fasted for eight hours for solid prior to surgery and premedicated with Tablet Ranitidine 150 mg on night before operation and 6am on the day of surgery. Patients were allocated alternately into two groups (Group A; n= 30 patients received 10ml of 0.25% bupivacaine and Group B; n= 30 patients received 10ml of normal saline instillation in the gall bladder fossa). Study medications were prepared by a post-graduate trainee who was not related to the study, in two identical syringes which had 10 ml of 0.25% bupivacaine or 10 ml of normal saline given in the gall bladder fossa to patients after gall bladder extraction at the end of the procedure.

In the preoperative room, IV line was secured, and maintenance fluid was given according to the Holliday and Segar formula.[13] In the operation theatre routine monitoring devices like pulse oximetry, non-invasive Blood Pressure (NIBP), electrocardiograph monitors were attached; and baseline blood pressure, heart rate and O_2 saturation values were recorded. Capnography was attached after intubation. The anesthetic regimen and surgical procedures were standardized for all patients.

The standard general anesthetic technique was administered to all the patients. Patients were premedicated with Inj. Midazolam 0.02mg/kg, Inj. Fentanyl 1.5µg/kg & induced by Inj. Propofol at the dose of 1.5 to 2.5 mg/kg body weight. Tracheal intubation was done by appropriate size endotracheal tube facilitated by Succinylcholine 1.5-2mg/kg and muscle relaxation was maintained with Vecuronium 100µg per kg body weight. A nasogastric tube was placed for emptying the gastric contents. Anaesthesia was maintained by O_2 and Isoflurane (1 to 2%). Intermittent doses of Vecuronium was given to maintain adequate muscle relaxation. Ventilation was controlled mechanically and adjusted to keep the end tidal carbon dioxide (ETCO2) at 30-35 mm of Hg throughout surgery. Intra operative HR, BP, SpO_2, ECG were monitored. Skin and abdominal wall were infiltrated with 0.25% bupivacaine before insertion of trocar at the port sites. During laparoscopic surgery abdomen was insufflated with CO_2 at a pressure of 10 to 12 mm Hg. After the completion of surgery, abdomen was deflated by the surgeon. At the end of the surgery, Group A patients received 10ml of 0.25% bupivacaine and Group B patients received 10ml of normal saline instillation in the gall bladder fossa.

After the surgery was over, the residual neuromuscular block was adequately reversed using Inj. Neostigmine (0.05mg/kg) and Inj. Glycopyrrolate (0.01mg/kg). The nasogastric tube was suctioned & removed and subsequently trachea was extubated once extubation criterion was met.

Pain assessment was done by anesthesiology residents not involved in study, who was unaware about the group allocation of the patient. The severity of postoperative pain was assessed by using VAS scale. VAS ruler used consisted of a 10 cm horizontal line, with ‘no pain’ at one end (end zero) and ‘pain as bad as it could be’ at other end (end 10). The intensity of pain was assessed by asking the patients to grade the severity of pain by marking on the 10 cm line scale at the point that corresponded to the level of pain they felt. A score of > 4 was considered as severe pain, 4 as moderate and <

4 as mild pain. Patients with severe pain score, that is >4 was treated with rescue analgesic. The time of arrival in the postoperative ward was defined as zero hour postoperatively. Pain intensity was measured at fixed time intervals of 6, 12 and 24 hours.

Injection Ketorolac 30mg IV was given as first line rescue analgesic at VAS>4. Injection Diclofenac sodium 75 mg intramuscularly was administered to any patient who still demanded analgesia or scored >4 on VAS after 30 minutes of administration of first line analgesia. The patients who had severe pain even after 30 minutes of the rescue analgesic were treated with Injection Tramadol 50mg intravenously. Standard analgesia was maintained with injection Ketorolac 30mg eight-hourly alternating with injection Paracetamol infusion 1gm (1%) eight-hourly.

The number of times the rescue analgesic was given and total analgesic consumption in the first 24 hours postoperatively was recorded. Any signs of systemic toxicity (tinnitus, metallic taste, circumoral numbness, blurred vision, dizziness, delirium, seizures) or hypersensitivity reaction or other adverse effects were treated accordingly and noted.

Statistical analyses were performed using SPSS Version 25.0. Continuous/Quantitative variables were reported as mean ± standard deviation and were analyzed using independent student's t-test. Categorical/Qualitative variables were reported as numbers/percentages and were analyzed using chi-square test. A P<0.05 was considered statistically significant.

RESULTS

Sixty patients were enrolled in the study. The patients were between the age group of 22 years to 60 years and had ASA physical status of I and II. There were 24(40%) patients of ASA I and 36(60%) patients of ASA II. Group A included 11(36.67%) male and 19(63.33%) female patients while group B included 10(33.33%) male and 20(66.67%) female. Age, sex and weight were comparable between the study groups (Table 1). VAS score was statistically significantly lower in group A (1.10± 0.76) compared to group B (2.73± 1.62) (p=0.00) at 6 hours post-operatively as presented in Table 2. VAS scores were comparable in both the groups at 12 and 24 hours post-operatively. At 6 hours postoperatively, only mild pain was complained by 30 (100%) of the patients in group A compared to 22 (73.3%) patients complaining of mild pain and 2 (6.7%) and 6 (20%) patients in group B complaining of moderate and severe degree of pain respectively. In the rest of the study duration; 6-12 hours and 12-24 hours, the pain severity and the requirement of rescue analgesic was comparable and statistically insignificant (p=0.79; p=0.64 respectively). The requirement of rescue analgesic (Table 4) was lesser in group A (0%) compared to group B (20%) in the first 6 hours post-operatively which was statistically significant (p=0.01). The total requirement of rescue analgesic in first 24 hours was comparable in both the groups as shown in Table no 5. No signs of systemic toxicity (tinnitus, metallic taste, circumoral numbness, blurred vision, dizziness, delirium, seizures) or hypersensitivity reaction or other adverse effects were noted in both the groups.

Table 1. Demographic variables of the study participants (n =60)

Demographic Variables	Group A	Group B	p-value
Age (Years)	44.17± 10.21	41.50± 11.18	0.34
Sex (M/F)	11/19 (36.67/63.33%)	10/20 (33.33/66.67%)	0.79
Weight (Kg)	63.23± **9**.31	61.43± **6**.98	0.40

Table 2. Comparison of VAS Scores between two groups at different time (n=60)

Time points	VAS Scores		
	Group A	Group B	p-value
6 hours	1.10± 0.76	2.73± 1.62	0.00
12 hours	3.47± 1.28	3.67± 1.45	0.57
24 hours	1.70± 1.26	1.26± 1.36	0.62

Table 3. Comparison of Pain severity between two groups at different time (n=60)

Pain Severity at 6 hours		
	Group A	Group B
Mild (VAS <4)	30 (100%)	22 (73.3%)
Moderate (VAS=4)	0	2 (6.7%)
Severe (VAS>4)	0	6 (20%)
Pain Severity at 12 hours		
	Group A	Group B
Mild (VAS <4)	15(15%)	14(46.7%)
Moderate (VAS=4)	6(20%)	6 (20%)
Severe (VAS>4)	9(30%)	10(33.3%)
Pain Severity at 24 hours		
	Group A	Group B
Mild (VAS <4)	28(93%)	27(90%)
Moderate (VAS=4)	0	0
Severe (VAS>4)	2(6.7%%)	3 (10%)

Table 4. Comparison of Requirement doses of rescue analgesic between two groups in different time intervals (n=60)

Time points	Requirement of rescue analgesic		
	Group A	Group B	p-value
0-6 hours	0 (0%)	6 (20%)	0.01
6-12 hours	9 (30%)	10 (33.33%)	0.79
12-24 hours	2 (6.67%)	3 (10%)	0.64

Table 5. Total requirement of rescue analgesic in first 24 hours (n=60)

Group	Rescue Analgesic Use	p-value
Group A	11 (36.67%)	0.07
Group B	19 (63.33%)	

DISCUSSION

Laparoscopic Cholecystectomy is considered the "gold standard" procedure for the surgical therapy of cholelithiasis.[14] Pain after LC demonstrates a high inter-individual variability in intensity as well as duration and is also mostly unpredictable.[15] The intensity of pain is highest on the day of surgery and the following day, subsequently declining to low levels within 2-3 days.[1] Our study demonstrated that patients who received bupivacaine experienced significantly lower pain scores and reduced need for additional analgesics compared to the control group in the first six hours post-operatively. This finding was similar to the results reported in previous studies.[16,17]

A past study conducted concluded that patients in the bupivacaine group had less pain in the early postoperative period and a lower incidence of pain in the right hypochondrium after instillation of bupivacaine in gall bladder bed.[6] Another study found that intraperitoneal instillation of bupivacaine causes good pain relief after LC.[8] One of the past Randomized Controlled Trial concluded that there was a significant reduction in the post-operative pain scores of bupivacaine instillation in subphrenic space, gall bladder bed and peritrocal site after elective LC.[18] However, in our study, we only used instillation of bupivacaine in the gall bladder bed and infiltration at the peritrocal sites which was effective for pain control.

In one of the past meta-analysis, the authors found out that intraperitoneal local anesthetics did not significantly reduce parietal pain of the abdominal wall and exhibited a favorable analgesic effect towards visceral pain and shoulder pain.[15] That finding may be attributed to the fact that the studies included did not use local infiltration at the peritrocal sites, whereas we used peritrocal infiltration in our study to address the parietal pain. Another study showed that the dosing of rescue analgesia was more frequent and the highest in patients who received normal saline in comparison to those that received bupivacaine.[19] Similarly, similar study revealed that the number of patients who needed postoperative analgesia with bupivacaine was significantly lower than control.[20] However our study showed the reduced need of rescue analgesics only in the first six post-operative hours and comparable demand of rescue analgesics in the first twenty four hours. This might be due to the low volume (10ml) and concentration (0.25%) of bupivacaine used in our study. Much longer duration of analgesia up to 48 hours has been reported in past study following intraperitoneal instillation 80ml of 0.125% bupivacaine with adrenaline (800,000 dilution) in patients undergoing diagnostic laparoscopy.[7] This longer duration of analgesia can be attributed to the use of intraperitoneal instillation of local anesthetic in patients undergoing diagnostic laparoscopy where injury to the visceral tissue is very minimal. However, another study found out the duration of postoperative analgesia with bupivacaine specifically in the first 12 hours postoperatively.[21] The longer duration of analgesic action can be due to the use of higher volume(20ml) and concentration(0.5%) of the drug than that used in our study.

A study compared lower concentrations of bupivacaine (0.125% and 0.25%) with normal saline and found no difference in the pain scores between the groups.[22] This could be due to the lower concentration of bupivacaine that was used in this study. There are a few other studies which concluded that administration of a local anesthetic did not show any efficacy. These failures could be due to the use of a lower drug dose, a lower concentration, or because the entire dose was

infiltrated only under the right hemidiaphragm.[5,23] On analyzing various reported literature, we can see the variation in the reduction in the postoperative analgesia requirements achieved with intraperitoneal instillation and peritrocal infiltration.[4,23–26] This variation can be considered as expected, as every investigator has its own study design, technique and methods of pain management.

Despite the reduction in pain in bupivacaine group during the immediate post-operative period, there was no overall difference in analgesic consumption in first 24 hours. A difference was probably not seen because the overall level of analgesic consumption in the two groups was small as LC itself being a minimal invasive surgery with less trauma to the tissues.

The limitations of this study include small sample size and limited to a single center. In addition, despite being a comparative study, yet no effort was made to find out etiologic factors, and hence, no analysis was therefore possible. Though the outcome of instillation of bupivacaine was comparable with previous evidence, to address these shortcomings, we suggest that large scale, randomized trials be conducted to identify the possible difference in the outcome of bupivacaine instillation to reduce frequency of the analgesia demand by the patient, time to mobilize after surgery and post operative hospital stay.

CONCLUSIONS

The postoperative pain was lower in patients who received bupivacaine instillation in gall bladder fossa than those who received normal saline during six post operative hours. However, Visual Analogue Scale scores and rescue analgesic requirements were comparable in the post-operative hours 6-12 and 12-24. Hence, we conclude that peritrocal and intraperitoneal instillation of local anaesthetic like bupivacaine is an easy, inexpensive, effective, non-invasive and relatively safe method to control immediate post-operative pain after LC.

CONFLICT OF INTEREST

None

SOURCES OF FUNDING

None

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