

Original Research Article

Evaluation of postoperative pain relief with intra-peritoneal bupivacaine instillation in laparoscopic cholecystectomy- a randomized control study

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ABSTRACT

Background: Laparoscopic cholecystectomy is the surgical procedure of choice for symptomatic cholelithiasis due to the improved postoperative course, but patients undergoing laparoscopic cholecystectomy during the first 24 hours postoperatively complaints of pain. This study was designed to study the efficacy of intraperitoneal bupivacaine in reducing the initial postoperative pain and also to evaluate the postoperative shoulder tip pain, nausea and vomiting.

Methods: Patients undergoing laparoscopic cholecystectomy were randomized into two groups the, study group received intraperitoneal bupivacaine 100mg at the end of the procedure and the control group received intraperitoneal saline. Post operatively patients were assessed for pulse rate, blood pressure, VAS, VRS, shoulder pain and nausea and vomiting at 0, 2, 6 and 24 hours.

Results: Among the 50 patients studied, our study proved that there is no statistical significant reduction in pain with intraperitoneal bupivacaine. The VAS at 0, 2, 6 and 24 hours calculated with non-significant p-value of 0.85, 0.29, 0.72 and 0.64 respectively and the VRS had p-value of 0.16, 0.08, 0.59 and 0.46 respectively and the doses of rescue analgesia consumed had p value of 0.67, 0.61 and 0.70 which were not significant statistically.

Conclusions: Instillation of 100mg bupivacaine did not significantly reduce the need for tramadol compared with saline.

Keywords: Laparoscopic cholecystectomy, Local anesthetics, Post-operative pain relief

INTRODUCTION

With the expanding role of ambulatory surgery and the need to facilitate an earlier hospital discharge, improving postoperative pain control has become an increasingly important issue for all surgeons and anaesthesiologist.¹

Uncontrolled postoperative pain has an adverse sequel of delayed resumption of normal pulmonary function,

restriction of mobility (thus contributing to thromboembolic complications), nausea and vomiting, increase in the systemic vascular resistance, cardiac work, and myocardial oxygen consumption through an increase in the catecholamine release induced by the stress response.²

Adequacy of postoperative pain control is one of the most important factors in determining when a patient can be

safely discharged from surgical facility and has a major influence on the patient's ability to resume their normal activities of daily living.³ Control of acute postoperative pain and the timing, and duration (e.g., pre-emptive analgesia), is important in facilitating short and long-term patient convalescence.⁴

Perioperative analgesia has traditionally been provided by opioid analgesics. However, extensive use of opioids is associated with a variety of perioperative side effects. It has been suggested by the Joint Commission on Accreditation of Health Organizations that excessive use of postoperative opioids analgesics leads to decrease patient satisfaction.⁵

In addition, the use of conventional method of administration of intramuscular opioids in standard prescribed doses, may be too large (causing side effects), or too small (causing inadequate analgesia). Therefore, anaesthesiologist and surgeons are increasingly turning to non-conventional techniques as adjuvant for managing pain during perioperative period to minimize the adverse effects of analgesic medications.⁶

From the non-conventional methods, the infiltration of long-acting local anaesthetics as an adjuvant for regional or local anaesthetic techniques, improve postoperative pain management, furthermore, when administered before surgery, these simple techniques can also decrease anaesthetic and analgesic requirement during surgery as well as reduce the need for opioid containing analgesic postoperatively.⁶ Intraperitoneal instillation of local anaesthetic in combination with general anaesthesia has been investigated in several interventional studies during laparoscopic cholecystectomy. Approximately half of these studies showed reduction in the postoperative pain significantly.

In spite of several advantages of laparoscopic procedures over laparotomy it does not take away the disadvantage like the post-operative pain which results in an unpleasant experience for the patient and there by delay the discharge. Pain usually occurs on the first day following surgery and it may be a visceral, parietal or shoulder pain.⁷

By evaluating the pathophysiology of pain it is shown that we can prevent or reduce pain by blocking the nociceptors before their stimulation by use of local anaesthetics.⁸ Bupivacaine is one such local anaesthetic which has a good safety profile, is long acting and free of side effects like gastritis due to NSAID's or nausea and vomiting and fear of drug dependence as in opioids.

Postoperative catheter infusion of bupivacaine into the subcostal incision during open cholecystectomy has been shown to decrease atelectasis, and reduce narcotic usage.⁹ Continuous postoperative infusion of local anaesthetic agent into the abdominal wounds has reduced both postoperative pain and narcotic requirements.^{10,11}

Bupivacaine has a half-life of 2.5 to 3.5 hours and has been reported to provide pain control for an average of 6 hours.¹² The margin of safety of the bupivacaine needed for analgesia is wide. Thus, pain relief and patient comfort during the early postoperative period becomes increasingly important, as the need for analgesic may delay discharge.

Several studies have described pain according to the presumed mechanism: visceral pain, which can theoretically be blocked by intraperitoneal instillation, and parietal pain, which can be blocked by port site infiltration.^{10,11,13} Present study is designed to evaluate the effect of intraperitoneal instillation of 0.5% bupivacaine with adrenaline for pain relief following laparoscopic cholecystectomy.

Visual analogue scale and verbal rating scale have been used to assess the difference between both groups.

Objective of the study

- Comparing the effect of intraperitoneal instillation of 0.5% bupivacaine with adrenaline versus saline for post-operative analgesia in laparoscopic cholecystectomy.
- To assess the need of rescue analgesics in post-operative period in both groups and to observe the side effects.

METHODS

It was a randomized clinical trial done on 50 adult patients of either gender admitted to department of surgery posted for elective laparoscopic cholecystectomy in the selected Hospital between age group 18 to 60 years. Prior to study, approval from the institutional ethical committee was obtained. All the patients were explained about the basis of the study and informed consent were obtained. All the participants with ASA-1 and ASA-2 undergoing elective laparoscopic cholecystectomy were randomly divided into two groups of 25 patients each. Obese patients with ASA grade III and IV, patients with chronic pain syndrome, history of previous abdominal surgery, allergy to protocol drug and patients who refused to participate were excluded.

Enrolled patients were explained about the use of visual analogue scale and visual rating scale. Visual analogue scale consists of a 10cm scale representing varying intensity of pain from 0 (no pain) to 10 (worst pain). Verbal rating scale (VRS) has up to 4 grades where 0- no pain on cough. 1- pain on cough but not on deep breathing 2- pain on deep breathing but not on rest. 3- slight pain at rest, 4- severe pain at rest.

All patients received alprazolam 0.5mg orally and ranitidine 150mg orally night before surgery and all patients underwent similar general anesthetic procedure.

Patients in group A received 20 ml 0.5% bupivacaine with adrenaline intraperitoneally at gall bladder bed and under right hemidiaphragm at the end of surgery through laparoscope port in trendelburg position. And patients under group B received 20 ml normal saline intraperitoneally at the same location

After the induction of anaesthesia patients were randomly assigned to one of two groups. Patients in group A (study group) received preoperative intraperitoneal and sub diaphragmatic 0.5% bupivacaine with 1 in 2 lakh adrenaline (10+10ml) at the end of surgery before the trocars were withdrawn; a total of 100mg, after instillation patient was maintained in trendelburg position for 5 minutes for the drug to stay at the injected site. Patients in group B (placebo group) received intraperitoneal and subdiaphragmatic saline (10+10ml) at the end of surgery before the trocars were withdrawn and trendelburg position was given for 5minutes.

The surgeon was blinded for the nature of the solution used. The residual CO₂ was evacuated carefully at the end of surgery by manual compression of the abdomen with open trocars. The nasogastric tube was removed after recovery from anaesthesia.

Post operatively the patients were assessed for pain utilizing visual analogue scale (VAS) and verbal rating Prince Henry scale (VRS). The time of arrival in the postoperative ward was defined as zero hour postoperatively. Pain intensity was measured at fixed time interval. The patients were also enquired about nausea, vomiting, number of times and dose of rescue analgesia using a predesigned proforma, which were assessed at 2, 4, 6, and 24 hour.

Rescue analgesics injection tramadol 50mg i.v, was given when VAS was more than 6 or VRS was more than 3 postoperatively, which was given by the ward staff who were unaware of the nature of the intraoperative analgesia. The time from the end of surgery until the first requested analgesia was recorded, and the doses of postoperative analgesia for breakthrough pain was assessed. Pain assessment was done by the investigator, who was blind to the group allocation of the patient and to any postoperative analgesia administered. The occurrence of nausea and/or vomiting was assessed by the ward nurses. If patients experienced nausea or vomiting, metoclopramide (0.1mg/kg) was given.

Patients were deemed ready for discharge from the hospital when they were afebrile, oral nutrition was tolerated without discomfort and bowel function (defined as presence of good intestinal sound or first passage of flatus) had returned.

Data analysis

Data was analyzed using SPSS (statistical presenting system software) for windows (version 15). Repeated

measure ANOVA, Student 't' test and paired 't' test was used. P-value <0.05 was considered statistically significant.

RESULTS

50 subjects participated in present study. The mean age of the participants in group A was 44.2±11.1 and in group B were 45.6±10.8. the number of females in both the groups were lower than the males.

52% of the participants were male and 48% were females. However, in group B 68% were males and 32% were females (Table 1).

Among the 50 patients studied, present study proved that there is no statistical significant reduction in pain with intraperitoneal bupivacaine.

Table 1: Demographic characteristics of participants.

Demographic variables	Group A	Group B
Mean age± SD	44.2±11.1	45.6±10.8
Age Groups (in percentage)		
Below 30	20.0	4
31-40	16.0	32.0
41-50	36.0	36.0
51-60	28.0	28.0
Gender		
Male	52.0	68.0
Female	48.0	32.0

Table 2: Comparison of pulse rate, systolic and diastolic BP among the groups.

Variables		Group A Mean±SD	Group B Mean±SD	P- value
Pulse Rate	0 hour	80.0±9.3	84.2±5.6	0.05
	2 hour	78.1±6.5	81.1±7.7	0.15
	6 hour	79.5±7.1	80.8±7.4	0.5
	24 hour	80.5±5.3	79.4±8.5	0.5
Systolic BP	0 hour	130±12	128 ±11.5	0.4
	2 hour	127±12	126.4±11.1	0.7
	6 hour	122.8±9.3	124.8±9.1	0.4
	24 hour	125.2±8.2	128.6±7.7	0.2
Diastolic BP	0 hour	82.1±8.6	84.0±7.6	0.3
	2 hour	80.8±9.0	82.6±6.2	0.5
	6 hour	78.9±6.4	79.2±6.4	0.8
	24 hour	80.4±6.1	80.8±4.0	0.7

The VAS at 0, 2, 6 and 24 hours calculated with non-significant p-value of 0.85, 0.29, 0.72 and 0.64 respectively and the VRS had p-value of 0.16, 0.08, 0.59 and 0.46 respectively and the doses of rescue analgesia consumed had p value of 0.67, 0.61 and 0.70 which were not significant statistically (Table 3).

Table 3: Comparison of VAS and VRS among the groups.

Variables		Group A	Group A	P-value
VAS	0 hour	3.5±2.1	3.6±1.0	0.8
	2 hour	3.9±1.9	4.4±1.2	0.2
	6 hour	4.6±1.1	4.4±1.1	0.7
	24 hour	5.1±1.8	4.9±1.1	0.6
VRS	0 hour	1.5±1.3	2.3±0.8	0.1
	2 hour	2.0±1.3	2.9±1.0	0.08
	6 hour	2.4±1.1	2.5±0.8	0.5
	24 hour	2.5±1.1	2.8±1.1	0.4

DISCUSSION

Although minimal invasive surgery is characterized by reduced pain, it is not painless. Patients undergoing laparoscopic cholecystectomy suffer considerable pain on the day of surgery frequently requiring narcotic analgesia.

Pain after laparoscopic cholecystectomy comprises of several components.¹⁴ The parietal pain is due to placement of trocars through the abdominal wall. The visceral pain is because of intraperitoneal dissection and insufflation of CO₂ resulting in distension of abdominal wall and prolonged elevation of diaphragm leads to shoulder tip pain.¹⁵⁻¹⁷ The parietal pain is superficial and can be located by the patient on the other hand visceral pain is dull, more diffuse in nature and difficult to locate. Studies show that blocking receptors before nociceptive stimulation eliminates the onset of pain. Visceral pain can theoretically be blocked by intraperitoneal infiltration; and parietal pain can be blocked by portside infiltration.^{18,19}

Present study was done to know analgesic efficacy of intraperitoneal bupivacaine versus intraperitoneal saline as postoperative analgesia following laparoscopic cholecystectomy.

Despite the large variation in the pain scores, we did not detect differences in Mean pain scores between the study and placebo group during the first 6 hours and was found to be statistically not significant. Although we expected the effect of the local anaesthetic to wear off after the period of 6-8 hours, there was no increase in the pain scores after 6 hours postoperatively in the patients who received bupivacaine. For the placebo group pain score was similar to the study group postoperatively. Therefore, the main effect of bupivacaine in this study seems to have been in amelioration of pain peak occurring during the initial 6 hours after the surgical procedure.

We have shown that intraperitoneal instillation of 100mg of bupivacaine at the end of laparoscopic cholecystectomy did not significantly reduced abdominal pain scores, and this was confirmed by the lower total dose of tramadol which was given postoperatively, which was similar for both the groups.

The incidence of shoulder tip pain, was absent in both the groups. Similar study done by Shalan H et al for laparoscopic pelvic surgery, found that pain score and analgesic dose required were lower in bupivacaine group.⁸ Goldstein A et al compared intraperitoneal 0.5% bupivacaine, 0.75% ropivacaine and saline instillation for postoperative pain relief found that local anaesthetics gave significantly good pain relief with ropivacaine being better than bupivacaine in both analgesia and opioid sparing effect.¹⁴

Bhardwaj et al, conducted study in patients undergoing laparoscopic cholecystectomy. He instilled 20ml 0.5% bupivacaine only at the end of surgery in the trendelenburg position. Post operatively they assessed for vital signs (heart rate, blood pressure and respiratory rate), pain scores (VAS, VRS and shoulder pain) and analgesic consumption. They found that it reduced post-operative cholecystectomy pain and analgesic consumption.²⁰ The efficacy of local anaesthetic instillation in pain control has been demonstrated in numerous other studies in laparoscopic cholecystectomy. Some used bupivacaine 0.25% while others used 0.125% bupivacaine and found a good post-operative pain relief.^{21,22} A systemic review and meta-analysis for the effect of intra-peritoneal local anaesthetic in laparoscopic cholecystectomy was done and 12 out of 24 studies reported a significant improvement in pain during early post-operative period.²³ The results correlate well with the results claimed in present study.

Local anaesthetics instillation has been found to be effective for post-operative analgesia in other laparoscopic surgeries. Intraperitoneal bupivacaine can significantly decrease post-operative pain and the need for additional analgesics in gynaecological laparoscopic surgeries. A systematic instillation is likely to be cost effective because it decreases resource utilization for the treatment postoperative pain and emesis.^{24,25}

The effect of pre-emptive and post-operative application of local anaesthetics in laparoscopic surgery was studied and concluded that pre-emptive application of local anaesthetics reduces the post-operative pain and analgesic requirements after laparoscopic fundoplication better than laparoscopic herniorrhaphy.²⁶

There are a few other studies in which local anaesthetic instillation has failed to show the efficacy. These failures were could be because of use of lower dosage, lower concentration or because the entire dose was instilled under right hemidiaphragm.^{21,27,28}

We observed that shoulder pain was less in both the groups; studies done shows that the result obtained by Pasqualucci et al demonstrated a statistically significant effect on surgical metabolic endocrine response (glucose and cortisol) and on postoperative pain scores by instillation of bupivacaine 100mg after creation of pneumoperitoneum and 200mg at the end of surgery.²⁹

The medical factor limiting hospital discharge is post-operative nausea and vomiting. Although we studied patients with chronic cholecystitis with a frequent incidence of post-operative nausea and vomiting related to the procedures, we found that no difference in both the groups. A study done by Andrei et al showed lower rate of post-operative nausea and vomiting in patients with bupivacaine.¹⁴ However, other studies showed no statistical difference in the incidence of Post-operative nausea and vomiting whether intraperitoneal local anaesthetic was used or not.³⁰

Of the 10 randomized controlled trails comparing bupivacaine or lidocaine with saline; wherein, in all trials the local anaesthetic was administered in the right sub diaphragmatic or gall bladder region in concentrations between 0.1% and 0.5%, 10 and 100mL at the beginning of the procedure, at the end, or both. Seven of the 10 trials found improved pain relief for at least one of the evaluated pain measures. In seven trials, overall pain scores were significantly reduced compared with the control patients. In most studies, pain scores were only reduced early postoperatively (2-8 hours) however, in two trials, reductions lasted up to 24 hours.^{29,31} In the three other trials; no effect on pain scores was observed.^{27,28,32}

Results from reports of intraperitoneal local anaesthetic after laparoscopic surgery revealed weak evidence for an effect on postoperative pain. Especially after laparoscopic cholecystectomy, the evidence was not compelling, and the clinical significance, at least regarding pain scores, was questionable. The differences between results in the various RCTs are difficult to explain.²³ Local anaesthetics are associated with toxicity which is dose related. Thus, the amount of local anaesthetics used may be of importance. Intraperitoneal instillation of 100mg of bupivacaine did not result in toxic plasma concentration, as also 300mg.^{29,33} Expression of neurological toxicity is a function of the cerebral concentration of local anaesthetic and its rate of increase; it is thus, caused by a direct intravascular injection or a rapid absorption. The maximal tolerated dose before manifestation of central nervous system toxicity is 12% to 25%.^{34,35} Based on these studies we conducted present study with 200mg bupivacaine, and there were no signs of any toxicity found.

Present study showed no statistically significant effect of intraperitoneal bupivacaine instillation in postoperative pain.

CONCLUSION

To conclude, bupivacaine is not effective at preventing pain after laparoscopic cholecystectomy. Present study showed, instillation of 100mg bupivacaine did not significantly reduced the need for tramadol compared with saline.

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Ethical approval: The study was approved by the institutional ethics committee

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