ORIGINAL ARTICLE

Intraperitoneal Pre-Insufflation of 0.125% Bupivaciane with Tramadol for Postoperative Pain Relief Following Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To compare the efficacy of intraperitoneal pre-insufflation of combined 0.125% bupivacaine and tramadol with bupivacaine alone in controlling postoperative pain among patients undergoing laparoscopic cholecystectomy.

Study Design: Randomized Controlled Trial

Place and Duration: The study was conducted at department of surgery, Holy Family, hospital, Rawalpindi from November 2016 to December 2017.

Methodology: Patients of either gender with ASA-1 and ASA-2 undergoing elective laparoscopic cholecystectomy were randomly divided into two groups of 50 each, by random number table method. The patients received the study drugs at the initiation of insufflation of CO2 in the intraperitoneal space by the operating surgeon under laparoscopic camera guidance over the gallbladder bed, tramadol 2 mg/kg in 30 ml of 0.125% bupivacaine was instilled in the gall bladder fossa under direct laparoscopic control in (study group) group A patients while group B patients received bupivacaine 30 ml of 0.125% solution only. Simultaneously, each group was assessed for intensity of pain at rest through VAS at 1, 4, 12 and 24 hrs after surgery.

Results: The mean age of group A (intervention group) was 43.25 ± 8.56 years and of group B (control group) was 44.89 ± 7.65 years. There were 24 (48%) male patients in group A and 29 (58%) in group B. In intervention group 34 (68%) patients and in control group 38 (76%) patients presented with ASA-I. The intervention group (Group A) had significantly (p-value < 0.05) lower mean values at 1 hour (3.89 ± 1.24 vs 5.79 ± 1.35), 4 hours (2.76 ± 2.13 vs 4.27 ± 1.08), 12 hours (2.28 ± 1.05 vs 4.89 ± 0.95) and 24 hours (2.16 ± 0.89 vs 3.23 ± 0.79) as compared with control group (Group B). The analysis showed that there was no statistically significant (p-value > 0.05) difference in side effects like nausea, vomiting, and shivering between both groups A and B.

Conclusion: Intraperitoneal instillation of bupivacaine plus tramadol reduces not only the intensity of postoperative pain but also the total rescue analgesic dose consumption after LC.

Keywords: Intraperitoneal bupivacaine plus tramadol, Postoperative pain, Laparoscopic cholecystectomy,

Introduction

Formerly cholelithiasis has been managed by open cholecystectomy technique but with advancement in technology laparoscopic cholecystectomy has become a method of choice for organization of cholelithiasis. There are many advantages of laparoscopic procedures like lesser haemorrhage, post-operative pain and recovery time.

Laparoscopic cholecystectomy significantly decreases hospital stay and expenditure. [1]

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. [2] 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. [3]

Postoperative pain control has a great importance in patient's prognosis after any surgical procedure and sufficient pain control is a marker for safely discharge of the patient from the hospital. The pain control has a major contribution for resumption of daily life activities. 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] The origin of pain after laparoscopic cholecystectomy is multifactorial. Pain arising from incision sites being somatic pain, whereas pain from the gallbladder bed being mainly visceral in nature, and shoulder pain is mainly due to the residual CO2 irritating the diaphragm. It is, therefore, likely that combined methods of analgesia can best reduce postoperative pain. [5]

The practice of intraperitoneal administration of local anesthetics is being used by many surgeons for postoperative pain control. The intraperitoneal infiltration of local anesthetics was first appraised in patients undergoing gynecological laparoscopic surgery. [6] Bupivacaine is a local anaesthetic and is used to control postoperative pain after laparoscopic procedures. In many studies 0.125 % to 0.5% bupivacaine is used intraperitoneally [7] or in the wound but with conflicting result. While in others, the use of intraperitoneal bupivacaine is found safe and effective. Technique for relieving postoperative pain control and is easy to perform in patients undergoing laparoscopic cholecystectomy. [8]

Tramadol, an atypical opioid analgesic, has been recently advocated to have local anesthetic action besides its central action on mu opioid receptors along with noradrenergic and serotonergic effects. The effect of tramadol on peripheral nerves has been confirmed in animal studies. [9] However, studies on the peripheral effect of tramadol by intraperitoneal route have shown inconsistent results. In a recent study by Memis et al., the combination of intraperitoneal bupivacaine plus tramadol was found to provide more effective analgesia than intraperitoneal bupivacaine alone after total abdominal hysterectomy.[10]

In a study conducted in India it was observed that overall VAS in 24 h was significantly lower (3.01 ± 0.48, 4.5 ± 0.92), time to first request of analgesia (min) was longer (118 ± 22, 55 ± 18) and total analgesic consumption (mg) was lower (85 ± 35, 175 ± 75) in combined group of bupivacaine plus tramadol and bupivacaine alone group. [11]

Postoperative pain after laparoscopic cholecystectomy (LC) is unpredictable, which explains the need for systematic prevention of pain before the patient wakes up from anesthesia. This study was planned to compare the efficacy of intraperitoneal administration of bupivacaine combined with tramadol in comparison to intraperitoneal bupivacaine alone among the patients undergoing laparoscopic cholecystectomy.

Methodology

This Randomized clinical trial study was conducted in the department of surgery, Holy Family, hospital Rawalpindi, from November 2016 to December 2017. Ethical approval was taken from hospital ethics committee before start of the study. The sample size was calculated by using WHO sample size calculator with mean VAS score of 5.9 and 3.62 in bupivacaine alone and bupivacaine plus tramadol group at 1 hour having pooled standard deviation of 4.0, [1a] with 5% level of significance and 80% power of test. The sample size was 50 patients in each group and a total of 100 patients. Patients of either gender admitted to department of surgery with ASA-1 and ASA-2 undergoing elective laparoscopic cholecystectomy were randomly divided into two groups by random number table method. 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.

Bupivacaine dose was limited to a maximum dose of 2 mg/kg. Preanesthetic evaluation was done on the evening prior to surgery. Patients were introduced to VAS and were instructed to point the intensity of pain on a 10 cm scale. Zero end of the scale is taken as no pain and 10 cm as maximum possible pain imaginable. All patients were premedicated with 10 mg diazepam per orally at night and 5 mg in the morning of the surgery. General anaesthesia was given to all the patients. Second generation cephalosporins

(cefuroxime) 1.5 g was injected i.v. before the induction of anaesthesia. Laparoscopic cholecystectomy was completed with the standard four port technique and carbon dioxide pnemoperitoneum. The patients received the study drugs at the initiation of insufflation of CO2 in the intraperitoneal space by the operating surgeon under laparoscopic camera guidance over the gallbladder bed, tramadol 2 mg/kg in 30 ml of 0.125% bupivacaine was instilled in the gall bladder fossa under direct laparoscopic control in (study group) group A patients while group B patients received bupivacaine 30 ml of 0.125% solution only. Simultaneously, each group was assessed for intensity of pain at rest through VAS at 1, 4, 12 and 24 hrs after surgery. All the patients were discharged 24 hours post operatively. The consumption of analgesics were also recorded. All the assessments were performed by a single observer (post graduate on duty) who was blinded to the group allocations.

Statistical Package for Social Sciences SPSS v 21 was utilized for data entry and analysis. Descriptive statistics were applied to describe the data on the basis of quantitative and qualitative nature of the data. Independent sample t-test was applied to compare the mean VAS and VAR values between both groups. P-value < 0.05 was considered significant.

Results

In this study a total of 100 patients were included consisting of two equal groups of 50 patients. The mean age of group A (intervention group) was 43.25 ± 8.56 years and of group B (control group) was 44.89 ± 7.65 years. Majority (38%) of the patients in group A had age in the interval of 41-50 years followed by (30%) patients in 51-60 years interval and in group B the main bulk (32%) of patient had age in interval of 41-50 years followed by (28%) in 31-40 years age interval.

There were 24 (48%) male patients in group A and 29 (58%) in group B. In intervention group (group A), 34 (68%) patients had ASA-I level and 16 (32%) had ASA-II level. In control group (group B) 38 (76%) patients presented with ASA-I and 12 (24%) presented with ASA-II. The mean duration of operation in group A was 62.78 ± 11.35 minutes and in group B it was noted as 64.35 ± 12.65 minutes (Table I).

According to the results of the study it was found that there was significant difference in mean value of visual analogue scale (VAS) at 1, 4, 12 and 24 hours between both groups. The intervention group (Group A) had significantly (p-value < 0.05) lower mean values at 1 hour (3.89 ± 1.24 vs 5.79 ± 1.35), 4 hours (2.76 ± 2.13 vs 4.27 ± 1.08), 12 hours (2.28 ± 1.05 vs 4.89 ± 0.95) and 24 hours (2.16 ± 0.89 vs 3.23 ± 0.79) as compared with control group (Group B). The duration of demand for additional analgesia was significantly greater in group A, (3.8 ± 1.37 vs 1.85 ± 1.33 hr, p-value = 0.000) as compared to group B. Similarly, the dose used in first 24 hours was significantly less in group A (115.5 ± 62.35 vs 183.5 ± 48.3 mg, p-value = 0.000) in comparison to control group B. The analysis showed that there was no statistically significant (p-value > 0.05) difference in side effects like nausea, vomiting, and shivering between both groups A and B as elaborated in Table II.

Table I: Distribution of demographic characteristics of patients

Variables	Group A		Group B	
	Frequency	Percentage	Frequency	Percentage
Age of patients				
Mean ± SD	43.25 ± 8.56		44.89 ± 7.65	
Age groups				
< 30	7	14.0%	9	18.0%
31-40	9	18.0%	14	28.0%
41-50	19	38.0%	16	32.0%
51-60	15	30.0%	11	22.0%
Total	50	100.0%	50	100.0%
Gender of patients				
Male	24	48.0%	29	58.0%
Female	26	52.0%	21	42.0%
Total	50	100.0%	50	100.0%
ASA categorization of the patients				
ASA-I	34	68.0%	38	76.0%
ASA-II	16	32.0%	12	24.0%
Duration of Operation (minutes)				
Mean ± SD	62.78 ± 11.35		64.35 ± 12.65	

Table II: Comparison of VAS, Time till first dose and dosage of analgesia and side effects between both groups

Characteristics	Group A	Group B	P-value
Pain on the basis of VAS at different time intervals (Mean ± SD)			
1 hour	3.89 ± 1.24	5.79 ± 1.35	0.000 *
4 hour	2.76 ± 2.13	4.27 ± 1.08	0.000 *
12 hour	2.28 ± 1.05	4.89 ± 0.95	0.000 *
24 hour	2.16 ± 0.89	3.23 ± 0.79	0.000 *

Duration until demand for analgesia (hour)			
mean ± SD	3.8 ± 1.37	1.85 ± 1.33	0.000 *
Dose of analgesia used in first 24 hours (mg)			
mean ± SD	115.5 ± 62.35	183.5 ± 48.3	0.000 *
Side effects			
Nausea	6 (12%)	11 (22%)	0.1832 **
Vomiting	2 (4%)	7 (14%)	0.0806 **
Shivering	11 (22%)	8 (16%)	0.4444 **

- Difference is significant at 5% level of significance
- ** Difference is not significant at 5% level of significance

Discussion

Laparoscopic surgeries produced medical revolution by bringing out many advantages and short incision, reduced blood loss, reduced stay in hospital and pain, that has brought down the cost of care process overall. However, patients undergoing laparoscopic procedures experience postoperative pain especially in back, abdomen and shoulder region that is one of the critical medical areas to be explored. However, it is associated with less pain and disability without increasing mortality or overall morbidity. [12]

The importance of postoperative pain control become more obligatory in laparoscopic cholecystectomy because it is a short stay procedure and sufficient pain control is necessary to discharge the patient from hospital.

During operation, interruption of nociceptive input and blockade of N-methyl d-aspartate activation by some drugs such as opioids or local anesthetics may be necessary to provide effective postoperative analgesia.[13] Instillation of intraperitoneal LA to reduce postoperative pain has been studied through randomized trials for more than 10 years. [14]

The local anaesthetic agents provide antinociception by affecting nerve membrane associated proteins and by inhibiting the release and action of prostaglandins which stimulates the nociceptors and cause inflammation. [15]

This present study was conducted to assess the effects of intraperitoneal administration of bupivacaine with intraperitoneal bupivacaine plus tramadol on pain relief after laparoscopic cholecystectomy. Different studies on this topic have revealed different results, some of them showing similar results with combination and alone drug groups[16] and majority showing better results in combined group. Some authors have suggested that the peritoneal instillation of local anesthetics or opioids before the nociceptive stimuli effectively suppresses the central neural sensitization and provides a greater reduction of postoperative pain. [17, 18]

The results of this present study showed that there was significant difference in mean value of visual analogue scale (VAS) at 1, 4, 12 and 24 hours between both groups. The intervention group (Group A) had significantly (p-value $<$ 0.05) lower mean values at 1 hour (3.89 ± 1.24 vs 5.79 ± 1.35), 4 hours (2.76 ± 2.13 vs 4.27 ± 1.08), 12 hours (2.28 ± 1.05 vs 4.89 ± 0.95) and 24 hours (2.16 ± 0.89 vs 3.23 ± 0.79) as compared with control group (Group B). Similar results showing significant ($P < 0.01$) reduction in postoperative pain, at 4 and 8 h postoperatively when bupivacaine plus tramadol group was compared with tramadol group alone. [19]

According to the results of this present study there was no significant difference (p-value $>$ 0.05) in both groups on the basis of side-effects like nausea, vomiting and shoulder tip pain. Parallel results have been found in literature with respect to side effects. Intercostal nerve block can be used to avoid the disadvantage of nausea and vomiting occurs with the use of opioids. Studies have shown that intercostal blockage have no severe systemic toxic reactions like pneumothorax associated with it.[20]

It can be concluded form findings of this study that combined use of bupivacaine and tramadol intraperitoneally have significantly better control of postoperative pain in comparison to intraperitoneal use of bupivacaine alone after laparoscopic cholecystectomy, without increasing any chance of hemodynamic instability or side effects like nausea, vomiting and shoulder tip pain. Similarly, this method has advantages of easy administration, high efficacy, safety and inexpensiveness. [21]

Conclusion

It can be concluded that intraperitoneal instillation of bupivacaine (0.125%) combined with tramadol in elective laparoscopic cholecystectomy significantly reduces the post-operative pain and significantly reduces the analgesic requirement in post-operative period as compared to bupivacaine alone. The combination also reduces the required dosage of rescue analgesia consumption without increasing risk of any side effect.

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