https://doi.org/10.29309/TPMJ/2024.31.02.7952

The Professional Medical Journal
www.theprofesional.com
2024, Volume, 31 Issue, 02

ORIGINAL ARTICLE

Effectiveness of port site bupivacaine infiltration in postoperative pain reduction after laparoscopic cholecystectomy: A randomized controlled trial from a tertiary care hospital.

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Article Citation: Shahid N, Rashid AM, Khan RA. Effectiveness of port site bupivacaine infiltration in postoperative pain reduction after laparoscopic cholecystectomy: A randomized controlled trial from a tertiary care hospital. Professional Med J 2024; 31(02):165-170. https://doi.org/10.29309/TPMJ/2024.31.02.7952

ABSTRACT… Objective: To determine the effectiveness of port site bupivacaine infiltration in postoperative pain reduction among patients undergoing LC in a tertiary care hospital in Karachi, Pakistan. **Study Design:** Randomized Controlled Trial. **Setting:** Department of Anesthesia, Hamdard Hospital, Karachi, Pakistan. **Period:** April 2022 to September 2022. **Material & Methods:** Patients of either gender aged between 18-45 years, undergoing elective laparoscopic cholecystectomy were included. Twenty ml of 0.25% bupivacaine solution were locally injected into the intervention group at the port locations. Treatment for the control group was consistent with standard of care. Post-surgery, to measure the severity of the pain, a visual analogue scale (VAS) was utilized and compared. **Results:** In a total of 170 patients, age, weight, systolic and diastolic blood pressure, ASA grade, SPO2, and the duration of the surgery were not substantially different between the two study groups at baseline ($p>0.05$). Post-operatively, from third hour till ninth hour pain score, abdominal pain, incisional pain and shoulder pain were significantly lower among the group received local infiltration of bupivacaine. No significant differences were seen at 12th hour. Median time to rescue analgesia was 12 (IQR=6-12) hours and 6 (IQR=6-9) hours among the intervention and control group ($p<0.001$). **Conclusion:** This study found lower pain intensity and higher time of rescue analgesia to be associated with local infiltration of bupivacaine at port as compared to control group in the early post-operative period among patients underwent laparoscopic cholecystectomy.

Key words: Bupivacaine, Local Infiltration, Laparoscopic Cholecystectomy, Post-operative Pain,Visual Analogue Scale.

INTRODUCTION

A minimally invasive surgical procedure, laparoscopic cholecystectomy (LC) is used to remove a sick gallbladder. Since the early 1900s, LC replaced open procedure for routine basis cholecystectomies.[1] Presently, LC is directed for the surgical management of chronic and acute symptomatic cholelithiasis, acalculous cholecystitis, cholecystitis, gallstone pancreatitis, gallbladder masses and biliary dyskinesia.[2]

The improved postoperative period has made laparoscopic surgery (LC) the standard surgical procedure for gallbladder illness.[3,4] Although this procedure results in lesser postoperative discomfort than traditional surgery, the treatment is not yet fully painless.[5,6] Laparoscopic cholecystectomy postoperative pain is still the most common complaint.[7,8] Following LC, pain is the most common complaint and the main factor contributing to a protracted recovery period. The first few hours following surgery are the most painful, and pain levels typically decrease over the next two to three days. Pain is the primary factor in 17-41% of patients' overnight hospital stays on the day of surgery.[9]

The application of local anesthetics at the trocar site, lowering pneumoperitoneum pressure, and fewer surgical ports are just a few of the methods that have been suggested so far to manage pain.[10,11] However, One method for

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Article received on: 20/09/2023
Accepted for publication: 22/11/2023

reducing postoperative pain after a variety of surgical operations has been the infiltration of the wound with local anaesthetics. The procedure reduces somatic pain brought on by the surgical wound without having any significant negative consequences.[12]

Bupivacaine is one of the local analgesics and was created in 1957 by Ekenstam. It eases pain and stiffness in the muscles, impairs proprioception and the ability to feel touch and warmth, and has an anti-inflammatory impact. As a result, bupivacaine has a wide range of uses, including infiltration, block, subarachnoid, sympathetic, and epidural anesthesia. It may be administered as 0.25 to 0.50% solution in form of direct application prior to wound closure or as a catheter infusion, allowing medication to be released to the wound gradually.[13]

Previously available literature studied bupivacaine effects in local infiltration for post-operative pain control in other surgical procedure.[12] However, findings relating to pain relief and analgesic consumption are differing and treatment still needs a complete evaluation. Further, there is also paucity of this data in Pakistan. Therefore, to fill this gap it was planned to determine the effectiveness of port site bupivacaine infiltration in postoperative pain reduction among patients undergoing laparoscopic cholecystectomy in a tertiary care hospital in Karachi, Pakistan.

MATERIAL & METHODS

This randomized controlled trial was conducted at the department of Anesthesia, Hamdard Hospital, Karachi, Pakistan, from April 2022 to September 2022. After acquiring the ethical approval (IRB#: HCM&D/346/2022) from the institutional committee, the study was commenced. Protocol was also registered in an international trial registry (https://www.clinicaltrials.gov/study/NCT05264805?term=NCT05264805&rank=1).

All study participants were asked to provide written and informed permission prior to being enrolled. Patients of either gender aged between 18-45 years, planned to undergo elective laparoscopic cholecystectomy under general anesthesia having ASA grade I to II were included. Patients known for allergic reactions to local anesthetics, converted to open procedure, developing intra-operative complications, having history of opioids, steroids, NSAIDs and alcohol use, obese and with multiple chronic illnesses were excluded.

Sample size was estimated considering mean pain score at 12th hour following LC among patients receiving local infiltration of bupivacaine and control group as 4.72 ± 0.61 and 6.08 ± 0.64 respectively at power of 80% and 95% confidence interval.[14] The calculated sample size was 8. For better reliability of our findings, total 170 patients were enrolled (85 in each group). Random allocation to both study groups was done following sequentially numbered opaque sealed envelope protocol.

Consultant surgeons having at least five years of experience performed the procedures. As per procedure, preoperative antibiotics were given within 30 minutes of incision. Using carbon dioxide, the abdomen was insufflated to a pressure of 15 mmHg. Then, four 10-mm-long incisions were made in the belly to implant the trocar. The gall bladder was pulled back over the liver using a laparoscope and lengthy devices. The abdomen was allowed to deflate to 8 mmHg for 2 minutes before hemostasis was reached. The gallbladder was taken out of the abdomen and placed in a sample pouch. All trocars were removed while being directly observed. In the intervention group, 20 ml of 0.25% bupivacaine solution was injected into the port sites; 6 ml was injected through the abdominal wall around each midline port site, and 4 ml was injected in the same way at the lateral port sites. Before ports closure, abdomen was compressed for evacuating the residual carbon dioxide. Control group received treatment as per the standard of care. Both the study groups were intra-operatively administered with nalbuphine at a dose of 0.1 mg/kg body weight through intravenous infusion.

Following the standard protocols, postoperative tramadol at dose of 50-100mg mg was intravenously infused as recuse analgesia on

demand of patients or when pain score was more than 5. The study outcome was pain status. The technique showing the lower pain score was considered as effective. To measure the severity of the pain, a visual analogue scale (VAS) was utilized. Patients were monitored as per the standard protocols. The assigned nursing staff monitored the patient for post-operative pain and analgesia requirement. Post-operative pain and analgesia requirement from 0 hours till 12 hours with interval of 3 hours were recorded. Number of patients reporting pain in abdomen, incisional site and at shoulder tip were also recorded in the pre-designed proforma. Arrival in the post-operative recovery room was defined as zero hours after surgery. Figure-1 depicts the CONSORT diagram.

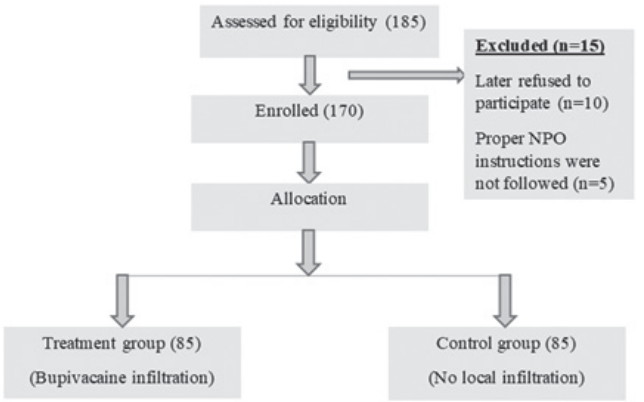

Figure-1. Consort diagram for the flow of patients involved in the study

The collected data was then analyzed by "IBM-SPSS statistics", version 24. Frequencies and percentages were computed for categorical variables. Non-normally distributed variables were expressed as median with inter-quartile range (IQR) while mean and standard deviation were calculated for normally distributed dat. Chi-square or Fisher-exact test were used to compare qualitative data. Mann-Whitney U test or independent sample t-test were applied to compare quantitative data. P-value < 0.05 was considered significant.

RESULTS

Total 170 patients were enrolled in this study (85 in each group). Table-I displays comparison of socio-demographic parameters among the two study arms. The two study arms did not differ on the basis of any socio-demographic characteristic except gender (p=0.036).

At baseline systolic blood pressure was 132 (IQR=128-142) mm Hg and 138 (IQR=135-141) mm Hg among intervention and control group respectively (p=0.013). Diastolic blood pressure 82 (IQR=76-86) mm Hg and 82 (IQR=79-86) mm Hg for intervention and control group respectively (p=0.237). SPO_2 was 98 (IQR=97-98) for intervention and control group 98 (IQR=97-98) (p=0.087). Table-II presents comparison of VAS score, analgesia consumption and incidence of pain at different time intervals among the two study groups. Post-operatively at 3rd hour, there median VAS score (p<0.001), incidence of abdominal pain (p=0.003) and incisional pain (p<0.001) were significantly higher in control group than intervention group. Following the 6th hour of surgery, median VAS score (p<0.001), analgesia consumption (p<0.001), incidence of abdominal pain (p=0.041), incisional pain (p<0.001) and shoulder pain (p<0.001) were significantly lower

Patients' Features	Total N (%)	Intervention Group N (%)	Control Group N (%)	P-Value
Age (in years)#	48 (46 – 53)	49 (46 – 53)	48 (46 – 54.5)	0.608
Weight (in Kg)#	68 (62 – 73)	69 (64 – 73)	68 (62 – 74)	0.933
Gender				
Male	21(12.4)	6(7.1)	15(17.6)	0.036
Female	149(87.1)	79(92.9)	70(82.4)	
ASA grade				
I	119(70)	63(74.1)	56(65.9)	0.241
II	51(30)	22(25.9)	29(34.1)	
Duration of surgery#	53 (51-54)	52 (51 – 54)	53 (51 – 54)	0.548

Table-I. Comparison of socio-demographic features among intervention and control group
Intervention group: bupivacaine solution; Control group: standard of care; #: Data is expressed as median with IQR

in group receiving local infiltration of bupivacaine. Median time to rescue analgesia was 12 (IQR=6-12) hours and 6 (IQR=6-9) hours among the intervention and control group (p<0.001).

Pain Status	Intervention Group N (%)	Control Group N (%)	P-Value
At 3rd hours			
VAS score#	0 (0 – 2)	2 (0 – 2)	<0.001
Analgesia consumption#	0 (0 – 0)	0 (0 – 0)	0.204
Abdominal pain	31(36.5)	58(68.2)	<0.001
Incisional pain	3(3.5)	56(65.9)	<0.001
Shoulder pain	5(5.9)	11(12.9)	0.115
At 6th hours			
VAS score#	2 (0 – 4)	4 (4 – 6)	
Analgesia consumption#	0 (0 – 0)	50 (0 – 50)	<0.001
Abdominal pain	38(44.7)	63(74.1)	<0.001
Incisional pain	19(22.4)	56(65.9)	<0.001
Shoulder pain	17(20)	66(77.6)	<0.001
At 9th hours			
VAS score#	4 (4 – 5)	6 (4 – 8)	<0.001
Analgesia consumption#	0 (0 – 50)	50 (1 – 100)	<0.001
Abdominal pain	45(52.9)	71(83.5)	<0.001
Incisional pain	26(30.6)	60(70.6)	<0.001
Shoulder pain	64(75.3)	83(97.6)	<0.001
At 12th hours			
VAS score#	6 (4 – 6)	6 (4 – 6)	0.169
Analgesia consumption#	50 (0–50)	50 (0 – 50)	0.119
Abdominal pain	67(78.8)	72(84.7)	0.321
Incisional pain	55(64.7)	62(72.9)	0.246
Shoulder pain	82(96.5)	85(100)	0.081

Table-II. Comparison of pain status among the two study arms at different time intervals

Intervention group: bupivacaine solution; Control group: standard of care; #: median with IQR

DISCUSSION

LC is a minimally invasive surgery that is frequently done in a day care setting. It is now widely accepted and preferred to remove the gallbladder using minimally invasive surgical procedures for the treatment of symptomatic gallstone disease. Avoiding a subcostal incision and manipulating the colon as little as possible reduce postoperative pain, speed up function recovery, and cut down on hospital stays overall. The cause of pain following LC is diverse and multifactorial in nature. Patients may have substantial postoperative pain, and numerous studies are currently being conducted to determine better methods to further lessen this suffering.[15,16]

In clinical practice, local anesthetics are frequently used to both prevent and treat pain during surgery. By raising the threshold for electrical excitation, local anesthetics typically prevent nerve cells from producing an action potential. From the amide category of local anesthetics, bupivacaine is a strong local anesthetic with distinctive properties.[17,18] One method for reducing postoperative pain after a variety of surgical operations has been the infiltration of local anesthetics to wound. The procedure reduces somatic pain brought on by the surgical wound without having any significant negative consequences.[19] Bupivacaine is reported to be injected intraperitoneally in amounts ranging from 10 to 100 ml at doses between 50 and 200 mg. Plain bupivacaine is administered intraperitoneally at a dose of 100–150 mg, producing plasma concentrations in the range of 0.9–1.14 g/ml, much below the lethal level of 3 g/ml.[20] This study used 20 ml of 0.25% bupivacaine solution for port site infiltration.

This study analyzed that median VAS score post-operatively from third to 9 hour with interval of 3 hours was considerably higher in control group than group received local infiltration of bupivacaine. A randomized control trial was conducted in Pakistan to study efficacy of large volume of diluted bupivacaine injected intraperitoneally during LC. This trial also observed significantly lower pain scores in group injected with bupivacaine than placebo group. From extubation till 12 hours following LC lower pain score was observed in intervention.[21] A double-blinded control trial from India reported that post-operative pain score was significantly lower in bupivacaine group than placebo group throughout the study period.[15] Another similar study from Bangladesh studied local wound

infiltration of bupivacaine versus placebo, reported that considerably higher pain score among placebo group from 2nd post-operative hour till 1oth post-operative hour.[14]

As in this study the pain score was higher in control group from third post-operative hour till ninth post-operative hour, likewise analgesic requirement was also higher in control group than intervention group. However this significantly higher requirement was seen at sixth and ninth post-operative hour. Another fact that we observed in this study was an increasing trend of pain score with time. In fact, there was increase in incidence of abdominal, incisional and shoulder pain with the time. Nevertheless the incidence of abdominal, incisional and shoulder pain and overall pain score were significantly lower for intervention group than control group. Although the difference was not seen in among the two groups at 12th hour post-operatively. Firstly, the most likely phenomenon for no difference in analgesic requirement at third hour may be the lower pain score for which patients did not demanded analgesia. Secondly, an explanation for increase in pain incidence and pain score with the time is the action time of anesthetic agent after which the pain incidence is usually higher. This increase in pain score with time is also evident in other studies.[15,21] In this study, a median time to rescue analgesia for bupivacaine group was 12 hours as compared to 6 hours in control group. Mana et al also reported higher analgesia duration among bupivacaine group than placebo group (16.53 ±2.65 versus 0.99 ±0.51).[21] Das et al reported mean duration of analgesia was 7.93±1.44 for bupivacaine group and 4.47±0.86 for placebo group with a significant difference.[15]

This study reported experience of a single center institute and we did not aim to observe complication like nausea and vomiting or others. Further post-operative length of stay and was also not determined in this study. Thus, we avoid to generalize the study results on entire population. However a larger sample size from multi-center institutions addressing the gaps of this study can verify our findings.

CONLSUION

This study found lower pain intensity and higher time of rescue analgesia to be associated with local infiltration of bupivacaine at port as compared to control group in the early post-operative period among patients underwent laparoscopic cholecystectomy.

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2	Asim Masroor Rashid	Study Protocol, Proof reading.	
3	Rizwan Ahmed Khan	Literature review, Critical review.	