The evaluation of efficacy and safety of paravertebral block for perioperative analgesia in patients undergoing laparoscopic cholecystectomy

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ABSTRACT

Background: Paravertebral block is a popular regional anesthetic technique used for perioperative analgesia in multiple surgical procedures. There are very few randomized trials of its use in laparoscopic cholecystectomy in medical literature. This study was aimed at assessing its efficacy and opioid-sparing potential in this surgery. **Methods:** Fifty patients were included in this prospective randomized study and allocated to two groups: Group A (25 patients) receiving general anesthesia alone and Group B (25 patients) receiving nerve-stimulator–guided bilateral thoracic Paravertebral Block (PVB) at T6 level with 0.3 ml/kg of 0.25% bupivacaine prior to induction of general anesthesia. Intraoperative analgesia was supplemented with fentanyl (0.5 µg/kg) based on hemodynamic and clinical parameters. Postoperatively, patients in both the groups received Patient-Controlled Analgesia (PCA) morphine for the first 24 hours. The efficacy of PVB was assessed by comparing intraoperative fentanyl requirements, postoperative VAS scores at rest, and on coughing and PCA morphine consumption between the two groups. **Results:** Intraoperative supplemental fentanyl was significantly less in Group B compared to Group A (17.6 µg and 38.6 µg, respectively, $P = 0.001$). PCA morphine requirement was significantly low in the PVB group at 2, 6, 12, and 24 hours postoperatively compared to that in Group A (4.4 mg vs 6.9 mg, 7.6 mg vs 14.2 mg, 11.6 mg vs 20.0 mg, 16.8 mg vs 27.2 mg, respectively; $P < 0.0001$ at all intervals). **Conclusion:** Pre-induction PVB resulted in improved analgesia for 24 hours following laparoscopic cholecystectomy in this study, along with a significant reduction in perioperative opioid consumption and opioid-related side effects.

Key words: *Laparoscopic cholecystectomy, opioid-sparing effect, paravertebral block, pre-emptive analgesia*

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INTRODUCTION

Laparoscopic cholecystectomy is one of the most commonly performed minimally invasive surgical procedures. Pain after laparoscopic cholecystectomy is complex and multifactorial. Adequate perioperative analgesia is an important requisite for improved patient outcome and functional recovery.

Studies have been done in the recent past to assess the nature and mechanism of pain following laparoscopic cholecystectomy,[1-3] and attempts have been made to tailor the various analgesic modalities according to the mechanism involved, eg, use of non-steroidal anti-inflammatory drugs such as ketorolac, tenoxicam; pre-emptive analgesic regimens containing ketamine or gabapentin; intraperitoneal local anesthetics; infiltration of the incision site with local anesthetics; and regional anesthesia techniques including thoracic epidural technique.

Paravertebral Block (PVB) is a regional anesthetic technique resulting in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous dermatomes above and below the site of injection. The last two decades have witnessed a renaissance in the application of PVB, with studies showing efficacy in inguinal herniorrhaphy, breast surgery, and thoracoscopic surgery.[4-6]

This present study was designed to assess the efficacy and safety of the PVB for analgesia in patients undergoing laparoscopic cholecystectomy.

METHODS

This study included 50 patients of American Society of Anesthesiologists (ASA) grades 1 and 2 who were scheduled for laparoscopic cholecystectomy. Departmental committee clearance was obtained and informed consent was taken.
Exclusion criteria:
a. Patient refusal to participate
b. Local sepsis at the site of block
c. Severe chest wall deformity, eg, scoliosis
d. Coagulation abnormalities
e. Known hypersensitivity to local anesthetics.

The patients selected for the study were randomly allocated to two groups: Group A consisted of 25 patients receiving general anesthesia alone and group B comprised 25 patients receiving bilateral PVB prior to induction of general anesthesia.

All selected patients underwent a routine pre-anesthetic assessment. Patients were informed regarding postoperative pain assessment with Visual Analog Scale (VAS) as well as postoperative analgesia with Patient-Controlled Analgesia (PCA) using morphine.

Patients in both groups were pre-medicated with oral diazepam, 0.2 mg/kg, two hours before the procedure. Baseline parameters including pulse, Non-Invasive Blood Pressure (NIBP) and SpO_2 were recorded before induction of general anesthesia.

Anesthesia was induced with fentanyl (2 µg/kg, IV) followed by propofol (2.5 mg/kg, IV). Intubation of the trachea with an adequate sized endotracheal tube was facilitated by muscle-relaxation using vecuronium bromide (0.1 mg/kg).

Anesthesia was maintained with oxygen and nitrous oxide (33%: 66%) isoflurane and vecuronium. Supplemental analgesia was provided intraoperatively with fentanyl (0.5 µg/kg) on the basis of presence of any one of the following parameters—rise in heart rate or systolic blood pressure by more than 20% of the baseline values, sweating, or lacrimation. The number of doses and the total amount of supplemental analgesia with fentanyl intraoperatively were recorded for comparison between the two groups.

Monitoring and observation during the intraoperative period included recording of pulse and NIBP every 15 min. The End-tidal CO_2 ($EtCO_2$) was maintained at 35-40 mm Hg.

Baseline VAS scores at rest and on coughing were noted in the recovery room in the immediate postoperative period, and the patients in both groups were provided PCA morphine (1 mg IV bolus with a lockout period of 10 minutes and a maximum dose of 24 mg in 4 hours). The patients were instructed to take boluses of PCA morphine when the VAS score became greater than 3. Pulse, NIBP, SpO_2, respiratory rates, and VAS scores were recorded at 0, 2, 6, 12, and 24 hours after the surgery. The total amount of PCA morphine used at 2, 6, 12, and 24 hours postoperatively were recorded for comparison between the groups. Side-effects such as nausea, vomiting, respiratory depression, hypotension, and chest pain were noted. The scale for assessing Postoperative Nausea And Vomiting (PONV) included a score of zero for no nausea or vomiting, one for an episode of nausea but no vomiting, two for an episode of vomiting or severe retching, and three for two or more episodes or vomiting. Patients with a score of two or higher received ondansetron (0.1 mg/kg, IV) as a rescue anti-emetic.

Respiratory depression was defined as respiratory rate less than 8 per minute or SpO_2 below 90%.

Paravertebral nerve block technique
Bilateral PVB was performed at the T5-6 level in patients belonging to group B, prior to induction of anesthesia. With the patient in sitting or lateral position, a point 2.5-3 cm lateral to the midline was marked, on either side. Following aseptic preparation of the skin, the sites of injection were infiltrated with lidocaine 2%. For proper localization of paravertebral space, a nerve stimulator-guided technique was used. A 21-G insulated needle attached to a nerve stimulator was introduced at a right angle to the skin at the marked point for injection, using the settings: 5 mA and 1 Hz. Direct muscle stimulation caused initial contraction of the paraspinal muscles. On further advancement of the needle, the contractions ceased as the tip of the needle reached the costo-transverse ligament. When the needle entered the paravertebral space, contractions of the ipsilateral rectus abdominis muscle were seen. The needle was then gently manipulated into a position to allow a muscle contraction with the reduction of the stimulating current to a predetermined minimum value (0.4-0.8 mA). Thereafter, 0.3 ml/kg of 0.25% bupivacaine was injected, and a similar approach was used for the PVB on the other side.

Statistical analysis
The data were recorded in 'Microsoft Excel 2000' format and analyzed using 'SPSS Version 15.0'. Continuous variables were compared and analyzed using Student's *t* test. Pain scores (VAS score) and PONV scores were compared using Mann–Whitney *U* test. Qualitative data were analyzed using the Chi-square test or Fischer's test, whichever applicable.

RESULTS

A total of 50 patients, scheduled for elective laparoscopic cholecystectomy were included in this prospective, randomized study and allocated to two groups consisting of 25 patients each. The demographic parameters (age, weight, sex, ASA physical status) of the patients in both the groups were comparable [Table 1]. The mean duration of surgery in the control and study groups were 77.0±18.48 minutes and 78.6±17.35 minutes, respectively. The intraoperative hemodynamic parameters (heart rate, Systolic Blood Pressure (SBP), diastolic blood pressure, SpO$_2$, EtCO$_2$) did not differ significantly between the groups. Hypotension was noted in one patient intraoperatively in the study group. The SBP decreased to 78 mm Hg in this patient, requiring three boluses of mephentermine (6 mg each bolus) to maintain the SBP >90 mm Hg during the surgery.

The patients receiving pre-induction PVB required significantly less supplemental fentanyl intraoperatively (38.6±23.16 μg in the control group compared to 17.60±19.20 μg in the study group, *P*=0.001). Eleven out of 25 patients (44%) in the PVB group did not require any additional intraoperative analgesia compared to only four patients (16%) in the control group.

The patients in the control group reported significantly more pain at rest and on coughing in the immediate postoperative period compared to those in the study group (as reflected in the VAS scores on arrival to the post-anesthesia care unit). The mean VAS score at rest was significantly higher in the control group in the immediate postoperative period (mean scores 5.68±1.34 vs 3.64±1.57 in the study group; *P*<0.001). Patients in the study group reported significantly less pain on coughing in the immediate postoperative period (mean VAS scores 5.24±1.5 and 7.04±1.24 in the study and control groups, respectively; *P*<0.001). The mean VAS scores at subsequent time intervals (2, 6, 12, and 24 hours) did not differ significantly between the two groups.

In the post-anesthesia care unit, the patients in both groups received PCA morphine for 24 hours. The cumulative PCA morphine requirement in the PVB group was significantly less compared to the control group (mean 16.80±3.37 mg compared to 27.24±5.08 mg in the control group; *P*<0.001) [Table 2].

The hemodynamic parameters on the first postoperative day did not differ significantly between the groups.

The patients in both the groups were observed for adverse effects postoperatively. None of the patients had respiratory depression and pneumothorax. Urinary retention was noted in two groups in the control group

Table 1: Comparison of demographic data

	Group A	Group B	*P*
Age (years) (mean±SD)	39.64±8.75	35.76±8.83	0.12
Weight (kg) (mean±SD)	58.92±6.79	57.20±8.58	0.43
Sex ratio (Male:Female)	5:20	7:18	0.90

Table 2: PCA morphine requirements

Time (hours)	Group A (mean±SD) mg	Group B (mean±SD) mg	*P*
2	6.92±1.077	4.44±1.26	*P*<0.001
6	14.24±2.74	7.60±2.17	*P*<0.001
12	20.04±3.96	11.68±2.75	*P*<0.001
24	27.24±5.08	16.80±3.37	*P*<0.001

compared to none in the study group. There was a higher incidence of PONV in the control group in the immediate postoperative period (mean rank 30.14 compared to 20.86 in the PVB group; *P*=0.01; Mann-Whitney *U* test). The PONV scores at subsequent time intervals were comparable between the two groups. The number of patients requiring rescue anti-emetic drug in the immediate postoperative period in the control group was 60% compared to 36% in the PVB group.

DISCUSSION

Adequate perioperative analgesia is an important requisite for improved patient outcome and functional recovery. Intensity of pain and the risk-benefit ratio of different analgesic modalities are procedure-related.[7] Procedure-specific pain management strategies for laparoscopic cholecystectomy are currently being investigated.[8] Hence, we assessed the efficacy and safety of PVB in laparoscopic cholecystectomy.

Analysis of our results revealed a significant decrease in intraoperative supplemental fentanyl consumption in the study group (mean requirements 38.6 μg vs 17.6 μg in the control and study groups, respectively; *P*<0.05). Since general anesthesia was administered in the study group immediately after the PVB in most patients, the success of the block by the loss of pin-prick or temperature sensation could not be assessed. Hence, the finding of reduced intraoperative fentanyl requirement in the study group assumes greater clinical relevance. Similar results have been reported in thoracoscopic surgery in patients receiving single-dose, multilevel (six injections of 5 ml of 0.5% bupivacaine each) PVB.[9] Naja *et al.* (2004) assessed the efficacy of bilateral PVB in laparoscopic cholecystectomy but did not compare intraoperative analgesic requirements between the groups.[10]

The mean VAS score at rest was significantly higher in the control group in the immediate postoperative period.

More patients in the control group reported moderate to severe pain (92% compared to 44% in the study group; $P<0.05$) immediately after awakening, while a significant number of patients in the PVB group awoke pain free. Fifty-six percent (56%) of the patients in the study group had a VAS score <3 compared to 8% in the control group, ($P<0.05$) after the surgery.

These findings affirm that the pre-induction PVB was effective in reducing pain intensity in a significant number of patients in the study group because the mean VAS score at rest was less in the study group despite less intraoperative fentanyl consumption.

The subsequent mean VAS scores at rest were less in our study group at 2, 6, 12, and 24 hours postoperatively, but the difference was not statistically significant. This can be explained by the use of PCA morphine postoperatively in both the groups and the wearing off of the PVB. The patients in the control group required more PCA morphine in order to keep the VAS score <3 throughout the first postoperative day compared to those in the study group.

Dynamic pain relief is crucial to facilitate early recovery in the postoperative period. The efficacy of PVB in attenuating dynamic pain was assessed in this study by comparing VAS scores on coughing between the groups. The patients in the study group reported significantly less pain on coughing in the immediate postoperative period (mean VAS scores 5.24±1.5 and 7.04±1.24 in the study and control groups, respectively; $P<0.001$).

However, VAS scores on coughing were comparable between the two groups during the subsequent postoperative recordings (2, 6, 12, and 24 hours). These findings can again be attributed to the PCA morphine consumption in both the groups.

The mean VAS scores on coughing were higher than those at rest in both the groups at all intervals. However, unlike those at rest, the mean VAS scores on coughing at 2, 6, 12, and 24 hours postoperatively in both the groups were >3, thus reflecting inadequate analgesia on coughing. A high percentage of patients reported moderate pain (VAS score: 4-6) on coughing at 2, 6, 12, and 24 hours postoperatively in both the groups (64%, 64%, 72%, and 80% in Group A and 72%, 60%, 64%, and 64% in Group B, respectively).

These findings suggest that neither the PCA morphine could adequately relieve the pain on coughing in the control group, nor could the PVB result in adequate dynamic pain relief in the study group.

The results in our study group are in contrast with those observed in the PVB group by Naja *et al.* (2004) because only 20%, 10%, and 14% of the patients reported mean VAS scores on coughing >3 in their study group at 6, 12, and 24 hours postoperatively.[10] This difference in results can be explained by the use of a combination of lignocaine, bupivacaine, fentanyl, and clonidine for PVB in their study compared to bupivacaine only in our PVB group. Adjuvants such as fentanyl and clonidine are of proven efficacy in enhancing the quality and duration of analgesia following peripheral nerve blocks.[11]

Patients in the PVB group in our study required significantly less PCA morphine compared to those in the control group, and the difference was significant statistically throughout the first postoperative day (mean cumulative PCA morphine requirements 16.80±3.37 mg vs 27.24±5.08 mg in the study and control groups, respectively; $P<0.05$).

The significant reduction in analgesic consumption for the first 24 hours in our study group was well beyond the reported duration of bupivacaine in peripheral nerve blocks. This finding may suggest the efficacy of PVB as a pre-emptive analgesic modality in laparoscopic cholecystectomy. Pre-incisional PVB may have led to inhibition of central sensitization and resulted in improved pain relief beyond the pharmacological duration of bupivacaine. In a study involving patients undergoing breast surgery, Greengrass *et al.* (1996) reported improved analgesia for 24 hours in patients receiving PVB with bupivacaine alone.[12] Kairaluoma *et al.* (2000) also demonstrated that pre-incisional PVB resulted in reduction of the prevalence of chronic pain for one year following breast surgery.[13]

Opioid-sparing effects of PVB

Laparoscopic cholecystectomy is now being increasingly performed on an outpatient basis, and hence effective analgesia with opioid-sparing attributes is being preferred to hasten postoperative recovery. The patients receiving PVB in our study required 38% less PCA morphine compared to those in the control group. Intraoperative supplemental fentanyl requirement in the study group was 54% less than the control group. Kehlet *et al.* (2005) have extensively reviewed opioid-sparing effects of different regimens and remarked that approximately 30% reduction in opioid requirement was clinically significant.[14]

An opioid-sparing analgesic technique should also result in decreased incidence of opioid-related side effects. Hence, we compared the occurrence of opioid-related adverse effects between the two groups.

PONV is one of the most unpleasant symptoms perceived by the patients following laparoscopic cholecystectomy. Patients in the PVB group reported significantly less PONV than those in the control group in the immediate

postoperative period in our study. Rescue anti-emetic was required by 15 of 25 patients (60%) in the control group immediately postoperatively compared to only 9 of 25 patients (36%) in the study group. This difference reflects significant opioid-sparing benefit of PVB in terms of reduced PONV but did not attain statistical significance, presumably, due to the small sample size. Similar limitation of various trials assessing opioid-sparing analgesic regimens had been reported by Kehlet *et al.* in 2005.[14] They suggested that the different trials estimated the sample size in order to demonstrate a certain reduction in opioid requirements for effective analgesia, but, subsequently, found it insufficient to reflect a similar difference in opioid-related side effects. Requirement of a larger sample size was suggested in order to find a statistically significant difference in the side effects.

Baumgarten *et al.* (2007) also remarked the efficacy of PVB in terms of reducing PONV after hernia surgery and recommended PVB as the anesthetic technique of choice in ambulatory hernia repair.[15]

Urinary retention was noted in 2 of 25 patients in the control group compared to none in the study group. This can be attributed to the greater PCA morphine requirement in the control group.

Hence, in summary, the use of PVB in our study resulted in significantly better pain relief, reduced opioid requirements for the first 24 hours, and a decreased incidence of opioid-related side effects.

Complications related to PVB

We also aimed to assess the safety of PVB in our study. Karmakar (2001) in his review of PVB reported the following complications—pleural puncture, pneumothorax, epidural spread, injection into the subarachnoid space, intravascular injection, and Horner's syndrome.[16]

None of the patients in the PVB group reported chest pain or breathlessness indicative of pneumothorax in our study. This could be attributed to the enhanced safety associated with the nerve-stimulator–guided technique of PVB. Improved safety with nerve-stimulator–guided technique has also been suggested in few previous studies.[17,18] Ultrasound guidance has further enhanced the safety of PVB as illustrated in some recent studies.[19,20]

Epidural and subarachnoid spread of local anesthetic injected into the paravertebral space has also been reported. One of 25 patients in our study probably had an epidural spread as reflected in the persistent intraoperative hypotension and mephentermine requirements. Klein *et al.* (2002) also noted epidural spread in one of 24 patients receiving PVB for inguinal herniorrhaphy.[21]

CONCLUSION

The results of improved, prolonged pain relief and reduced opioid-related adverse effects in our study group reflected two important attributes of PVB in laparoscopic cholecystectomy—pre-emptive effect and opioid-sparing efficacy. Dynamic pain, unlike pain at rest, was inadequately relieved by PVB with bupivacaine alone. Further studies might be needed to assess the efficacy of adjuvants in PVB in reducing dynamic pain postoperatively.

REFERENCES

1. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalescence after laparoscopic cholecystectomy. Eur J Surg 2001;167:84-96.
2. Wills V, Hunt D. Pain after laparoscopic cholecystectomy. Br J Surg 2000;87:273-84.
3. Joris J, Thiry E, Paris P, Weerts J, Lamy M. Pain after laparoscopic cholecystectomy: Characteristics and effect of intraperitoneal bupivacaine. Anesth Analg 1995;81:379-84.
4. Klein SM, Greengrass RA, Weltz C, Warner DS. Paravertebral somatic nerve block for outpatient inguinal herniorrhaphy. An expanded case report of 22 patients. Reg Anesth Pain Med 1998;23:306-10.
5. Klein SM, Bergh A, Steele SM, Georgiade GS, Greengrass RA. Thoracic paravertebral block for breast surgery. Anesth Analg 2000;90:1402-5.
6. Soni AK, Conacher ID, Waller DA, Hilton CJ. Video-assisted thoracoscopic placement of paravertebral catheters. A technique for postoperative analgesia for bilateral thorascopic surgery. Br J Anaesth 1994;72:462-4.
7. Rowlingson JC, Rawal N. Postoperative pain guidelines – targeted to the site of surgery. Reg Anesth Pain Med 2003;28:265-7.
8. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: A critical assessment of the evidence. Anesthesiology 2006;104:835-46.
9. Hill SE, Keller RA, Smith MS, Grichnik K, White WD, D'Amico TA, *et al.* Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures. Anesthesiology 2006:104:1047-53.
10. Naja MZ, Ziade MF, Lonnqvist PA. General anaesthesia combined with bilateral paravertebral blockade (T5-6) vs. general anaesthesia for laparoscopic cholecystectomy: A prospective, randomized clinical trial. Eur J Anaesthesiol 2004;21:489-95.
11. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996;83:1046-50.
12. Greengrass R, O'Brien F, Lyerly K, Hardman D, Gleason D, D'Ercole F, *et al.* Paravertebral block for breast cancer surgery. Can J Anaesth. 1996;43:858-61.
13. Kairaluoma PM, Bachmann MS, Rosenberg PH, Pere PJ. Preincisional paravertebral block reduces the prevalence of chronic pain after breast surgery. Anesth Analg 2006;103:703-8.
14. Kehlet H. Postoperative opioid sparing to hasten recovery: What are the issues? Anesthesiology 2005;102:1083-5.
15. Baumgarten RK, Greengrass RA, Wesen CA. Paravertebral block: The holy grail of anesthesia for hernia surgery? Anesth Analg 2007;104:207.
16. Karmakar MK. Thoracic paravertebral block. Anesthesiology 2001;95:771-80.
17. Wheeler LJ. Peripheral nerve stimulation end-point for

thoracic paravertebral block. Br J Anaesth 2001;86:598-9.

18. Lang SA. The use of a nerve stimulator for thoracic paravertebral block. Anesthesiology 2002;97:521-2.

19. Cowie B, McGlade D, Ivanusic J, Barrington MJ. Ultrasound-guided thoracic paravertebral blockade: A cadaveric study. Anesth Analg 2010;110:1735-9.

20. Renes SH, Bruhn J, Gielen MJ, Scheffer GJ, van Geffen GJ. In-plane ultrasound-guided thoracic paravertebral block: A preliminary report of 36 cases with radiologic confirmation of catheter position. Reg Anesth Pain Med 2010;35:212-6.

21. Klein SM, Pietrobon R, Nielsen KC, Steele SM, Warner DS, Moylan JA, *et al.* Paravertebral somatic nerve block compared with peripheral nerve blocks for outpatient inguinal herniorrhaphy. Reg Anesth Pain Med 2002;27:476-80.

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