



Evaluation of Continuous Thoracic Paravertebral Block for Post-Operative Pain Relief in Patients Undergoing Open Cholecystectomy

KEYWORDS

Paravertebral Block, Postoperative Pain, Open Cholecystectomy, Post-operative Nausea and Vomiting, Dynamic Pain

*Dr Pravin Kumar Das

Associate Professor, Department of Anesthesiology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, INDIA * Corresponding Author

Dr Abinash Patro

Senior Resident, Department of Anesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, INDIA.

Dr Sujeet Gautam

Assistant Professor, Department of Anesthesiology, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, INDIA.

ABSTRACT

Background: The aim of this prospective, randomized, single blind study was to evaluate the efficacy of continuous thoracic paravertebral block for post-operative pain relief in patients undergoing open cholecystectomy. **Methods:** Sixty adult patients undergoing open cholecystectomy under general anaesthesia were randomized into two groups; Group C patients received systemic analgesics alone; Group P patients received intra-operative and post-operative paravertebral infusion of a solution containing 0.1% bupivacaine with 1 µg ml⁻¹ fentanyl at 7 ml hr⁻¹ in addition to systemic analgesics. Primary outcome measures were postoperative pain during rest (static pain) and coughing (dynamic pain); secondary outcome measures were post-operative patient controlled fentanyl consumption, post-operative nausea and vomiting, requirement of rescue antiemetic, hypotension, sedation, pruritus, motor block and respiratory depression; these were assessed at 6 hourly intervals for a period of 48 hrs in the post-operative period. Results were analyzed by the student's T-test, Chi square test, Mann Whitney test and fisher's exact test. P value <0.05 was considered significant. **Results:** The two groups were similar with regard to demographic factors (P>0.05). Paravertebral analgesia group caused a significant reduction in VAS scores during rest and coughing (static and dynamic pain) and post-operative patient controlled fentanyl consumption as compared to the control group (P<0.05). The incidence of side effects were similar in the two groups (P>0.05). **Conclusions:** Continuous thoracic paravertebral block reduces the post-operative static and dynamic pain along with post-operative patient controlled fentanyl consumption in patients undergoing open cholecystectomy.

Introduction

Cholecystectomy is one of the commonly performed abdominal surgeries indicated in biliary colic secondary to cholecystitis, choledocholithiasis or biliary pancreatitis; currently most of the cholecystectomies are done by laparoscopic approach, however open cholecystectomy is indicated in patients with suspicion of malignancy, cholecystoenteric fistula, and patients unable to tolerate pneumoperitoneum due to haemodynamic instability or severe cardiorespiratory comorbidity. There are different approaches for open cholecystectomy: the midline incision or right subcostal, Kocher's incision.

Right subcostal incision is widely acceptable as it provides good exposure to the surgical site; but the incision size is very large and it involves significant muscle cutting in the subcostal area. This results in severe post operative pain and impaired diaphragmatic function giving rise to impaired pulmonary function after open cholecystectomy (1, 2). Hence, patients undergoing open cholecystectomy require a good post operative pain relief to decrease post operative pulmonary complication and early mobilization.

Pain relief in patients undergoing this procedure is usually provided by thoracic epidural analgesia and or systemic analgesics. Epidural analgesia is considered as a highly effective option for postoperative pain management in abdominal surgeries, but associated complications and contraindications may limit its usage (3-6). Systemic analgesics in the form of intra-venous opioid analgesia may cause opioid-related side effects and often provide inadequate analgesia (7). Hence, alternative safer approaches of post-operative pain management are required.

Paravertebral block (PVB) has been increasingly being used for post-operative pain management and shown to be as efficient as epidural analgesia in patients undergoing thoracic or abdominal surgeries (8). The better deafferentation provided by PVB in comparison to epidural analgesia provides better preservation of lung functions; it also provides better haemodynamic stability by providing unilateral analgesia. It has also been reported to be effective in open cholecystectomy (9); however, the effectiveness of continuous thoracic PVB has not been evaluated in patients undergoing open cholecystectomy.

In this prospective, randomized, single blind study we have compared the post-operative pain relief provided by continuous thoracic PVB with systemic analgesics in patients undergoing open cholecystectomy.

Materials & Methods:

Study Design

The present study was a prospective, randomized, single blind study; the study protocol was approved from the institutional ethical committee and written informed consent was obtained from all the patients.

Inclusion Criteria

Adult patients (18-70 yrs) of either sex, ASA physical status I and II, scheduled for open cholecystectomy under general anaesthesia were included in the study.

Exclusion Criteria

Patient refusal, coagulation disorders, signs of local or systemic infection, history of regular intake of analgesics, anatomical abnormalities.

Randomisation, Group Allocation and Study Intervention

Sixty patients meeting the inclusion criteria during the pre-anesthetic evaluation were randomly assigned into two equal groups of 30 each with the help of a computer generated table of random numbers; Group C patients received systemic analgesics alone; Group P patients received intra-operative and post-operative paravertebral infusion of a solution containing 0.1% bupivacaine with 1 µg ml⁻¹ fentanyl at 7 ml hr⁻¹ in addition to systemic analgesics; the infusion was provided by an elastomeric pump (Baxter Healthcare Corporation, California, USA).

A random allocation sequence concealed in 60 consecutively numbered, sealed envelopes, determining group distribution, were computer generated by a project nurse not involved in the trial. The envelopes were opened on the morning of surgery by the preoperative nurse, not involved in the study.

An 18G epidural catheter was placed in the paravertebral space at T 6 or T7 level in Group P patients, under local anesthesia prior to induction, by an anesthesiology resident not involved in the study; the paravertebral catheter was placed using loss-of-resistance technique according to Eason and Wyatt (10); before catheter placement 15ml 0.1% bupivacaine with 1 µg ml⁻¹ fentanyl was injected in the paravertebral space. The paravertebral infusion via elastomeric pump was started after induction of anesthesia. The Anesthesia technique was standardized in all the patients. Patients were induced with fentanyl 2-3 µg kg⁻¹ and propofol 1.5-2.5 mg kg⁻¹; orotracheal intubation was facilitated by vecuronium 0.1 mg kg⁻¹. Anesthesia was maintained with propofol, isoflurane and oxygen air mixture. A reduction in systolic blood pressure of more than 20% or a systolic blood pressure below 90 mm Hg was considered as hypotension and was treated by infusion of isotonic sodium chloride or mephentramine 5 mg intravenously in incremental doses. At the end of surgery residual neuromuscular paralysis was antagonized with neostigmine 0.04 mg.kg⁻¹ and glycopyrrolate 0.01 mg.kg⁻¹. Following satisfactory recovery, the patients were extubated and shifted to the post-anesthesia care unit. In the post-operative period patients received IV fentanyl via patient controlled analgesia device with patient activated dose of 10µg/mL, lock out interval of 5 minute; with a maximum allowable fentanyl dose being 2µg kg⁻¹ hr⁻¹.

Outcome Measures and Patient Assessment

Primary outcome measures were postoperative pain during rest (lying supine: static pain) and coughing (dynamic pain); secondary outcome measures were post-operative patient controlled fentanyl consumption, post-operative nausea and vomiting (PONV), requirement of rescue antiemetic, hypotension, sedation, pruritus, motor block and respiratory depression. All these measures were assessed by acute pain nurse blinded to group allocation.

All patients were assessed on arrival to post anaesthesia care unit (PACU) (0 hr), then at 6 hourly intervals for a period of 48 hrs in the post-operative period. Assessment of pain was done by a 100mm visual analogue scale (VAS); 0= no pain, 100mm= worst imaginable pain. All patients received acetaminophen 1 g intravenously (IV) every 6 hr during this period. Motor block was measured using the modified Bromage scale (0 = no motor block, 1 = inability to raise extended leg, 2 = inability to flex knee, 3= inability to flex ankle) (11). The severity of PONV was graded on a 4 point ordinal scale (0 = no nausea or vomiting, 1 = mild nausea, 2 = moderate nausea, and 3 = severe nausea

with vomiting) (12). Rescue antiemetic ondansetron 4 mg IV, was given to all patients with PONV of grade >2. The Ramsay sedation scale (Awake levels were: 1- anxious, agitated or restless; 2- cooperative, oriented and tranquil; 3- responds to command; asleep levels were dependent on patient's response to a light glabellar tap or loud auditory stimulus; 4- brisk response; 5- a sluggish response; 6- no response) was used to assess the sedation; patients with a sedation scale of > 4 were considered as sedated (13). Respiratory depression was defined as respiratory rate < 8 breaths/min and oxygen saturation < 90% without oxygen supplementation.

Sample Size Estimation

Sample size calculation was based on the findings of a pilot study performed at our institute. Assuming that the therapeutic drug would reduce postoperative pain VAS scores by 30% as compared to the placebo a sample size of 25 patients was required in each group for the results to be significant (with $\alpha = 0.05$ and power=80%); To take care of any drop outs we enrolled 30 patients in each group.

Statistical Analysis

Demographic data were analyzed with student's T-test for continuous variables and chi square test for categorical variables. The VAS scores were analyzed with Mann Whitney test; post-operative patient controlled fentanyl requirement was analyzed with student's T-test; the incidence of PONV, sedation, motor block and respiratory depression were analyzed with Fisher's exact test. The package SPSS 22.0 (SPSS Inc, Chicago, IL) was used for statistical analysis. $P < 0.05$ was considered significant.

Results

A total of ninety eight patients were assessed for eligibility between September 2015 to March 2016, out of which sixty patients were randomized into two groups; fifty eight patients i.e. 96% of the randomized patients completed the study (Fig. 1). The reasons for patients not being randomized were refusal to participate in the study (25 patients), chronic analgesic consumption (5 patients) and inability to operate patient controlled analgesia device (8 patients). Two patients were excluded from the study following initial randomization and were therefore not subjected for further analysis (2 patients needed re-exploration on account of postoperative bleed). There was no difference amongst the groups as regards to age, sex, weight distribution, duration of anesthesia, duration of surgery and intra-operative fentanyl consumption ($P > 0.05$) (Table 1).

Paravertebral analgesia group caused a significant reduction in VAS scores during rest and coughing (static and dynamic pain) at all points of observation (Table 2) and post-operative patient controlled fentanyl consumption (Table 3) as compared to the control group ($P < 0.05$); however, there was no significant difference in VAS scores during rest between the two groups at 0 hr. The incidence of side effects were similar in the two groups ($P > 0.05$) (Table 4).

Discussion

We observed that continuous thoracic paravertebral block reduces the post-operative static and dynamic pain along with post-operative patient controlled fentanyl consumption in patients undergoing open cholecystectomy. Different techniques have been tried to address post-operative pain management in patients undergoing open cholecystectomy aiming for better post operative experience along with reduced incidence of post operative nausea and vom-

iting, early mobilization and reduced hospital stay. Standard techniques used for post operative pain management in open cholecystectomy are epidural analgesia and systemic analgesics in the form of opioids. Epidural analgesia is considered as the gold standard as it provides excellent analgesia. However the common side effects due to epidural block like hypotension, itching, vomiting/nausea and urinary retention limits its use; in addition, technical difficulties with insertion have been reported in up to 11% of patients along with a failure rate ranging from 17% to 37% (14-16).

Opioids have been the mainstay for the treatment of post-operative pain as it carries a low risk profile; however, opioids don't reduce dynamic pain and surgical stress (17) and develop clinically relevant resistance in hours (18-19). To add on opioids are associated with PONV and other side effects (7); therefore, management of post operative pain with opioid-sparing regimens may be helpful in minimizing post operative pain and PONV (7). In our study we have observed that continuous thoracic PVB decreases the postoperative opioid consumption significantly; the fentanyl consumption decreased by 35 % during first 24 hr and up to 44% during the second day in the PVB group.

PVB is currently being utilized for many surgical procedures both as an anesthesia technique (20) and for postoperative pain management (21). By providing unilateral analgesia it has minimal hemodynamic effects compared with spinal or epidural block; in addition it can be performed even in patients under anticoagulant therapy or with coagulopathies. The neural structures in the paravertebral space include the anterior and posterior ramus of the intercostal nerve, the rami communicantes, the sinu-vertebral nerve, and the sympathetic chain of ganglia. Blockade of sympathetic chain ganglia, which is unique in thoracic PVB, might be related to its ability to inhibit stress response. (22-23) The deafferentation provided by PVB is superior to that of epidural block resulting in better preservation of physiologic function such as functional residual capacity of the lungs (24). This intense deafferentation with resultant decrease in opioid requirements postoperatively helps in minimizing the incidence of chronic pain (25).

Open cholecystectomy involves a right sub-costal incision of 10-15 cm which offers a wide operative field; cutting of anterior rectus sheath and abdominal muscles including external oblique, internal oblique and transverse abdominis give rise to significant post-operative pain and longer recovery period owing to large painful scar (26). This also hampers effective coughing, deep breathing, and patient's mobility (1, 2). This pain hampers effective coughing, deep breathing, and patient's mobility; in addition it gives rise to chronic pain in 30-40% patients undergoing open cholecystectomy (27, 28).

Thoracic paravertebral block is a safe alternate for post-operative pain management in open cholecystectomy with minimal side effects and good quality of analgesia. Data on the use of thoracic PVB in patients undergoing cholecystectomy via a subcostal incision are limited, and the results are inconclusive (29). Giesecke et al. reported that a single preincisional thoracic paravertebral injection of bupivacaine 0.5%, 20 ml before cholecystectomy, attenuates the stress response to surgical stimuli during isoflurane anesthesia and provides complete pain relief for 1-6 h (23). In contrast, Bigler et al. (30) reported that TPVB with 0.5% bupivacaine, a 15-ml bolus dose followed by an infusion of 5 ml/h postoperatively, is inadequate as the only analgesic

after cholecystectomy, whereas a thoracic epidural infusion of bupivacaine 0.5% (5 ml/h) and morphine (0.2 mg/h) produced total pain relief. Pain scores were higher in the paravertebral group, as was the use of systemic morphine (30).

The effectiveness of continuous thoracic PVB has not been evaluated so far. In the present study we observed that continuous thoracic PVB reduces the post-operative static and dynamic pain along with post-operative patient controlled fentanyl consumption in patients undergoing open cholecystectomy. However, the incidence of side effects remained the same as in the systemic analgesic group; hence a multimodal approach involving thoracic PVB with systemic analgesics is a useful option in patients undergoing open cholecystectomy. One of the limitations of the present study is that we have evaluated thoracic PVB at a single rate of drug infusion and local anesthetic concentration; comparison of different rates and different concentration would provide more valuable information. Secondly, a number of comparisons of side effects in the two groups have been done; however, the sample size is not adequate to comment on these and we therefore suggest further studies with larger sample size which could adequately address these issues.

Conclusion:

To conclude, we observed that continuous thoracic paravertebral block reduces the post-operative static and dynamic pain along with post-operative patient controlled fentanyl consumption in patients undergoing open cholecystectomy. We therefore suggest routine usage of continuous thoracic paravertebral block for management of post-operative pain in patients undergoing open cholecystectomy.

Table 1: Demographic data

Groups Variables	Group C (N=29)	Group P (N=29)
Age (yr)	42.3 ± 10.1	45.8 ± 8.1
Weight (kg)	54.5 ± 7.6	57.2 ± 7.9
Sex (M/F)	12/ 17	10/ 19
Duration of anesthesia (min)	149.3 ± 28.4	157.2 ± 34.2
Duration of surgery (min)	115.7 ± 23.6	119.0 ± 32.2
Intra-operatively fentanyl consumption (µg)	228.1 ± 32.1	249.6 ± 46.7

Data are presented either as mean + SD or numbers; Group C: Control Group; Group P: Paravertebral Analgesia Group. *Denotes P<0.05 during intergroup comparison

Table 2: Postoperative pain (Visual Analogue Scale Scores)

	Pain		Coughing	
	Rest		Group C	Group P
	Group C	Group P	Group C	Group P
0hr	35 (13)	30 (18) *	NA	NA
6 hr	50 (35)	40 (20) *	50 (35)	40 (15) *
12 hr	50 (15)	30 (15) *	45 (35)	40 (15) *
18 hr	50 (30)	25 (15) *	55 (25)	35 (10) *
24hr	60 (25)	30 (15) *	40 (25)	30 (10) *
30 hr	50 (30)	25 (13) *	50 (30)	30 (18) *
36 hr	50 (30)	30 (15) *	40 (20)	25 (10) *
42 hr	50 (20)	25 (20) *	40 (28)	25 (15) *
48 hr	40 (15)	25 (10) *	40 (15)	35 (15) *

Data are presented as median (inter-quartile range); Group C: Control Group; Group P: Paravertebral Analgesia Group; *Denotes P<0.05 during intergroup comparison

Table 3: Post-operative Patient Controlled Fentanyl Consumption (μg)

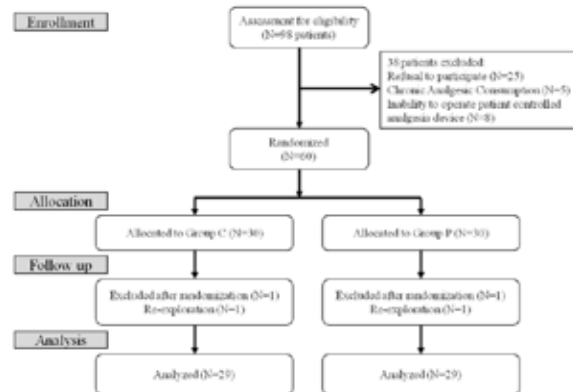
	Group C (N=29)	Group P (N=29)
0-24 hrs	677.2 \pm 55.2	402.1 \pm 68.8 *
24-48 hrs	882.8 \pm 128.5	486.9 \pm 103.8 *

Data are presented as mean values + SD; Group C: Control Group; Group P: Paravertebral Analgesia Group. *Denotes $P < 0.05$ during intergroup comparison

Table 4: Incidence of side effects

	Group C (N=29)	Group P (N=29)
PONV	3	5
Hypotension	1	0
Pruritus	1	0
Respiratory Depression	0	0
Motor Block	0	0
Sedation	0	0
Requirement of rescue antiemetic	5	6

Data are presented as numbers; Group C: Control Group; Group P: Paravertebral Analgesia Group; *Denotes $P < 0.05$ during intergroup comparison

Legend for Figures**Figure 1: Study Design**

Group C: Control Group; Group P: Paravertebral Analgesia Gr

References:

- Zahoor MU, Masroor R, Khurshid T, Azhar M et al Thoracic epidural anaesthesia for open cholecystectomy. *Journal of the college of physician and surgeon*; 2011; 21: 654-8.
- Bablekos GD, Michaelides SA, Roussou T, Charalabopoulos KA. Changes in breathing control and mechanics after laparoscopic vs. open cholecystectomy. *Arch Surg* 2006; 141: 16-22.
- Dajczman E, Gordon A, Kreisman H, Wolkove N. Long-term post-thoracotomy pain. *Chest* 1991; 99: 270-4.
- Tiipana E, Nilsson E, Kalso E. Post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. *Acta Anaesthesiol Scand* 2003; 47: 433-8.
- Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg* 2003; 75: 1349-57.
- Matthews PJ, Govenden V. Comparison of continuous paravertebral and extra-dural infusion of bupivacaine for pain relief after thoracotomy. *Br J Anaesth* 1989; 62: 204-5.
- Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: time for a reconsideration? *J Clin Anesth* 1996; 8: 441-5.
- Joshi GP, Bonnet F, Shah R, et al: A systematic review of randomized

- trials evaluating regional techniques for post-thoracotomy analgesia. *Anesth Analg* 2008; 107: 1026-1040.
- Paleczny J, Zipser P, Pysz M. Paravertebral block for open cholecystectomy. *Anestezjol Intens Ter* 2009; 41: 89-93.
- Eason MJ, Wyatt R. Paravertebral thoracic block-a reap praisal. *Anaesthesia* 1979; 34: 638-642.
- Cousins M, Bromage P. Epidural neural blockade. In: Cousins M, Bridenbaugh P, eds. *Neural blockade in clinical anesthesia and management of pain*. 2nd ed. Philadelphia: JB Lippincott 1988: 309-10.
- Gautam S, Agarwal A, Das PK, Agarwal A, Kumar S, Khuba S. Evaluation of the efficacy of methylprednisolone, etoricoxib and a combination of the two substances to attenuate postoperative pain and PONV in patients undergoing laparoscopic cholecystectomy: a prospective, randomized, placebo-controlled trial. *Korean J Pain* 2014; 27: 278-84.
- Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. *Br Med J* 1974; 2: 656-9.
- Dolin SJ, Cashman JN, Bland JM. Effectiveness of acute postoperative pain management: evidence from published data. *British Journal of Anaesthesia* 2002; 89: 409-23.
- Scott DA, Chamley DM, Mooney PH, Deam RK, Mark AH, Hagglof B. Epidural ropivacaine infusion for postoperative analgesia after major lower abdominal surgery – a dose finding study. *Anesthesia and Analgesia* 1995; 81: 982-6.
- Stenseth R, Sellevoid O, Breivik H. Epidural morphine for postoperative pain: experience with 1085 patients. *Acta Anaesthesiologica Scandinavica* 1985; 29: 148-56.
- Walder B, Schafer M, Henzi I, Tramér MR. Efficacy and safety of patient-controlled opioid analgesia for acute postoperative pain. A quantitative systematic review. *Acta Anaesthesiol Scand*. 2001; 45: 795-804.
- Chia YY, Liu K, Wang JJ, Kuo MC, Ho ST. Intraoperative high dose fentanyl induces postoperative fentanyl tolerance. *Can J Anaesth* 1999; 46: 872-7.
- Guignard B, Bossard AE, Coste C, Sessler DI, Lebrault C, Alfonsi P et al. Acute opioid tolerance: intraoperative remifentanyl increases postoperative pain and morphine requirement. *Anesthesiology*. 2000; 93: 409-17.
- Coveney E, Weltz CR, Greengrass R, Leight GS, Steele SM, Lyerly HK. Use of paravertebral block anesthesia in the surgical management of breast cancer: Experience in 156 cases. *Ann Surg* 1998; 227: 496-501.
- Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy- a systematic review and metaanalysis of randomized trials. *Br J Anaesth* 2006; 96: 418-426.
- Richardson J, Lonnqvist PA, Naja Z. Bilateral thoracic paravertebral block: Potential and practice. *Br J Anaesth* 2011; 106: 164-71.
- Giesecke K, Hamberger B, Jarnberg PO, Klingstedt C. Paravertebral block during cholecystectomy: Effects on circulatory and hormonal responses. *Br J Anaesth* 1988; 61: 652-6.
- Richardson J, Sabanathan S, Jones J, Shah RD, Cheema S, Mearns AJ. A prospective, randomized comparison of preoperative and continuous balanced epidural or paravertebral bupivacaine on postthoracotomy pain, pulmonary function and stress responses. *Br J Anaesth* 1999; 83: 387-392.
- Kairaluoma PM, Bachmann MS, Rosenberg PH, Pere PJ. Preincisional paravertebral block reduces the prevalence of chronic pain after breast surgery. *Anesth Analg* 2006; 103: 703-708.
- Stiff G, Rhodes M, Kelly A, Telford K, Armstrong CP, Rees BI. Long-term pain: less common after laparoscopic than open cholecystectomy. *Br J Surg* 1994; 81: 1368-70
- Post-cholecystectomy symptoms. A prospective study of gall stone patients before and two years after surgery. *Gut* 1987; 28: 1500-4.
- Wilson RG, Macintyre IMC. Symptomatic outcome after laparoscopic cholecystectomy. *Br J Surg* 1993; 80: 439-41.
- Karmakar MK. Thoracic paravertebral block. *Anesthesiology* 2001; 95: 771-80.
- Bigler D, Dirkes W, Hansen R, Rosenberg J, Kehlet H. Effects of thoracic paravertebral block with bupivacaine versus combined thoracic epidural block with bupivacaine and morphine on pain and pulmonary function after cholecystectomy. *Acta Anaesthesiol Scand* 1989; 33: 561-4.