

OPIOID SAVING STRATEGY: BILATERAL SINGLE-SITE THORACIC PARAVERTEBRAL BLOCK IN RIGHT LOBE DONOR HEPATECTOMY

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Abstract

Background and Objectives: Postoperative analgesia after hepatectomy remains a challenge, mainly because of limited therapeutic index of the conventional opioids. The aim of this study is to evaluate the efficacy of bilateral single-site thoracic paravertebral block for the management of postoperative pain following right lobe donor hepatectomy (RLDH) using a prospective, randomized and controlled study design.

Methods: Twenty four adult patients, aged 18-50 years, ASA-I-II, of both sexes scheduled for right lobe donor hepatic resection, were enrolled in this study. Patients were randomly allocated into 2 equal groups of 12 patients each. Before induction of general anesthesia, all patients received bilateral single-site thoracic paravertebral injection at the level of T7-8 in the sitting position. Patients of Group B were injected with 25 mL of bupivacaine 0.25% with epinephrine 1:200.000 on each side. Patients of Group P were injected with 25 mL of 0.9% NaCl (placebo). General anesthesia was standardized in all patients. Postoperative pain score, analgesic requirements and the incidence of

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postoperative nausea and vomiting were recorded.

Results: Bilateral single-site thoracic paravertebral block significantly decrease the pain visual analogue score parameters. Total morphine consumption in the first 24 hours postoperatively was decreased by more than 50% in Group B (21.76 ± 6.8 mg compared to 44.12 ± 9.2 mg in Group P). There was significant prolongation in time to rescue analgesia (104.08 ± 2.04 min in Group B, and 31.5 ± 6.14 min in Group P). Postoperative nausea and vomiting was significantly less in the active Group B when compared to the controlled Group P.

Conclusion: Bilateral single-site thoracic paravertebral block is easy, safe and efficient technique for postoperative pain management in patients undergoing right lobe donor hepatectomy.

Key words: (Analgesics, opioid: Anesthetic technique: paravertebral block; Anesthetics, local: bupivacaine. Pain: postoperative. Surgery: Hepatic resection).

Introduction

Partial liver donation for related liver transplantation is gaining popularity due to the shortage of cadaveric livers, and it is considered relatively safe, given the gradual advances made in surgical skills and perioperative patient care. Inevitably, however, all donors are subjected to severe postoperative pain because of the nature of the operation. Also, living donors are generally known to have a particularly low tolerance to pain because they are healthy individuals¹. Cywinski et al² reported that right lobe donors complained more of postoperative pain than patient who underwent major hepatic resection for tumor. Therefore, the efficient management of postoperative pain should be given the important priority in living donors. Poor postoperative pain control may have a significant impact on the quality of life of an otherwise healthy donor.

Remarkable improvements in patient-controlled analgesia delivery devices and the introduction of Acute Pain Service have expanded the

routine practice of patient-controlled analgesia using different types of opioids mainly morphine. Postoperative side effects of opioids are very annoying to living liver donors including nausea, vomiting, prolonged postoperative ileus and prolonged hospitalization³.

The role of thoracic paravertebral block (TPVB) for postoperative analgesia in patients undergoing thoracic or abdominal surgical procedures is well established⁴. TPVB is the technique of injecting local anesthetic adjacent to the thoracic vertebra close to where the spinal nerves emerge from the intervertebral foramina. This results in somatic and sympathetic nerve blockade in multiple contiguous thoracic dermatomes above and below the site of injection⁵.

The aim of this study was to evaluate the safety and the efficacy of bilateral single-site thoracic paravertebral block in controlling postoperative pain after living liver donor and its effect on postoperative morphine consumption.

Methods and Materials

After approval from the Hospital Ethics Committee, twenty-four patients, aged 18-50 years ASA-I-II of both sexes were recruited in this study. Informed written consent was obtained from each patient. The same anesthesiologist and surgical team performed all procedures. Exclusion criteria included allergy to local anesthetics, history of cardiac disease, coagulopathy, infection at the site of TPVB placement, morbid obesity, and patient receiving regular analgesics. All patients received premedication in the form of midazolam 15 mg orally, 30 minutes before surgery.

Patients were equally assigned into two different groups (B & P), twelve patients each, by pre randomized sealed envelopes technique.

Bilateral Thoracic Para vertebral Block technique

Prior to induction of GA, a bilateral paravertebral injection was performed at T7-8 level with the patient in the sitting position. According to the guidelines described by Moore⁶ and Katz⁷, two sites of injection were marked 2.5 cm lateral to the midline on both sides. Following aseptic preparation of skin, each injection site was infiltrated with 0.5-1.0 ml of Lidocaine 1%, using a 29-G needle.

In each side, a 22-gauge Tuohy needle attached via extension tubing to a syringe, was advanced anteriorly in the parasagittal plane (perpendicular to the back in all planes) until it contacted the transverse process. The needle was then withdrawn to the subcutaneous tissue and angled to walk off the caudal edge then advanced anteriorly approximately 1 cm. After careful aspiration of the syringe, patients of group (B) received 25 mL of 0.25% bupivacaine with 1:200,000 epinephrine injected over at least one minute. Patients of group (P) received 25 mL of 0.9% NaCl (placebo). All patients were then returned to the supine position. Drug preparation in unlabelled coded syringes for all patients and the efficacy of the block in group (B) patients only, was done by another anesthetist (blinded to the study protocol) by recording warming at the dermatomes T4-T12 (Dermatemp, infrared temperature scanner) and testing by pin prick method. Failed TPVB in group B patients were excluded from the study.

The General Anesthesia technique

General anesthesia was induced with IV remifentanyl 1 µg/kg, propofol 2 mg/kg and atracurium 0.5 mg/kg was used to facilitate orotracheal intubation. Anesthesia was then maintained with remifentanyl 0.1-0.4 µg/kg/min and propofol 4-10 mg/kg/hr using 2 separate infusion syringes (Diprifusor™, Graseby 3500 by SIMS Watford Herts, UK). Remifentanyl and propofol infusion rates together with intraoperative fluid

management were titrated to maintain blood pressure and heart rate within 20% of preinduction values. Chevron incision was used to achieve surgical exposure with the same surgical retractor system used in all cases. Ventilation was maintained with 40-50% oxygen in air and mechanically adjusted to maintain $P_{ET}CO_2$ between 4.6-5.2 KPa with an anesthetic/respiratory analyzer (Capnomac Ultima, Datex, Finland). Muscle relaxation for surgical exposure was provided with additional doses of atracurium. Anesthesia monitoring included electrocardiography, blood pressure via the radial artery, central venous pressure via the right internal jugular vein, pulse oximetry, capnography, urine output, neuromuscular blockade, and esophageal temperature. (Solar 8000M, GE, Freiburg, Germany).

At the cessation of surgical procedure, remifentanyl and propofol infusions were stopped and I.V morphine 0.01 mg/kg was given to all patients. Residual neuromuscular blockade was reversed with I.V neostigmine 0.05 mg/kg and glycopyrrolate 5 μ g/kg, and then trachea was extubated (defined as end of surgery), when the patient was awake.

In The Post Anesthesia Care Unit (PACU)

Postoperative pain was evaluated using Visual Analogue Scale (VAS), where 0 means no pain and 10 the worst imaginable pain. In PACU, all patients received 50 μ g/kg of IV morphine as a rescue analgesic, when VAS is 4 or higher, every 6 minutes to control postoperative pain.

In the ward, patient controlled analgesia was used with morphine concentration 1 mg/ml, demand bolus of 2 mg, lockout time of 6 minutes, no initial bolus and no basal infusion.

Nurses in the PACU and Acute Pain Service team in the ward collected the data were blinded to the patient's group and the study protocol.

Measurements

1 - Visual Analogue Scale (VAS) was assessed on admission to and on discharge from PACU.

2 - The time to first analgesic requirement (minutes).

3 - Postoperative morphine consumption during the first 2 hours and after 24 hours was recorded.

4 - The incidence of complications including respiratory depression (RR less than 10), oxygen desaturation ($\text{SaO}_2 < 87\%$) on admission to PACU, re-intubation during the first 24 hours postoperatively, and the incidence of nausea and vomiting (N & V) were recorded, as the number of patients needed medical treatment in each group.

Statistical Power

A power analysis with a pain score as the primary criterion (Power = 0.90, [alpha] = 0.05 unilateral, with Bonferroni correction) on the basis of previous studies^{7,8} revealed that 10-12 patients were mandatory in each group

Statistical analysis

ANOVA test was used to compare and analyze results between groups, while subgroup analysis was achieved by Tukey's approach. The statistical analysis of means within the groups is achieved via paired t test. A p value < 0.05 was considered significant.

Results

There was no significant difference between the two groups of patients with regard to demographic data, body mass index, duration of surgery, ASA physical status and intraoperative fluid balance management (Table 1).

Table 1
Demographic and intraoperative data

	Group B N = 12	Group P N = 12
Age (Yr)	32.8 ± 9.32	34.3 ± 8.18
Gender (male/female)	9/3	10/2
BMI (kg/m ²)	26.1 ± 6.2	25.2 ± 2.9
Duration of surgery (min)	421.2 ± 59.8	417.5 ± 44.6
ASA (n (%))		
I	3 (25.0)	4 (33.3)
II	9 (75.0)	8 (66.6)
Estimated blood loss (mL)	708 ± 212.4	716 ± 209.8
Administered IV fluids:-		
Crystalloid (mL)	3510.5 ± 980.2	3560.4 ± 980.8
Colloid (mL)	742.4 ± 255.4	768 ± 240.8
Urine output (mL)	687.8 ± 180.4	692.6 ± 206.6

● Data are expressed as Mean ± SD.

Pain scores were statistically lower in patients of Group B as compared to Group P, both on admission and on discharge from PACU, 2 hours postoperatively, (Table 2).

Table 2
Postoperative Pain Scores Measured on 10 Visual Analogue Scale (VAS)

	Group B N = 12	Group P N = 12
On Admission to PACU	2	5*
On Discharge from PACU	1	4*

Data are expressed as Median.

* Statistically significant (P <0.05).

The time to first analgesic requirement was significantly longer in

Group B (104.08 ± 2.04 min) when compared to Group P (31.5 ± 6.14 min). ($P < 0.01$) (Table 3).

Table 3
Time for Rescue Analgesia and Morphine consumption in PACU and 24Hour after Surgery

	Group B N = 12	Group P N = 12
Time to Rescue Analgesia (min)	104.08 ± 2.04	$31.5 \pm 6.14^*$
Morphine Consumption on discharge from PACU (mg)	4.1 ± 1.16	$9.21 \pm 2.18^*$
Total Morphine Consumption 24 h after Surgery (mg)	21.76 ± 6.8	$44.12 \pm 9.2^*$

Data are expressed as Mean \pm SD.

* Statistically significant ($P < 0.05$).

The morphine consumption in Group B was significantly lower than Group P both on admission and on discharge from PACU (4.1 ± 1.16 mg compared to 9.21 ± 2.18 mg) and after 24 hours (21.76 ± 6.8 mg) compared to 44.12 ± 9.2 mg.

In Group B, 3 patients (25.0%) suffered from postoperative vomiting compared to 7 patients (58.3%) in Group P ($P < 0.01$).

Discussion

After initiating the liver transplantation program at our Institution, we observed that donor patients experienced significant postoperative pain, despite the use of different opioid-based patient controlled analgesic regimens. The use of the epidural route has proven very effective in the postoperative care of patients with similar laparotomy surgeries³; however, the possibility of a bloody tap from needle or catheter placement or continuing trauma due to the presence of an epidural catheter, has been widely described and may occasionally result in spinal bleeding.

Epidural hematoma is a rare event, and is always related to deranged hemostatic capacity or complete anticoagulation⁸. Although our patients had a normal coagulation state at the time of surgery, there is no doubt that after liver resections, patients usually have a significant derangement in the anticoagulation profile during the second and third day, and the presence or removal of the epidural catheter at that time constitutes a potential risk.

Using strict exclusion criteria, we controlled the factors known to interfere with postoperative pain course changes during the observation period. The demographic data were not significantly different between the two groups. To minimize bias, all anesthesia conductions were done by the same anesthetist and the surgeries were done by the same surgical team, using the same incision and retractor type. Because the depth of anesthesia may influence the postoperative analgesic requirements², we standardized the anesthetic technique and intraoperative fluid management used in this study. Therefore, we believe that the comparison of postoperative pain course variables between the two groups, is valid.

In agreement with this study, TPVB was proven to be technically easy to learn⁹, has a high success rate regardless of the number of blocks performed, and does not appear to be operator dependant⁹. The failure rate varies from 6.8 to 10%^{9,10} which is comparable with that of other commonly used regional blocks¹⁰. Based on published data, it is difficult to quote the true complication rate of TPVB, but it appears to be relatively low, ranging from 2.65%⁹ to 5%¹¹. Lonnqvist et al¹⁰ prospectively evaluated complications after PVB in 367 patients and observed the following frequency of complications: hypotension 4.6%, vascular puncture 3.8%, pleural puncture 1.1% and pneumothorax 0.5%. Dural puncture related complications such as intrathecal injection¹¹, spinal anesthesia¹², postural headache¹² and Horner syndrome appear to be exclusive to medial approach and closer proximity of the needle to the dural cuff and intervertebral foramen¹⁰⁻¹². No fatality directly related to TPVB has been reported to date.

In the present study, patients in Group B with bilateral single-site TPVB at the level of T7-8, showed statistically significant longer time to

the first rescue analgesic, lower VAS values (both in the PACU and 24 hours in the ward), and more than 50% reduction in the total morphine requirement in the first postoperative day, reflecting an excellent opioid saving strategy for bilateral TPVB in such cases.

The surgical incision of the donor hepatic resection may extend from T-6 down to T 10-11 dermatomes bilaterally², thus, in order to provide adequate pain relief, both high quality afferent somatic and visceral pain blockade are most likely necessary in order to successfully treat post liver resection pain. TPVB has been reported to provide high quality afferent blockade with abolishment of somatosensory evoked potentials and has also been found capable of attenuating the postoperative stress response associated with traditional abdominal surgeries¹³. A combined somatic and visceral analgesic effect has also been described for intrapleural anesthesia¹⁴, a nerve blocking technique that to a large extent exerts its effect by diffusion of local anesthetics into the paravertebral space.

Adequate somatic and visceral blockade will require that the bilateral injections at T7-8 are able to spread to multiple adjacent thoracic segments. Such spread between segments has been verified in both patients and cadaveric studies¹⁵, and single level injection of local anesthetic has been also found to result in a multi-segmental anesthesia¹⁶.

The efficacy of a single-site TPVB is explained by the its spread. TPVB injection may remain localized to the level injected¹⁷, or it may spread to the contiguous levels above and below¹⁸, the intercostals space laterally¹⁹, the epidural space medially²⁰, or a combination of the above to affect ipsilateral somatic^{13,21} and sympathetic nerves^{13,22}, including the posterior primary rami in multiple contiguous thoracic dermatomes^{5,13,22}.

Eason and Wyatt⁵ found that at least four intercostals spaces could be covered by a single 15 ml of 0.375% bupivacaine. More recently, 15 ml of bupivacaine 0.5% injected in the TPVB has been shown to produce mean unilateral somatic block over 5 (range 1-9) dermatomes and sympathetic block over 7 (range 6-10) dermatomes²¹. Similarly, 1.5 mg/kg bupivacaine 0.5% produced sensory loss at the level of injection with a mean superior spread of 1.4 (range 0-4) dermatomes and a mean inferior spread of 2.8 (range 0-7) dermatomes¹³. Current evidences suggest that a single-site

injection of 0.375-0.5% bupivacaine, 15-20 ml or 0.3 ml/kg^{5,21} is as effective as multiple-sites injection of 0.5% bupivacaine 3-4 ml per site²³, in producing unilateral anesthesia over four to five thoracic dermatomes.

The analgesic effect of TPVB appears to be stronger and to last longer than predicted. Based on the local anesthetic kinetics alone²⁴, the explanation of this is unclear when compared with other forms of neuroaxial block e.g., epidural anesthesia¹³. TPVB has been shown to be uniquely effective in eliminating cortical responses to thoracic dermatomes stimulations. This may perhaps inhibit a central reflex involved in pain. Weltz et al²⁵, reported that the block (4 ml, 0.5% bupivacaine with 1:400,000 epinephrine injected at each level, C7-T7) provides postoperative analgesia for an average of 23 hours (range, 9-38 hours). TPVB has significantly improved the quality of recovery, experienced less postoperative pain and required less analgesic²³.

Significantly lower incidence of postoperative nausea and vomiting (PONV) in Group B when compared to Group P can be easily explained by their lower morphine consumption. Many studies proved that the higher the doses of morphine consumption in the postoperative period, the higher the incidence of PONV^{3,26}.

Conclusion

Thoracic paravertebral block is effective in controlling the postoperative pain and has a smoother postoperative course in comparison to the traditional general anesthesia alone for patients undergoing right lobe donor hepatectomy. This technique deserves more widespread use in patients undergoing liver resection.

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