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ORIGINAL ARTICLE

Paravertebral block for percutaneous nephrolithotomy: a prospective, randomized, double-blind placebo-controlled study

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Abstract

Purpose Percutaneous nephrolithotomy (PCNL) is performed commonly in patients with large kidney stones, but the management of their postoperative pain presents a major challenge. While it is not routinely performed in PCNL patients, paravertebral block (PVB) has been described as an effective strategy for pain control after various non-urologic surgeries. This trial aims to assess the effect of paravertebral blockade on intraoperative and postoperative opioid use as well as postoperative pain control in patients undergoing PCNL.

Methods This was a prospective, randomized, double-blind, placebo-controlled study. Patients who consented to participate were randomly assigned to undergo either PVB or a placebo intervention preoperatively. The patient, surgeon, and anesthesia team were all blinded to the randomization. The outcome parameters were intraoperative opioid requirement, postoperative visual analog scale (VAS) pain scores, postoperative opioid use, and postoperative antiemetic use.

Results 23 patients were enrolled in each arm of the study, and the two groups had no significant differences in baseline demographic or clinical characteristics. Patients in the PVB group had significantly lower intraoperative opioid use, postoperative opioid use, frequency of opioid use, and antiemetic. Patients in the PVB group also had lower postoperative VAS pain scores. There were no patients who suffered from complications attributable to PVB.

Conclusion The results of this randomized, double-blind, placebo-controlled trial suggest that PVB should be considered an effective strategy to reduce opioid requirement and improve pain control for patients undergoing PCNL.

Keywords Nephrolithiasis · Percutaneous nephrolithotomy · Pain management · Paravertebral · Nerve block

Introduction

Nephrolithiasis affects millions of Americans each year. In the year 2000, there were over 2 million outpatient visits for kidney stones with a total estimated annual expenditure of $2.1 billion [1]. There are a variety of strategies used to manage nephrolithiasis including medical expulsive therapy, extracorporeal shock wave, ureteroscopy, open surgery and percutaneous nephrolithotomy (PCNL). PCNL is favored over other forms of kidney stone management especially

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in cases of large stone burden (> 2 cm), staghorn calculi, or when other methods of management fail [2]. The procedure is considered to be one of the most effective kidney stone procedures with success rates of up to 95% [3].

While PCNL is a minimally invasive procedure, a major challenge in these patients' postoperative care is pain and discomfort at the nephrostomy tract. Postoperative pain can increase the average length of stay after PCNL, cause nausea and vomiting, and aggressive management with opioids alone can result in respiratory depression [4]. In the current healthcare climate, providers are striving to find ways to reduce perioperative opioid use and regional anesthesia is rapidly gaining popularity.

Urologists have worked with anesthesiologists to employ a number of different strategies to control postoperative PCNL pain. Some of the strategies previously investigated include the use of single-dose spinal anesthesia, intrapleural blocks, as well as instillation of local anesthetic within the skin, nephrostomy tract, and renal capsule [5-10]. A paravertebral block (PVB) is a regional nerve block technique that involves injection of local anesthetic adjacent to the vertebra to block spinal nerve roots in a dermatomal distribution. PVB has been studied extensively in breast, thoracic, and gastrointestinal surgery [11-17]. There have also been several studies describing the use of PVB in various urological procedures, as well as its use in PCNL [18-27]. All of the previous trials evaluating PVB in PCNL have demonstrated promising results thus far, but significant methodological variations exist in regard to blinding, timing of the block, and anesthetic agents. To our knowledge, this is the first randomized, double-blind, placebo-controlled trial investigating the effect of preoperative paravertebral blockade on intraoperative and postoperative opioid use as well as postoperative pain control in patients undergoing PCNL.

Materials and methods

This study was approved by the Institutional Review Board and registered with Clinical Trials. Our primary outcome was postoperative pain as measured by the visual analog scale (VAS) in patients who received the PVB as compared to patients who received a placebo intervention. The secondary outcomes were comparisons of intraoperative opioid requirement, postoperative intravenous and oral opioid use, time to first postoperative opioid dose, and need for antiemetic medication. A two-tailed error of 5% and a beta error of 10% were accepted into the detection of differences of 1.5 points on the VAS pain scale between the block group and the control group. Based on these calculations, the required sample size per arm was 34 patients but enrollment was halted after only 46 patients were recruited. This was influenced by various factors: the availability of internal funding was limited, patients were requesting PVB rather than risking randomization to the control arm, and the surgeons also wanted to offer PVB globally in an effort to reduce opioid usage.

Patients aged 18–80 who consented to undergo unilateral PCNL between 2013 and 2016 were included in this study. Exclusion criteria were refusal to participate, inability to fill out study documents due to physical or mental conditions, inability to use a patient-controlled analgesia (PCA) due to physical or mental conditions, infection at the site of the proposed block, anatomy that prevents the ability to safely perform the block including morbid obesity, coagulopathy, pregnancy, allergy to local anesthetics, and patients undergoing bilateral PCNL.

Randomization

All patients who consented to participate in the study were transferred to the preoperative area approximately 1 h prior to surgery and then randomized to one of two groups: PVB group and control group. At our institution, a separate anesthesia team, the Acute Pain Service (APS), manages all regional anesthesia and the randomization designation was kept in sealed envelopes available only to the team administering the block. Importantly, the randomization was blinded from the patient, the surgeon, and the treating anesthesia team, both intraoperatively and in the recovery unit.

Paravertebral block technique and control group technique

After randomization, the APS team confirmed the study consent with the patient and administered midazolam intravenously to all patients. All patients were placed in the sitting position. Using a low-frequency (2–6 mHz) curvilinear ultrasound probe, the T10 paravertebral space was visualized in the paramedian sagittal plane. The skin of all patients was aseptically prepared using chlorhexidine in isopropyl alcohol and infiltrated with 3 mL of lidocaine 2%. An injection into the paravertebral space will spread to multiple adjacent dermatomes, so exact identification of a specific level is not necessary. An in-plane needle approach was used; the endpoint for successful block was anterior displacement of the pleura by injected local anesthetic. For those patients in the control group, pressure was held for several minutes with the lidocaine syringe to mimic performance of a paravertebral block. For patients who were randomized to the PVB group, using a 17 g Tuohy needle, an in-plane PVB was performed at T10 with a single injection of 20 cc of 0.5% bupivicaine. This typically provides a block that covers dermatomes T7-L1, however, we did not test the block to prevent unblinding the patient.

Anesthesia

Following administration of either the PVB or the control intervention, general anesthesia was induced using a standardized protocol (Appendix A) including propofol, rocuronium, and fentanyl. General anesthesia was maintained with desflurane in oxygen and air. The depth of anesthesia was monitored using the standard anesthetic practice of observation for changes in vitals signs such as heart rate, blood pressure, and respiratory effort in response to surgical stimulation as well as end-tidal desflurane monitoring. Additional 50 mcg boluses of fentanyl were given as deemed necessary by the anesthesia provider based on intraoperative hemodynamic changes, which is the universal practice and consistent with international standards.

Operative technique

The patients included in this study were operated on by three urologists in our institution with identical techniques. Percutaneous renal access was obtained by an interventional radiologist the day prior to each procedure. A urethral catheter was placed at the start of each procedure and the surgery was performed in the prone position. The tract was dilated using a balloon dilator, and a 30-French access sheath was placed under fluoroscopic guidance. Using a combination of rigid and flexible nephroscopy, lithotripsy was performed with an ultrasonic lithotripter and/or the holmium laser depending on stone size, location, and hardness. When appropriate, antegrade ureteroscopy was performed to extract any significant stone fragments from the ureter. A 20-French council-tip nephrostomy catheter was placed over a 5-French double open-ended ureteric catheter at the conclusion of all procedures. The nephrostomy catheters for all patients were removed within 24 h of the procedure. No ureteral stents were utilized.

Postoperative measurements

Our postoperative pain management was kept consistent with our current practices to most closely mimic our clinical setting. In the recovery room, nursing was allowed to provide intravenous fentanyl in a manner that is consistent with standard practices (25 mcg every 5 min as needed for VAS 7–10). A morphine PCA with standard settings was started once the patient was transferred to the ward. Patients allergic or intolerant to morphine were given a dilaudid or fentanyl PCA and morphine equivalents were calculated for the purpose of the study. Patient also could receive addition oral Norco (tylenol–hydrocodone) on an as-needed basis. Antiemetic medications, most commonly ondansetron, were also administered on an as-needed basis.

The VAS pain scale was completed by the patient at 2, 4, 8, 12, and 24 h following surgery. This 24-h cutoff for pain measurement was based on the expected length of bupivacaine's effect. The location of the pain was also marked on the diagram by the patient. Both intravenous and oral opioid consumption were recorded for a 24-h postoperative period. The time from exiting the operating room to the first dose of an opioid medication was recorded in minutes. The use of antiemetic medications in the 24-h study period was also recorded.

Statistical analysis

Analysis was performed using Microsoft Excel. Data were presented as number (%) or mean ± SD. Between groups, continuous variables were analyzed using the Student's *t* test, and categorical variables were analyzed using the Chi square test. *P* value of < 0.05 was considered statistically significant.

Results

A total of 46 patients were enrolled in the study and randomized. One patient randomized to the PVB group elected to withdraw from the study prior to receiving any intervention and was not included in the analysis, thus there were 22 patients in the PVB group and 23 in the control group for the final analysis.

Demographic parameters, operative time, estimated blood loss, ASA score, and presence of intercostal access did not differ between the two groups. The PVB group was slightly older than the control group. There were no major complications (Clavien III or higher) in the study population. There were no complications attributed to the PVB or postoperative opioid use (Table 1).

The VAS pain score was lower in the PVB group as compared with the control group at all time points, except the 8-h time point at which they were similar. The difference was statistically significant at the 24-h time point and also when comparing the overall VAS pain score of the two groups (Fig. 1).

The intraoperative fentanyl requirement and recovery room fentanyl use were greater in the control group when compared with the PVB group (Fig. 2). Intraoperatively, there was a 49.5% decrease in the fentanyl dose when the PVB was used. In the recovery room, there was an 83.3% decrease in the fentanyl dose in the PVB group. The median time from exiting the operating room to the first postoperative dose of opioids was much longer in the PVB group as compared to the control group (119.7 min vs. 31.9 min, $p < 0.01$). Postoperative opioid use from the PCA was significantly more in the control group and the control group has a much higher frequency of demand on the PCA (i.e., the number of times the button was pressed in a 24-h period)

Table 1 Demographic properties

	PVB group ($n=22$)	Control group ($n=23$)	P value
Age (years)	58.2 (10.9)	49.9 (11.8)	0.02
Gender (% male)	39.1	54.5	0.13
Operative time (min)	69.4 (34.9)	72.2 (37.2)	0.80
Estimated blood loss (mL)	86.1 (48.5)	115.9 (137.9)	0.33
ASA score	2.60 (0.66)	2.31 (0.48)	0.10
Intercostal access (%)	34.8	36.4	0.80
Complication rate (Clavien III or higher) (%)	4.3	4.5	0.83
Multiple accesses (%)	8.7	9.1	0.83

Means and standard deviations are reported where appropriate

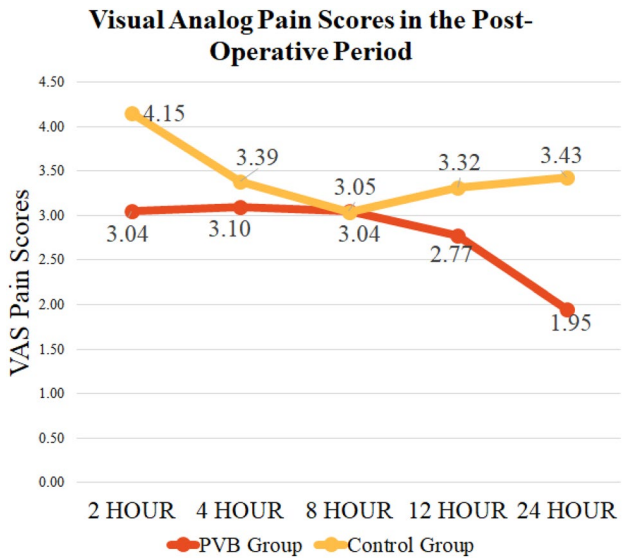

Fig. 1 VAS scores in the postoperative period

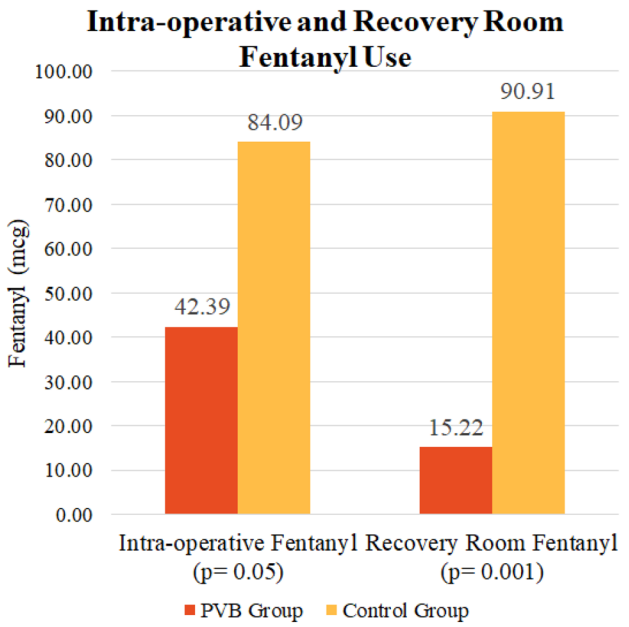

Fig. 2 Intraoperative and recovery room fentanyl use

(Table 2). The control group also requested supplemental oral opioids at a high rate than the opioid group (61.9% vs. 30.4%, $p<0.001$) (Table 2). There was a higher need for antiemetic medication during the 24 h study period in the control group (52.4% vs. 30.4%, $p<0.001$) (Table 2).

Discussion

Postoperative pain is a major complaint of patients undergoing percutaneous nephrolithotomy, the management of which generally includes opioids. The ubiquitous use of opioids in the United States has led to an opioid epidemic with more than 630,000 deaths from drug overdose between 1999 and 2016, and most of these deaths were due to opioids prescribed for pain [28]. Shah et al. demonstrated that opioid dependence and overdose affect 1 of 1111 patients following urological surgery; these rates were the highest in stone surgery, which made up 27.3% of the overall cohort [29]. Numerous modalities for adequate analgesia following PCNL have been studied, including oral and parenteral analgesics, as well as spinal and peripheral nerve blocks. In this study, we sought to investigate the effect of preoperative thoracic paravertebral block on pain control following PCNL as well as on intraoperative and postoperative opioid use.

Regional anesthesia or nerve blockade reduces the risk of postoperative opioid use through one of two mechanisms [30]. First, nerve blockade is thought to block the transmission of pain impulses thus preventing central sensitization and chronic neuropathic pain. Second, regional anesthesia is well established to treat and reduce acute postoperative pain in many different surgeries and body areas. Acute postoperative pain is an established predictor of the development of chronic pain, thus any reduction is beneficial to prevent dependence [30]. Recently, PVB has garnered more

Table 2 Outcome parameters comparing the PVB group versus the control group

	PVB group	Control group	*P* value
Average postoperative VAS pain score	2.78 (2.14)	3.48 (2.31)	0.03
Intraoperative fentanyl use (mcg)	42.39 (61.0)	84.09 (80.75)	0.05
Recovery room fentanyl use (mcg)	15.22 (35.15)	90.91 (99.27)	< 0.001
Total PCA morphine equivalents dose (mg)	17.5 (15.0)	31.1 (21.6)	0.02
Frequency of PCA demand (n)	14.4 (11.1)	26.9 (15.7)	0.004
Time to first analgesic administration (min)	119.7 (133.6)	31.9 (32.0)	0.006
Rate of supplemental oral narcotic use (%)	30.4	61.9	< 0.001
Rate of antiemetic use (%)	30.4	52.4	< 0.001

attention in the PCNL setting. Elbealy et al. demonstrated the benefits of a preoperative PVB over epidural anesthesia in lowering VAS scores and postoperative morphine requirement [23]. Ak et al. reported postoperative PVB with levobupivacaine was more effective than placebo in reducing postoperative pain and opioid consumption [24]. Borle et al. used a preoperative bupivacaine PVB and found that it reduced intraoperative fentanyl requirement as well as VAS scores postoperatively [25]. Maheshwari et al. described the use of post-PCNL PVB with ropivacaine to reduce postoperative pain and requirement for rescue analgesia [26]. Our study is the first known investigation of this concept in a randomized, double-blinded, placebo-controlled manner utilizing bupivacaine for preoperative single-injection paravertebral blockade.

We observed that in patients undergoing PCNL, single-injection preoperative PVB reduced intraoperative and postoperative opioid consumption, postoperative pain, and the need for antiemetics. The reduction in opioid use likely leads to improved nausea as reflected in decreased antiemetic use. We feel that the impressive reduction in opioid use in the intraoperative and postoperative period is the most valuable finding in our study. If adequate perioperative pain control can be achieved, while reducing opioid requirement, anesthesiologists and urologists alike can make significant contributions to the fight against opioid overconsumption.

This study did have a few notable limitations. Naturally, the use of VAS scores can be complicated by the subjective nature of experiencing pain; while it is a validated tool, its imperfections are well-known. Some patients who complained of severe bladder spasms from their Foley catheter may have recorded exaggerated VAS scores for non-surgical site pain; we were unable to control for this scenario. We also had some missing VAS data, specifically for overnight checkpoints when the nurses were reluctant to awaken the patients. Additionally, we were unable to control for preoperative acute opioid use, which is often encountered in patients undergoing nephrolithiasis treatment and can affect postoperative opioid requirement. However, we attempted to mitigate this by excluding any patients using chronic opioids. Furthermore, based on the operative techniques that were used in this trial, its findings are limited to standard PCNL and may not translate to less invasive PCNL techniques. Finally, the generalizability of this study is affected because general practice patterns have already shifted away from the use of PCA after PCNL. Even in the setting of these design-based limitations, the ultimate contribution of this project cannot be understated, as it highlights the advantages of using nonopioid pain management techniques.

Conclusions

Given the benefits of improved pain control, reduced opioid use, and decreased opioid-associated side effects, PVB should be considered an effective strategy to reduce pain in patients undergoing PCNL. In the current healthcare climate, given a global push to minimize the use of and exposure to unnecessary opioids, proven techniques such as paravertebral blockade may pave the path for alternative analgesic strategies. Future studies are needed to determine optimal timing of the block, the safety of bilateral blocks, and the benefits of continuous infusion as compared to a single injection.

Author contributions KGB: Project development, data collection, data analysis, manuscript writing. PMP: Manuscript writing/editing. GDS: Project development, data collection. CE: Project development, data collection. AF: Data collection, Manuscript editing. ERM: Manuscript editing. SB: Project development, data collection. TMT: Project development, data collection.

Compliance with ethical standards

Research involving human participants Approval for this study for obtained from the Loyola University Chicago Health Sciences Division Institutional Review Board for the Protection of Human Subjects. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards."

Informed consent Informed consent was obtained from all individual participants included in the study.

Appendix A

See Appendix Table 3

Table 3 Anesthetic protocol for percutaneous nephrolithotomy

Premedication	
Midazolam 1–2 mg IV	
Induction of anesthesia	
Propofol 2 mg/kg IV	Note: weight is based on estimated lean body mass, with supplemental 0.5 mg/kg as needed for hemodynamic responses
Fentanyl 2 mcg/kg IV	
Rocuronium 1 mg/kg IV	Note: weight is based on estimated lean body mass. Use 1.2 mg/kg for rapid sequence induction
Maintenance of anesthesia	
Inhalational agent: desflurane	Note: this is delivered in combination with O_2 and air, as tolerated. No nitrous
Opioids: fentanyl IV	Note: this is dosed in 1 cc increments in response to surgical stimulation, as necessary
Muscle relaxant: rocuronium	Note: this is titrated to maintain 'train-of-four' < 3 twitches [31]

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