ORIGINAL CLINICAL RESEARCH

A Comparison between Ultrasound Guided Erector Spinae Block using Bupivacaine versus Bupivacaine and Dexmedetomidine for Postoperative Analgesia in Patients Undergoing Percutaneous Nephrolithotomy: A Randomized Controlled Double-Blinded Study

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Abstract

Background: The erector spinae plane block (ESPB) effectively provides extensive somatic and visceral analgesia in percutaneous nephrolithotomy (PCNL). The role of dexmedetomidine as an adjuvant to the local anesthetic is debatable. This study this study assessed the efficacy and safety of using dexmedetomidine as an adjuvant to bupivacaine in ESPB for postoperative pain management in patients undergoing PCNL.

Methods: This double-blinded, parallel-group, randomized, clinical trial enrolled 50 adult patients aged more than 21 years with American Society of Anesthesiologists physical status I or II who were scheduled for PCNL. All participants received ultrasound guided erector spinae block. In the control groups, 25 participants received only 30 mL of bupivacaine 0.25%. In the combined block group, 25 participants received 30 mL of bupivacaine 0.25% plus 2 mL of dexmedetomidine (0.5 μg/kg). The primary outcome was the total postoperative consumption of morphine. Secondary outcomes encompassed intraoperative fentanyl usage, hemodynamic measurements during the operation, and any adverse events.

Results: The addition of dexmedetomidine to bupivacaine produced a significant decrease in the total postoperative morphine consumption ($p<0.001$), heart rate ($p<0.005$), and mean arterial pressure ($p<0.005$). The combined block group experienced a statistically significant reduction in the incidence of postoperative nausea ($p=0.049$), while the decrease in the incidence of postoperative vomiting was not statistically significant ($p=0.490$).

Conclusion: In PCNL, dexmedetomidine proves to be a safe and effective adjuvant to bupivacaine, significantly reducing postoperative analgesic consumption in patients receiving an ultrasound guided erector spinae block.

Keywords: Bupivacaine; dexmedetomidine; erector spinae block; morphine consumption

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Introduction

Percutaneous nephrolithotomy (PCNL) is currently considered the preferred method for treating patients with renal calculi due to its minimally invasive nature, shorter duration, and reduced risk of infection compared to open surgical procedures. Additionally, it is associated with decreased morbidity rates and expedited recovery.[1] However, the insertion of a nephrostomy tube results in peritubal pain, requiring analgesic medication. Inadequate administration of analgesic medication can cause delayed mobilization, compromised respiration, and prolonged hospitalization, resulting in increased costs.[2]

There is a lack of consensus regarding the standardized approach to postoperative pain treatment following PCNL. Several potential choices are available, such as the utilization of systemic opioids, non-steroidal anti-inflammatory medications, patient-controlled analgesia pumps, epidural analgesia, and local anesthetic infiltration.[3]

The utilization of opioid-based analgesia is a crucial component in managing postsurgical pain following PCNL. Nevertheless, the administration of opioids carries the potential for notable adverse effects, such as nausea and vomiting, as well as more serious events like respiratory depression. These consequences have been linked to extended hospital stays and increased costs.[4] Given the heightened occurrence of adverse events in patients receiving higher doses of opioids, it is crucial to investigate other measures to reduce opioid usage in the postoperative phase following PCNL.[1]

Multimodal analgesic techniques are frequently utilized in clinical settings. However, recent research has revealed unfavorable outcomes.[5] Regional anesthetic procedures are the most efficient methods for postoperative pain management. Tailored recommendations for pain management after specific procedures are based on empirical evidence and consider the impact of surgical techniques and anesthesia.[6]

The erector spinae plane block (ESPB) was first reported in 2016, when it was introduced as a regional block technique for managing thoracic neuropathic pain.[7] It is technically simple and safe, hence it is frequently implemented in various surgical procedures, such as those related to the spine, breast, and, most recently, the heart.[7]

The application of bupivacaine infiltration into the nephrostomy tract has the

potential to reduce postoperative discomfort following tubeless and conventional PCNL procedures.[8] However, the use of an adjuvant to bupivacaine can have a synergistic effect and prolong the postoperative analgesia compared to the bupivacaine only.[9]

Dexmedetomidine is an α_2-adrenergic receptor agonist known for its strong selectivity. It exhibits notable efficacy as a sedative and analgesic agent.[10] The roles of dexmedetomidine as an adjuvant in peripheral nerve blocks are debatable.[11] Incorporating dexmedetomidine into the local anesthetic solution has demonstrated favorable outcomes, as evidenced by earlier studies.[9, 12-14] These advantages encompass amelioration of tissue and nerve damage, prolongation of both sensory and motor block duration, and reduction of postoperative pain.[15] Therefore, the aim of this study is to assess the efficacy and safety of using dexmedetomidine as an adjuvant to bupivacaine in ESPB for postoperative pain management in patients undergoing PCNL.

Materials and Methods

Ethical considerations

The study was approved by the Research Ethics Committee, Faculty of Medicine, Misr University of Science and Technology, Egypt. This trial was registered at Pan African Clinical Trial Registry; (Trial ID: PACTR202311772437904; https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=26958; Date: November 6, 2023). Informed written consents were obtained from the study participants after being informed of the study aim and methods. The participants' data were kept confidential.

This double-blinded, parallel-group, randomized, controlled, clinical trial was conducted at the Urosurgery Theater at Souad Kafafi University Hospital, Misr University of Science and Technology, Egypt between January 2021 and June 2021.

The study included 50 adult patients, aged 21 to 72, of both gender, who were scheduled for PCNL under general anesthesia and were classified as American Society of Anesthesiologists physical status I or II. Patients with coagulation disorders, skin lesions, or injection site infections, a known history of allergic reactions to any of the studied medications, neurological or mental disease, and those who consumed opioids within 48 hours before the surgery were excluded. Additionally, patients who required conversion to open surgery or refused to participate were excluded.

A computer-generated table was used to randomly assign 50 patients into two groups. The randomization sequence was concealed using the sealed opaque envelopes method.16 To guarantee blinding, one researcher coded the administered drugs according to the computer-based system, while another researcher was responsible for delivering the ESPB, and a third researcher observed and recorded the data.

All patients received ultrasound guided ESPB after induction of general anesthesia. The control group received local infiltration anesthesia with 30 mL bupivacaine 0.25%. The combined block group received 30 mL of bupivacaine 0.25% plus 2 mL of dexmedetomidine (0.5 μg/kg).
All Patients were subjected to history taking, complete physical examination, and routine laboratory investigations. Preoperative medications, including midazolam (0.03 mg/kg), metoclopramide (10 mg) and ranitidine (50 mg), were administered intravenously (IV). Upon arrival at the operating room, pulse oximeter, noninvasive blood pressure, and six-lead electrocardiogram were applied and monitored continuously.

For induction of general anesthesia, propofol (1-2 mg/kg), fentanyl (1-2 μg/kg), and atracurium (0.5 mg/kg) were administered IV to all patients. For maintenance of anesthesia, isoflurane concentration was adjusted to maintain a minimum alveolar concentration of 1- 1.3, and incremental doses of atracurium were administered IV.

During intraoperative monitoring, if there was a sustained increase in either the systolic blood pressure or the heart rate greater than 20% of baseline for more than 5 minutes, fentanyl was administered in increments of 0.5 μg/kg.

Block performance

Patients were placed in the prone position and the skin was sterilized using chlorhexidine. The eighth rib's location was determined by a sequential counting method, starting from the first rib, while employing ultrasonography. Subsequently, the identified site was demarcated on the skin surface. Following the placement of a linear probe with a frequency range of 5–12 MHz parallel to the vertebral axis at the level of the 10^{th} rib, the probe was subsequently moved in a transverse direction from the lateral side to the medial side to detect any alterations in form that occurred within the rib and transverse process. The 18-G Tuohy needle (Perifix, B. Braun Melsungen AG, Melsungen, Germany) was placed in a cephalad-to-caudal direction towards the

trapezius and erector spinae, as well as the T10 trigger point, using the plane technique. This was done after the round shadow of the rib was transformed into the rectangular shape of the transverse process. Upon the needle's contact with the target tissue, it was determined that the fascial plane exhibited clear separation, as evidenced by the successful injection of 2 mL of saline. Subsequently, the administered drugs were injected as per the assigned groups. Following the completion of the block, a deliberate 10-minute wait was implemented for the skin incision to facilitate the optimal distribution of the infiltrating medicines. [17]

The patients' mean arterial pressure and heart rate were initially measured prior to general anesthesia induction (T0), followed by assessment before block commencement (T1), and again 30 minutes post-block (T2). The visual analogue scale was employed to assess the patients' perceived pain intensity. Following the surgical procedure, IV morphine was administered every 6 hours at a prescribed dosage of 0.05 mg/kg, with a maximum amount of 0.2 mg/kg. This intervention was initiated when the patient's visual analogue scale surpassed 4, indicating the presence of significant pain. The cumulative dosage of morphine and fentanyl were calculated.

Study outcomes

The primary outcome was the total postoperative morphine consumption over 24 hours. Secondary outcomes included the patient's hemodynamics, fentanyl consumption during surgery, and the occurrence of any postoperative complications.

Sample size

G*Power version 3.1.9.2 (Franz Faul, Universitat Kiel, Germany) was used to calculate the sample size. Assuming that a two-sided independent samples T-test will be conducted, with an alpha level of 0.05, a power of 0.95, an allocation ratio of 1, and an effect size of 1.123, the minimal sample size per group was 22 patients. The effect size was derived from the study by Reddy and Bisht[18] that reported that the total postoperative opioid consumption was 140.33 ± 37.55 and 107.33 ± 17.80 mcg in the bupivacaine and bupivacaine plus dexmedetomidine groups, respectively. A 15% was added to each group to account for any drop out of patients, so the final sample size was 25 patients per group.

Statistical analysis

Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

Kolmogorov-Smirnov and Shapiro-Wilk tests were used for normality. Data was presented as mean ± SD or median and range. Student t-test, Mann-Whitney test, Chi-square test and Fisher's Exact test were used. Repeated measures ANOVA test was used to compare heart rate and mean blood pressure to study the changes over time within each group. Bonferroni's post-hoc test was used for pair-wise comparisons when the ANOVA test was significant. The significance level was set at $P \leq 0.05$.

Results

A total of 67 patients were assessed for eligibility, 13 declined to participate, and 4 did not fulfil eligibility criteria. Fifty patients were randomly allocated to two equal groups. All patients received ultrasound guided ESPB during PCNL. The control group received bupivacaine alone. The combined block group received dexmedetomidine as an adjuvant to bupivacaine (Figure 1).

Demographic data including gender, age, and body mass index, were not statistically significantly different between the two groups (Table 1). Before induction of anesthesia, the mean values of heart rates and mean arterial blood pressure were comparable (p=1). At T2, the combined block group had a significantly lower heart rates and mean blood pressures (61.84 ± 6.67 vs 69.88 ± 6.42 and 74.32 ± 5.53 vs 83.80 ± 5.36) compared to the control group (Table 2). The postoperative morphine consumption showed a statistically significant decrease in the combined block group compared to control group (0.033 versus 0.051, p<0.001). There was no difference between the two groups in terms of fentanyl consumption (Table 2). Postoperative complications including vomiting, bleeding, and organ injury were not significantly different between the two groups. Patients in the control group had a statistically higher incidence of nausea than the combined block group (28% vs 4%, p=0.049, Table 3).

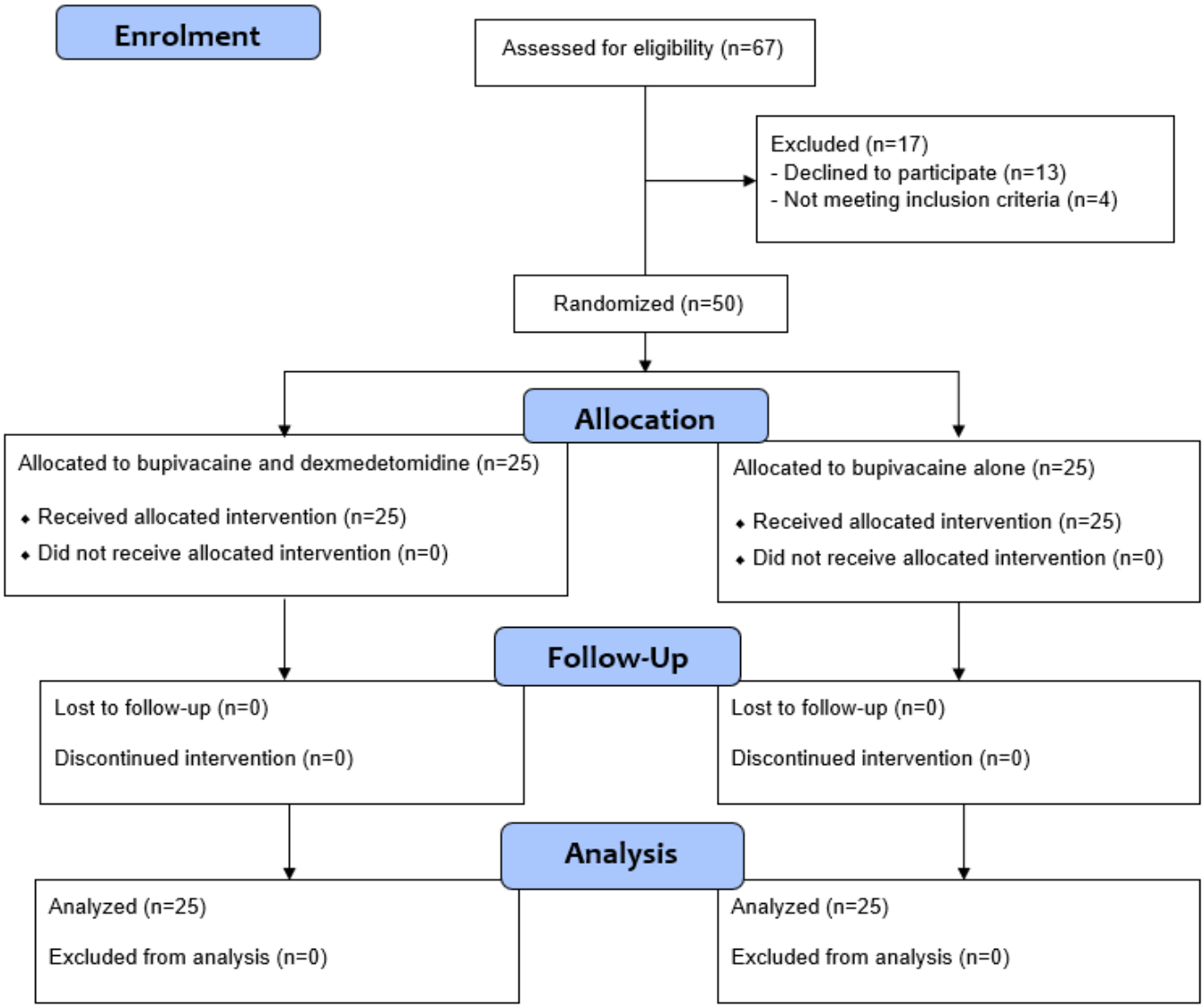

Figure 1. The CONSORT flow diagram of the trial

Table 1. Demographic data

		Control group (n = 25)	Combined block group (n = 25)	P-value
Gender, n (%)	Female	10 (40.0%)	11 (44.0%)	0.774
	Male	15 (60.0%)	14 (56.0%)	
Age, year	Mean ± SD	44.72±10.22	45.68±9.51	0.733
Body mass index	Mean ± SD	26.40±3.1	25.88±2.44	0.513

SD: standard deviation; n: numbers

Table 2. Hemodynamics, fentanyl, and morphine consumption

		Control group (n = 25)	Combined block group (n = 25)	P-value
Heart rate, Mean ± SD	T0	77.84±7.27	76.24±8.79	1.00
	T1	72.60±7.05	71.56±7.97	1.00
	T2	69.88±6.42	61.84±6.67	0.005
P value for time effect		0.005	0.005	
Mean arterial blood pressure, Mean ± SD	T0	102.76±11.07	101.68±10.91	1.00
	T1	88.52±6.14	87.48±6.40	1.00
	T2	83.80±5.36	74.32±5.53	0.005
P value for time effect		0.005	0.005	
Fentanyl consumption, μg/kg, median (range)		0.210 (0-0.560)	0.200 (0-0.300)	0.183
Morphine Consumption, mg/kg, median (range)		0.051 (0.030-0.078)	0.033 (0.020-.300)	<0.001

T0: The first time before induction of general anesthesia; T1: time before starting the block; T3: time at 30 minutes after the end of the block; SD: standard deviation; n: numbers

Table 3. Postoperative complications

		Control group (n = 25)		Combined block group (n = 25)		P-value
		n	%	n	%	
Nausea	Yes	7	28.0%	1	4.0%	0.049
	No	18	72.0%	24	96.0%	
Vomiting	Yes	2	8.0%	0	0.0%	0.490
	No	23	92.0%	25	100.0%	
Bleeding	Yes	4	16.0%	3	12.0%	1.00
	No	21	84.0%	22	88.0%	
Organ Injury	Yes	0	0.0%	0	0.0%	1.00
	No	25	100.0%	25	100.0%	

Discussion

Erector spinae plane block is a feasible peripheral nerve block for providing postoperative analgesia.[19] There is a necessity for alternative approaches to prolong the analgesic efficacy of single-shot nerve blocks after PCNL. The role of dexmedetomidine as an adjuvant agent to bupivacaine is debatable. Hence, this study aimed to examine the utilization of dexmedetomidine as a supplementary agent to bupivacaine for ESPB in patients undergoing PCNL.

Our main results revealed that patients who received combined bupivacaine and dexmedetomidine had lower total morphine consumption, heart rate, mean arterial blood pressure, and incidence of postoperative nausea and vomiting compared to patients who received bupivacaine only.

The etiology of acute pain after PCNL involves visceral discomfort originating from the kidneys and ureters, as well as somatic pain radiating from the incision site. The transmission of renal pain is facilitated through the 10^{th} thoracic vertebra (T10) to first lumbar vertebra (L1) spinal nerves, whereas the transmission of ureter pain is facilitated through the T10–L2 spinal nerves. Furthermore, it is noteworthy that the cutaneous innervation of the incision site is predominantly supplied by the T10-T11 spinal nerves.[2]

The administration of the ESPB at the T7-9 level is effective in providing comprehensive analgesia for both the somatic and visceral abdominal regions. This method can provide a thorough sensory block spanning the T2 to L4, with additional coverage extending to the L1 and L2.[20] Muñoz et al.[21] reported that the suggested mechanism of action of the ESPB involves the inhibition of the dorsal, ventral rami of the thoracic spinal nerves and sympathetic nerve fibers. According to Chin et al.,[22] radiographic findings indicate that administering local anesthetic at the erector spinae plane results in its diffusion in both cranial and caudal directions, as the anatomical plane remains uninterrupted down the vertebral column. According to Muñoz et al.,[21] the ESPB provides evidence of analgesic effects at the cervical, thoracic, and lumbar levels.

Regarding PCNL, Soni et al.[9] assessed the effectiveness of ropivacaine with either fentanyl or dexmedetomidine during the infiltration of the nephrostomy tract. The inclusion of dexmedetomidine alongside ropivacaine yielded superior results compared to fentanyl in terms of

extending the duration of pain relief provided by local anesthesia in nephrostomy tract block while also inducing temporary and mild drowsiness. Moreover, Gao et al.[23] provided evidence supporting the notion that the use of dexmedetomidine (1 μg/kg) as an adjunct to ESPB with ropivacaine resulted in an extended duration of sensory block and diminishes the need for opioid medication during the postoperative period. Several studies[14, 24, 25] have indicated that the administration of perineural dexmedetomidine has the potential to prolong the duration of nerve block, delay the onset of the first postoperative patient-controlled analgesia request, and decrease the requirement for postoperative rescue analgesia. Prior research has elucidated potential pathways that are linked to the efficacy of dexmedetomidine in enhancing blockage. One possible factor to consider is the possible interaction between dexmedetomidine and local anesthetics. According to Zhang and Bai[26] and Yoshitomi et al.,[27] the administration of dexmedetomidine has been found to induce vasoconstriction in the vicinity of the injection site. This vasoconstriction phenomenon has been observed to impede the absorption of local anesthetics, hence extending their duration of action. Furthermore, it has been shown that the administration of perineural dexmedetomidine has a direct impact on the activity of peripheral nerves. This effect serves to mitigate the occurrence of acute perineural inflammation generated by local anesthetics, all while avoiding any potential harm to the nerves themselves. Additionally, it has been found that perineural dexmedetomidine can inhibit the hyperpolarization-activated cation current.[28] In addition, it is worth noting that dexmedetomidine possesses inherent analgesic capabilities and exhibits analgesic-sparing characteristics. Furthermore, the involvement of peripheral α2A-adrenoceptors has been identified as the underlying mechanism via which dexmedetomidine effectively alleviates pain in the context of peripheral nerve block. The stimulation of presynaptic α2 adrenoceptors has been observed to exert an inhibitory effect on the release of neurotransmitters from primary afferent axons. The stimulation of postsynaptic α2 adrenoceptors at the spinal cord level has resulted in an increase in acetylcholine concentrations in the superficial dorsal horn. This increase in acetylcholine levels leads to the inhibition of nociceptive neurotransmission by reducing

the release of certain neurotransmitters, including substance P and glutamate.[29, 30]

Furthermore, Mohamed et al.[31] reported that the effective dose of dexmedetomidine was 0.5–1 μg/kg, which enhanced analgesia quality and duration without any significant adverse effects. According to Fritsch et al.,[32] administering dexmedetomidine in a dosage range of 100-150 μg reduced heart rate while having no significant impact on blood pressure. Carollo et al.[33] found that dexmedetomidine has been linked to hypotension and bradycardia. It was advised that those with substantial cardiovascular conditions or those who were susceptible to hypotension should be cautious while considering the use of this medication. In this study, heart rate and mean arterial blood pressure decreased in the combined dexmedetomidine and bupivacaine group compared to the control group. We used 0.5 μg/kg of dexmedetomidine, that was found to be both safe and efficacious for patients classified as ASA I–II who had PCNL.

Postoperative nausea was significantly reduced in the combined block group. In contrast, no significant variation between the two groups was observed in terms of vomiting. Notably, the incidence of vomiting seemed to be slightly lower in the combined bupivacaine and dexmedetomidine group, though this could be attributed to the comparatively lower morphine consumption in that group. Furthermore, earlier studies[14, 34] have demonstrated a decrease in postoperative nausea and vomiting following laparoscopic surgery with the use of dexmedetomidine as a supplement to ropivacaine. This result is potentially due to the antiemetic properties of dexmedetomidine. The existence of pain is broadly recognized as a significant risk factor for postoperative nausea and vomiting.[34, 35] Within the control group, it is possible that occurrence of severe pain could have led to a higher incidence of postoperative nausea and vomiting.

Limitations

In future research, we recommend conducting multicenter trials with a larger sample size to ascertain the statistical significance of the observed disparity in body mass index. The present study employed a relatively moderate dose of dexmedetomidine. An increase in the duration of analgesia could be observed with higher doses of dexmedetomidine. Hence, future research should give priority to investigating the potential for improved analgesic efficacy with increased dexmedetomidine dosage in the context of the ESPB.

Conclusion

The addition of dexmedetomidine to bupivacaine during ultrasound guided ESPB is a safe and effective adjuvant in reducing postoperative analgesic consumption, maintaining the hemodynamics, and decreasing the occurrence of postoperative nausea and vomiting in patients undergoing PCNL.

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None.

Conflict of interest

The authors declare no competing interests.

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