Influence of gender on postoperative pain in percutaneous nephrolithotomy: A prospective observational study

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Abstract

Background and Aims: Percutaneous nephrolithotomy (PCNL) is the procedure of choice for managing large renal calculi. Although minimally invasive, it is associated with pain due to dilatation of renal capsule, parenchymal tract, and nephrostomy tube placement. Gender differences in pain perception and analgesic requirement have not been studied in PCNL surgeries. This study was done to evaluate the influence of gender on pain.

Material and Methods: It was a prospective observational study including 60 ASA physical status I and II patients. The number of males and females were 29 and 31, respectively. Analgesic requirement and postoperative pain score were assessed by visual and dynamic visual analog scales (VAS, DVAS) score fourth hourly for first 24 h. Rescue analgesia was IV paracetamol 1 g when pain score exceeded four. VAS scores were assessed using Mann–Whitney test. Rescue analgesia was calculated as frequency and proportions. A *P* value of <0.05 was considered statistically significant.

Results: The mean pain score values (VAS P = 0.361; DVAS P = 0.332) and postoperative fentanyl (P = 0.703) did not show a statistically significant difference in males and females. The requirement of rescue paracetamol was higher in females with 30 out of 31 females demanding a rescue analgesic in comparison to 15 out of 29 male patients (P = 0.001).

Conclusion: No significant difference was observed in postoperative pain among males and females in patients undergoing PCNL surgery. The analgesic requirement, however, was found to be more in females than in males.

Keywords: Gender, percutaneous nephrolithotomy, postoperative pain, visual analog scale

Introduction

Percutaneous nephrolithotomy (PCNL) is the procedure of choice for managing large renal calculi and is the preferred technique for staghorn calculi.^[1] It is a minimally invasive procedure. Nevertheless, it is associated with pain due to dilatation of the renal capsule, the parenchymal tract, and placement of the nephrostomy tube.^[2]

There has been a substantial increase in research, analyzing the sex differences in pain and its perception. There is enormous

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literature suggesting that men and women differ as to how they respond to pain. Females have a higher pain sensitivity and an increased risk of perception of pain.^[3] However, the mechanisms underlying these differences are not fully understood.^[4]

The effect of gender on pain in PCNL surgeries has not been studied before. The primary objective of the study was to assess the influence of gender on the postoperative pain in patients undergoing PCNL. The secondary aim was to assess the analgesic requirement in the immediate and late postoperative period.

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Material and Methods

After obtaining ethics committee approval, EC/NIMS/1841/2017 with Clinical Trial Registry number CTRI/2017/02/007833, 60 patients were enrolled in this prospective observational study after taking a detailed informed written consent. The inclusion criteria were ASA I and II physical status patients of age group 18–60 years in whom PCNL procedures were done with a single puncture and a nephrostomy tube was placed. The exclusion criteria were patients with uncontrolled diabetes mellitus or hypertension, a history of cardiac and/or hepatic dysfunction, and the presence of any coagulation disorders or sepsis. Patients were excluded from the study post-induction if there was more than one puncture, blood loss was more than 10% of the blood volume during the procedure, duration of surgery exceeded 3 h, delayed recovery, or patient required postoperative ventilation.

Patients were explained about the visual analog scale (VAS) score and an informed consent was taken. Minimum mandatory monitoring included heart rate (HR), noninvasive blood pressure, pulse oximetry (SpO2), and end-tidal carbon dioxide (ETCO2) for all patients. Intravenous access was obtained and a standard general anesthesia technique was followed for all the patients. Fentanyl 2 μ g·kg⁻¹ dose was given at induction to all patients and they were placed in prone position during surgery. Nephrostomy tubes of size 10 French were inserted in all patients. At the end of the procedure, peritubal infiltration^[5] with 10 ml of 0.25% bupivacaine was given to all patients with 23 gauge spinal needle, at 6 and 12 o' clock positions under fluoroscopic guidance.

The trachea was extubated in supine position after reversing the residual neuromuscular blockade and the immediate postoperative requirement of fentanyl was noted. Patients were transferred to the postoperative care unit and followed up for 24 h postoperatively. Pain score was noted by a trained postoperative nurse on a VAS scale, every fourth hourly for the next 24 h. Dynamic VAS (DVAS) scores were also assessed by asking the patient to cough and with deep breathing. When VAS score was four or more, IV paracetamol 1000 mg was given as rescue analgesia and the number of doses given was noted, with the total dose not exceeding 4 g in 24 h.

Statistical analysis

Statistical analysis was done using the software Statistical Package for the Social Sciences SPSS version 22 (Chicago, IL, USA). Raua *et al.* analyzed the sex differences in reported pain across 11,000 patients captured in electronic medical records and observed that the pain scores used to extract the average pain levels had a mean score of 4.9 ± 0.6 for men and 5.4 ± 0.5 for women.^[6] One study reported the mean

VAS scores 4 ± 1.5 in males and 5.2 ± 0.68 in females undergoing ankle surgery.^[7] Another study by Hartwig *et al.* reported a mean VAS score of 4.9 ± 2.7 in males and 5.9 ± 2.6 in females undergoing laparoscopic gastric bypass surgery.^[8] Taking the mean VAS score in males to be 4 ± 2 and 6 ± 2 in females, a sample size of 27 was estimated in each group, with an alpha error of 0.5 and beta error of 95%.

The parametric data was calculated using student's *t*-test for independent samples. The VAS scores were compared using the Mann–Whitney test. Proportions were compared using the Chi-square test. The significance level of the test was targeted at P value <0.05.

Results

A total of 68 patients were enrolled for the study, 34 males and 34 females. Five males were excluded (three patients had two punctures and two patients had surgery more than 3 h). Three females were excluded (two females had more than one puncture and one patient had blood loss >10% of blood volume). The total patients analyzed for the study were 60, out of which 29 were males and 31 females.

There was no difference in the demographic data like age and vital parameters noted-like HR, blood pressure, saturation, and recovery times between males and females (P > 0.05) [Table 1]. The recovery time was calculated from the time of extubation till the patient was shifted to the recovery after gaining consciousness.

Static and dynamic VAS scores were assessed in all the groups using Mann–Whitney test. It was found that females showed a lower pain score in the immediate postoperative period (VAS = 0.50, DVAS = 1.45 in females and VAS = 0.9, DVAS = 1.83 in males) and a higher score after subsequent assessments [Table 2]. However, the mean pain score values did not show a statistically significant difference in males and females (VAS P = 0.361; DVAS P = 0.332) except at the 20th hour where VAS score depicted a P value

Table 1: Demographic and intraoperative data of males	
and females	

	Male (<i>n</i> =29)	Female (n=31)	P (t-test)
Age; years	42.45 (9.9)	40.65 (11.16)	0.512
Heart rate; bpm	82 (12.47)	83 (14.70)	0.657
Systolic BP; mmHg	132.1 (17.03)	129.03 (18.33)	0.505
Diastolic BP	79.38 (11.48)	81.32 (11.90)	0.532
Mean BP	99.14 (13.03)	98.52 (14.00)	0.860
Recovery time; min	12.76 (3.91)	12.26 (4.05)	0.887
Duration of surgery; min	128.45 (37.84)	130.00 (33.36)	0.867
*Values are mean (SD)			

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of 0.04 and DVAS 0.019. The requirement of postoperative fentanyl in the immediate postoperative period also did not show a statistically significant difference (P = 0.703) in both the genders. The requirement of rescue paracetamol was found to be higher in females with 30 out of 31 females demanding a rescue analgesic in comparison to only 15 out of 29 male patients (P = 0.001) [Table 3].

Discussion

The present study was done to assess the influence of gender on postoperative pain in patients undergoing PCNL surgery. PCNL is the procedure of choice for managing large renal calculi and is the preferred technique for staghorn calculi.^[1] The placement of a nephrostomy tube ensures an adequate drainage and helps in keeping the tract patent for a second nephroscope. However, it ensues a considerable distress to a substantial number of PCNL patients in the form of significant postoperative pain.^[2] Postoperative pain is one of the important factors affecting morbidity of the cardiovascular, pulmonary, and psychological systems in surgical patients. Continuous efforts to provide adequate analgesia during the postoperative phase not only decreases complications, but also facilitates faster recovery.^[9]

With the advent of tubeless PCNL, the placement of nephrostomy tubes has significantly decreased. Although they have an advantage of decreasing postoperative pain and length of hospital stay, there is insufficient evidence for tubeless PCNL in supine PCNL, multiple, complex and staghorn stones, concurrent pelviuretric junction obstruction, and a nephrostomy tube is placed.^[10] The patients included in the study were operated for staghorn calculi. Placement of nephrostomy tube is done routinely in our institute for staghorn calculi.

Compared to men, women have reported more pain and a lower pain threshold and tolerance to pain stimuli in various studies.^[3,4,6] A notable difference has also been observed in the response to nonpharmacological as well as pharmacological pain relief modalities.^[3] Various studies have shown an appreciable gender difference in pain in surgeries like laparoscopic cholecystectomy^[11] and arthroscopic surgeries.^[12] Hussain et al. conducted a study in 120 patients undergoing laparoscopic cholecystectomy, 60 of either sex and observed that pain scores were found to be higher in females during the first hour after surgery and necessitated higher doses of opioid to attain a similar degree of pain relief in comparison to the male group.^[11] The lower pain score in females in the immediate postoperative period in our study (VAS = 0.50, DVAS = 1.45 in females and VAS = 0.9, DVAS = 1.83 in males) could be due to better response to analgesics.^[3,13]

Rosseland et al. conducted three randomized controlled trials on intra-articular analgesics where no analgesia was given postoperatively until there was moderate-to-severe pain with a VAS of more than four within 2 h postoperatively. Intra-articular catheter was placed in all patients. They observed that females had a higher incidence of moderate intensity pain than males.^[12]

Wu HT et al retrospectively analyzed the risk factors for moderate-to-severe postoperative pain after PCNL in 331 patients they found that 221 patients had moderate-to-severe

and females[†] **Tim; hours** Visual analog scale Dynamic visual analog scale Female (n=31) P Female (n=31) P Male (n=29) Male (n=29) 0 0.9 ± 0.86 0.58 ± 0.81 0.147 1.83 ± 1.0 1.45 ± 0.88 0.056 4 1.14 ± 0.64 1.03 ± 1.22 0.680 1.93 ± 0.84 1.94±1.18 0.716 8 2.00 ± 1.13 2.39 ± 1.17 0.200 2.97 ± 1.27 3.06 ± 1.12 0.627 12 2.79 ± 1.08 3.10 ± 1.19 0.307 3.48 ± 1.09 3.84±1.39 0.106 2.84 ± 1.00 0.361 3.58 ± 1.00 16 2.59 ± 1.12 3.31 ± 1.10 0.471 20 2.21 ± 0.82 2.74 ± 1.15 0.044 3.00 ± 0.75 3.42 ± 1.08 0.019 24 2.13 ± 1.02 2.07 ± 0.65 0.789 3.06 ± 1.09 0.335 2.90 ± 0.77 0.361 2.90 ± 1.10 Total 1.95 ± 0.95 2.11 ± 1.02 2.77 ± 0.97 0.332

Table 2: Comparison of visual analog scale (VAS) scores and dynamic VAS (DVAS) scores every fourth hourly in males

*Values are mean (SD). Mann-Whitney test used for statistical analysis

Table 3: Comparison of postoperative fentanyl and rescue paracetamol in male and females‡					
	Postoperative fentanyl (1 mcg/kg)	Р	Rescue paracetamol (1000 mg)	Р	
Gender					
Male $(n=29)$	2 (6.9%)	0.532	15 (51.7%)	0.001	
Female $(n=31)$	3 (9.7%)		30 (96.8%)		

\$Values are number (percentage). Chi-square test used for statistical analysis

pain and there were no significant differences in age (P=0.705) and gender (P=0.709).^[14] This was validated in our study as well.

Interestingly, we observed that there was a moderately significant difference (P = 0.04) in VAS scores as well as the DVAS (P = 0.019) at the 20th hour between males and females. This could be corresponding to the weaning off of the analgesic effect and routine morning care causing patient movement and shifting from postoperative care unit to the ward.

Although the use of postoperative fentanyl did not show a statistically significant difference in both the genders, the postoperative rescue analgesia requirement was found to be higher in females than in males (P = 0.001). This is consistent with the various studies that have shown the analgesic requirement to be higher in females in the postoperative period in other surgeries.^[11,15] This may be due to females being more vocal about their pain perception and analgesic requirement.

There were few limitations in our study. All patients received a peritubal block which might have caused a lower VAS score. We have not taken the hormonal state or the phase of menstrual cycle in the female group, which has been found to influence pain status. Furthermore, pain is a complex mechanism involving an interplay of various factors and further studies are warranted to assess the influence of gender on pain mechanisms. This is a single center study.

In conclusion, no significant difference was observed in postoperative pain among males and females in patients undergoing PCNL surgery in our study. However, the analgesic requirement was found to be more in females than in males. Further multicentric studies are warranted to corroborate our findings.

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Conflicts of interest

There are no conflicts of interest.

References

- 1. Ganpule AP, Vijayakumar M, Malpani A, Desai MR. Percutaneous nephrolithotomy (PCNL) a critical review. Int J Surg 2016;36:660-4.
- Pietrow PK, Auge BK, Lallas CD, Santa-Cruz RW, Newman GE, Albala DM, et al. Pain after percutaneous nephrolithotomy: Impact of nephrostomy tube size. J Endourol 2003;17:411-4.
- Bartley EJ, Fillingim RB. Sex differences in pain: A brief review of clinical and experimental findings. Br J Anaesth 2013;111:52-8.
- Fillingim RB, King CD, Ribeiro-Dasilva MC, Rahim-Williams B, Riley JL. Sex, gender, and pain: A review of recent clinical and experimental findings. J Pain 2009;10:447-85.
- Jonnavithula N, Pisapati MV, Durga P, Krishnamurthy V, Chilumu R, Reddy B. Efficacy of peritubal local anesthetic infiltration in alleviating postoperative pain in percutaneous nephrolithotomy. J Endourol 2009;23:857-60.
- Ruau D, Liu LY, Clark JD, Angst MS, Butte AJ. Sex differences in reported pain across 11,000 patients captured in electronic medical records. J Pain 2012;13:228-34.
- Storesund A, Krukhaug Y, Olsen MV, Rygh LJ, Nilsen RM, Norekvål TM. Females report higher postoperative pain scores than males after ankle surgery. Scand J Pain 2016;12:85-93.
- Hartwig M, Allvin R, Bäckström R, Stenberg E. Factors associated with increased experience of postoperative pain after laparoscopic gastric bypass surgery. Obes Surg 2017;27:1854-8.
- Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg 2013;26:191-6.
- 10. Agrawal MS, Agrawal M. Tubeless percutaneous nephrolithotomy. Indian J Urol 2010;26:16-24.
- 11. Hussain A, Khan F, Ahmed A, Chawla T, Azam S. Effect of gender on pain perception and analgesic consumption in laparoscopic cholecystectomy: An observational study. J Anaesthesiol Clin Pharmacol 2013;29:337-41.
- Rosseland LA, Stubhaug A. Gender is a confounding factor in pain trials: Women report more pain than men after arthroscopic surgery. Pain 2004;112:248-53.
- Gear RW, Miaskowski C, Gordon NC, Paul SM, Heller PH, Levine JD. Kappa–opioids produce significantly greater analgesia in women than in men. Nat Med 1996;2:1248-50.
- Hao-Tian Wu, Tian-fu Ding, Huan Zhang *et al*. Risk Factors for Moderate-to-severe Postoperative Pain After Percutaneous Nephrolithotomy: A Retrospective Study doi: [10.21203/ rs.3.rs-396652/v1]
- Mobini A, Mehra P, Chigurupati R. Postoperative pain and opioid analgesic requirements after orthognathic surgery. J Oral Maxillofac Surg 2018;76:2285-95.