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Comparison of post-operative shivering, nausea and vomiting between pre-intubation and pre-extubation intravenous paracetamol in percutaneous nephrolithotripsy under general anaesthesia

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Abstract

Background: Post-operative shivering, nausea and vomiting is frequently observed in patients undergoing percutaneous nephrolithotripsy [PCNL] under general anaesthesia. It is not only distressing to patients but can also be detrimental because of the increased oxygen consumption, coagulopathies, delayed recovery and increased blood pressure. Prophylactic paracetamol administration has shown to be effective in reducing post-operative shivering by decreasing the hypothalamic temperature set point. When paracetamol is administered prior to extubation, it can reduce nausea and vomiting by reducing the post-operative pain. We aimed to compare the effects of prophylactic pre-induction and pre-extubation intravenous paracetamol on post-operative shivering, nausea and vomiting. Correlation of severe post-operative shivering with patient's age, BMI, and amount of irrigation fluid used were also evaluated.

Methods: This prospective observational study was carried out on 72 patients undergoing PCNL under GA. Patients receiving intravenous 1gm paracetamol 20 minutes prior to intubation were grouped as PI-PCM while those receiving it 20 minutes prior to extubation over 20 minutes were grouped as PE-PCM. We recorded age, BMI, core body temperature (Pre-induction, before giving muscle relaxant and then 30 minutes thereafter, after extubation and just before shifting to the post-operative recovery), duration of PCNL, amount of irrigation fluid, post-operative shivering using Crossley & Mahajan score and PONV using the Apfel score every 10 minutes for 2 hours.

Results: Demographic data such were comparable between the PI-PCM and PE-PCM groups. The occurrence of severe post-operative shivering (Crossley-Mahajan grade >II) was significantly higher (p 0.033) in the PE-PCM group as compared to the PI-PCM group. Post-operative shivering had statistically highly significant negative correlation with BMI and positive correlation with the amount of irrigation volume used. Incidence of PONV was statistically higher (p0.023) in the PI-PCM group as compared to the PE-PCM group.

Conclusion: Prophylactic intravenous paracetamol administration can significantly reduce post-operative shivering in PCNL patients under GA. Similarly, its administration prior to extubating can significantly decrease the post-operative nausea and vomiting.

Keywords: Post-operative shivering, nausea, vomiting, percutaneous nephrolithotripsy

Introduction

Percutaneous Nephrolithotomy (PCNL) is an established method for removal of large size renal calculi (>1.5– 2 cm), staghorn calculi, upper tract calculi not responding to other modalities of treatment, lower pole stones, cystine nephrolithiasis, and stones in anatomically abnormal kidney [1]. General Anaesthesia (GA) is preferred because of its advantages that include safety as the patient's airway is secured in prone position, feasibility to control tidal volume during percutaneous access puncture to minimize injury to the pleura and lungs, and prolonged anaesthesia duration allowing the surgeon to make multiple and higher punctures with minimal patient discomfort [2].

GA facilitates redistribution of the temperature from the central tissues to the peripheral tissues causing peri-operative hypothermia which complicates a large percentage of surgeries [3]. Moreover, despite the relatively non-invasive nature of the procedure, the use of large quantity of irrigation fluid causes rapid fluid absorption in nearly 78% in PCNLs [4], resulting into peri-operative hypothermia and thus post-operative shivering in patients under GA.

The incidence of post-operative shivering (POS) is 5-65% of patients receiving general anaesthesia^[5]. Post-operative shivering has many side effects such as oxygen consumption, blood pressure changes, distressing patient with coronary artery disease, pain, discomfort in patients, coagulation disorders and delayed recovery. POS increases oxygen consumption 400% and sometimes up to 600%^[6] that leads to arterial hypoxemia raise in carbon dioxide production and lactic acidosis and blood pressure and is occasionally associated with harmful sequelae especially in high risk patients.

Furthermore, there are several variables apart from anaesthesia impacting POS including sex, BMI, age, type of procedure, blood loss etc^[7, 8, 9]. Postoperative shivering can occur even in normothermic patients during the perioperative period.

There are two ways to reduce shivering, including forced air warming of the patient^[10] and use of pharmaceutical agents. Anti-shivering drugs decrease the shivering threshold^[11, 12]. Many opioids, alpha 2 agonists, steroids etc have been found useful for prevention of post-operative shivering but can cause sedation, respiratory depression, delayed recovery, nausea, vomiting and impairment of hypothalamic thermoregulation^[13-16]. Intravenous paracetamol administration has become popular for post-operative analgesia and reducing opioid consumption^[17]. It acts through a centrally mediated prostaglandin inhibition to decrease the hypothalamic temperature set point. Its prophylactic use has shown to reduce post-operative shivering significantly^[18].

Post-operative nausea and vomiting (PONV) occurs in about 30% of patients undergoing GA. It has been found that intravenous prophylactic paracetamol given before the surgery can reduce the incidence of PONV, mainly mediated through superior pain control^[19].

In this study, our primary aim was to compare the incidence and severity of post-operative shivering, nausea and vomiting with use of pre-induction and pre-extubation intravenous paracetamol administration in PCNL patients undergoing GA. Correlation of severe post-operative shivering with patient's age, BMI, and amount of irrigation fluid used were also evaluated as secondary outcomes.

Materials and methods

This prospective observational study was carried out in the urology operation theatre of our institute from October 2019 to September 2021 after the clearance from the Institutional ethics committee. Based on previous study by G. Khalili et al^[20], considering 5% level of significance and 95% power value, the required sample size was 66. Considering 10% dropouts, 72 cases were included in this study. Sampling method used was non-probability convenient consecutive consenting patients. Patients having allergy to paracetamol, diabetics, on beta blockers, vasodilators, CCBs, ACE I, hypo/hyperthyroidism and febrile were excluded from the

study. A valid informed consent by all the participants was taken for the study.

As per the protocol, participants age in years, weight in kilograms, height in centimeters, Body mass index and peripheral body temperature were noted and starvation confirmed.

Our operation theatre room temperature is always maintained at 22 to 24 °C. On the operation table, baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, oxygen saturation, peripheral and core temperature. Following premedication with IV glycopyrrolate 0.04mg/kg, fentanyl 1-2 ug/kg, GA with endotracheal intubation was carried out with titrated doses of propofol upto 2 mg/kg and atracurium 0.75mg/kg. PCNL was carried out in prone position.

Intravenous paracetamol 15mg/kg was administered intravenously over 20 minutes either before induction or just before extubation for analgesia depending upon the senior anaesthetist's discretion. Cases were accordingly divided into two groups depending upon their timing of receiving paracetamol; pre-intubation or pre-extubation.

Intra-operatively the patients were covered with sheets of gamgee and sterile surgical drapes. Forced air warmer at 37 °C was used to keep the patient warm. After extubation, patient were transferred to post-operative recovery, covered with a blanket and provided with oxygen at the rate 1-2L/min via nasal prongs and were observed for atleast 2 hours before shifting to the ward.

Parameters recorded were age, BMI, skin and core body temperatures, (Pre-induction, before giving muscle relaxant and then 30 minutes thereafter, after extubation and just before shifting to the post-operative recovery), duration of surgery in hours and amount of irrigation fluid in ml at the end of surgery.

Post-operative shivering severity was graded as per the Crossley and Mahajan scoring^[21] [Table:1] and post-operative nausea and vomiting severity as per Apfel scoring^[22] [Table:2] after shifting to postoperative recovery every 10 minutes upto 2 hours. Shivering and nausea-vomiting of grade > II is considered as severe.

Results

Mean and standard deviation of quantitative variables were calculated using SPSS 16. Paired and unpaired t tests were used to assess statistical significance for discrete and categorical data. Association between variables was analyzed by Pearson and Spearman's correlation coefficient. A p value <0.005 was considered as significant p value < 0.001 was considered as highly significant statistically.

Demographic data such as age [Fig:1], BMI [Fig:2] and gender [Fig:3] were comparable (p > 0.05) between the PI-PCM and PE-PCM groups. Baseline core body temperatures between both the groups was also statistically insignificant. (p0.385, independent t test)

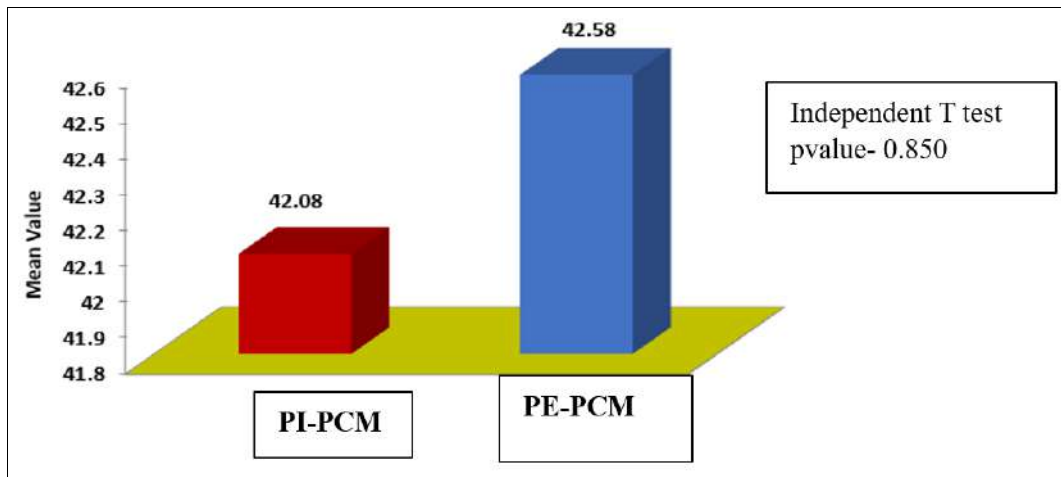


Fig 1: Comparison of mean age between PI-PCM & PE-PCM

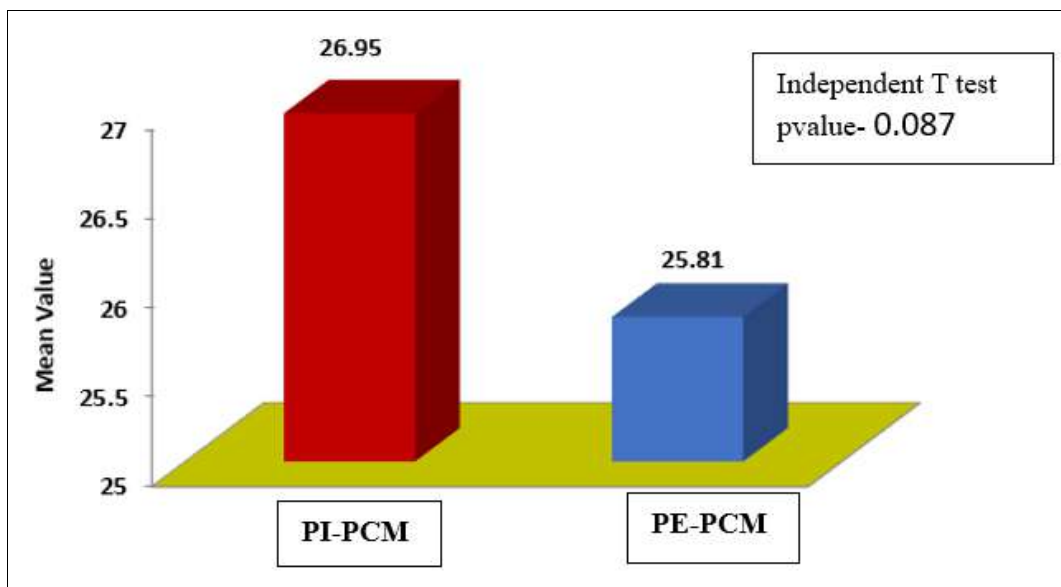


Fig 2: Comparison of BMI between PI-PCM & PE-PCM

Mean with standard deviation of core body temperatures [Table: 3] at different timepoints during PCNL shows a fall during the procedure but comparison done using

independent t test between PIPCM and PE-PCM is non-significant ($p > 0.05$) during perioperative period.

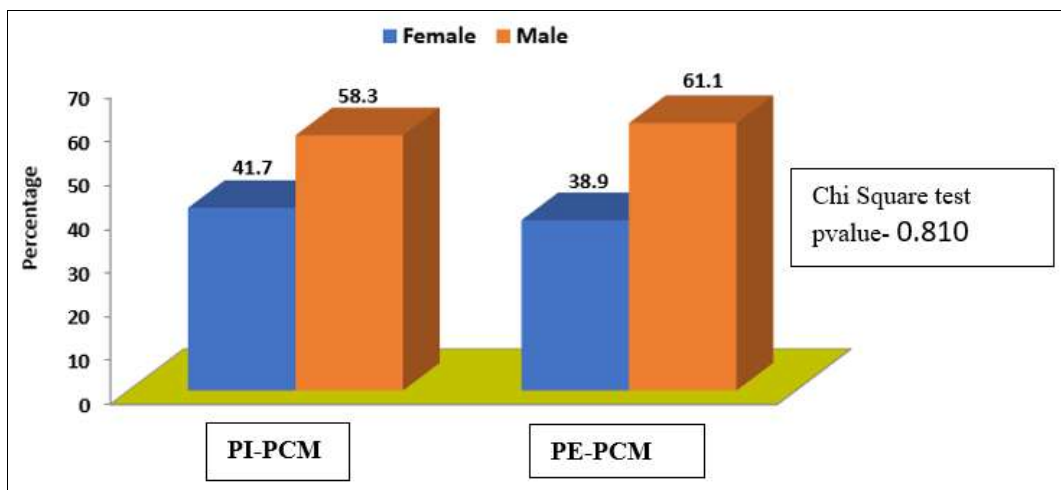


Fig 3: Comparison of gender population between PI-PCM & PE-PCM

The occurrence of severe post-operative shivering (Crossley-Mahajan grade >II) was significantly higher in the PE-PCM group as compared to the PI-PCM group.

[Fig:4] 15/36 of PI-PCM and 24/36 in PE-PCM group required treatment for severe shivering.

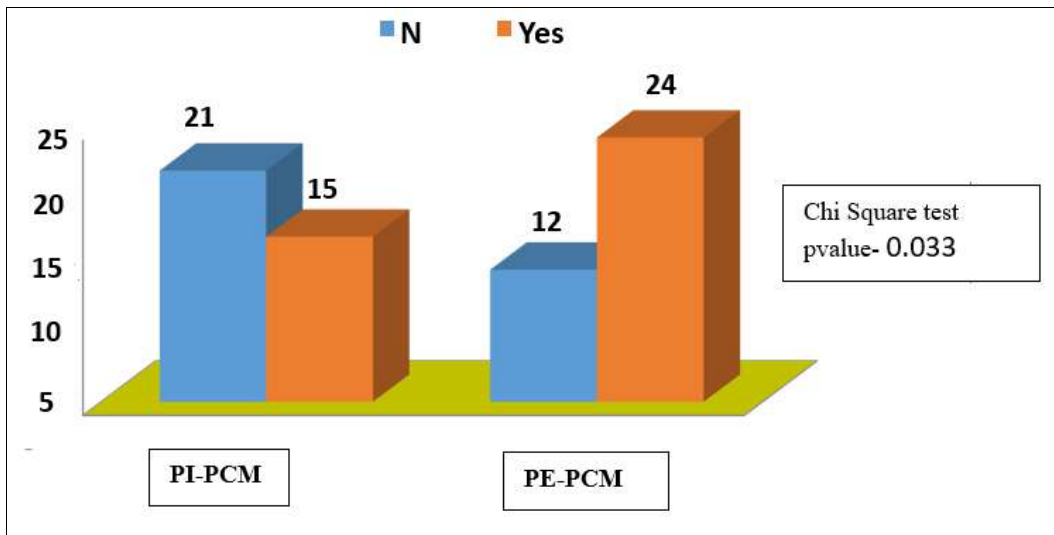


Fig 4: Comparison of incidence of post-operative shivering between PI-PCM & PE-PCM

Pearson’s correlation coefficient of post-operative shivering with patients age, BMI and amount of irrigation fluid was calculated for the entire sample population. There was no significant correlation of POS with age, statistically highly significant negative correlation with BMI and positive correlation with the amount of irrigation volume used.

[Table:4]

It was observed that the incidence of PONV was statistically higher and significant i.e. $p=0.023$, in the PI-PCM group (33.33%) as compared to the PE-PCM group (11.11%) [Fig:5]

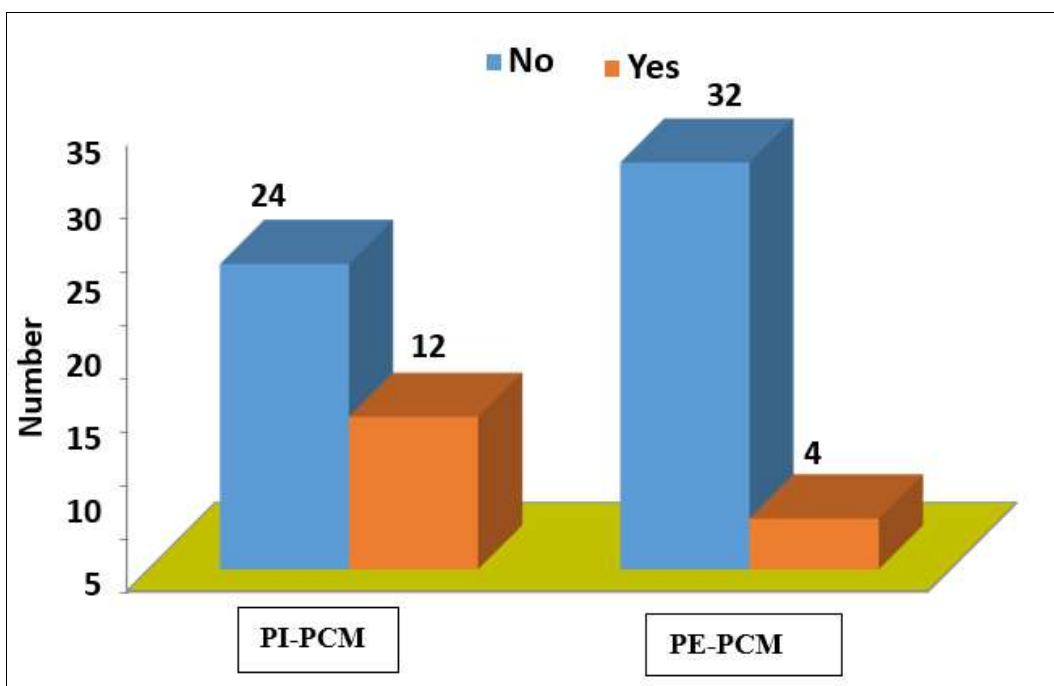


Fig 5: Comparison of incidence of post-operative nausea-vomiting between PI-PCM & PE-PCM

Discussion

Regional anaesthesia for PCNL has its own merits in the form of less postoperative pain, less blood loss, and early recovery and discharge thereby reducing stay in the hospital [23-25]. GA is more comfortable for the patients in prone position and also safer, in case the procedure was prolonged [26]. The many specific anesthesia concerns in PCNL mandate a fine coordination between the surgical and anesthesia teams for optimal results. The choice of anesthesia depends, to a great extent, upon the patient’s preference, the position for surgery favored by the surgeon, surgical expertise, and estimated time of the procedure determined by the stone size, number, and location.

Perioperative hypothermia, core temperature below 36.0 °C, transpires due to disruption of thermoregulation by general anesthesia coupled with cold exposure to procedural surroundings and cleansing agents. The clinical consequences of perioperative hypothermia are multiple and include patient discomfort, shivering, platelet dysfunction, coagulopathy, and increased vasoconstriction associated with a higher risk of wound infection [6]. Furthermore, postoperative cardiac events occur at a higher rate; although it is unclear whether this is due to increased oxygen consumption or norepinephrine levels. Hypothermia may also affect pharmacokinetics and prolong postoperative recovery times and hospital length of stay.

PCNL is a procedure where large quantity of irrigation fluid absorbed and thus again contribute to perioperative hypothermia and its complication. Prophylactic paracetamol infusion has been found to reduce the post-operative shivering [27-29] and nausea vomiting [19]. Here, we have also correlated incidence of post-operative shivering with patient's age, BMI, and amount of irrigation fluid.

Both the groups i.e. PI-PCM and PE-PCM were comparable in terms of demographic variables of age in years, BMI and gender.

Post-operative shivering occurs in patients recovering from general anaesthesia and most of the times is preceded by central hypothermia and peripheral vasoconstriction indicating that it almost is always thermoregulatory mechanism. Shivering is an important complication of hypothermia, it is a complicated response of the body that includes at least three different patterns of muscular activity. Despite the availability of various drugs and technologies to prevent hypothermia it continues to remain an ongoing problem in the perioperative period. Here in our study on PCNL patient use of irrigation fluid and its absorption make patients more prone for perioperative hypothermia and thus post-operative shivering. There was a fall in a core body temperature in both groups which was statistically significant. However, the baseline and intra-operative core body temperature between the 2 groups was comparable.

Post-operative shivering differs between 5% and 65% depending upon the kind of general or regional anesthesia [4]. On analysing the data, we have found that, the incidence of post-operative shivering in patients receiving preoperative paracetamol was 41.66% which is significantly less than in compare to patients receiving pre-extubation paracetamol which was 66.66%. This effect observed mainly is due to suppressing the temperature set point of hypothalamus and thus avoiding it to trigger a response. The mechanism of action observed with paracetamol in reducing post-operative shivering is different with that of other drugs which act by lowering threshold for shivering. Previous studies have demonstrated the effect of intravenous paracetamol for postoperative shivering in different surgeries and shown the effects of paracetamol in lowering core and peripheral body temperature and its effect in controlling post-operative pain and PONV. Gholamreza Khalili et al [6], have shown the beneficial effects of paracetamol in post-operative shivering and pain reduction and on the core and peripheral temperature using the drug as a pre-drug and recommended in patients undergoing surgery with general anesthesia. Similarly, Gholami et al [5] and Takehiro Kinjo et al [28], concluded effects of prophylactic intravenous paracetamol for prevention of shivering after general anesthesia.

Shivering was graded by using scale devised by Crossley-Mahajan [9]. Any grade above II can cause discomfort in the patients and hence it would require treatment. It was found that patients receiving prophylactic pre-intubation paracetamol infusion had significantly lower incidence of post-operative shivering as comparing to the patients who received it before extubation.

We also done Pearsons correlation coefficient for post-operative shivering with various variable like age, BMI, and amount of irrigation fluid used as the secondary outcome of the study. It was observed that there is negative correlation of shivering with patients BMI and positive correlation with amount of irrigation fluid used. No significant correlation

was found between age and post-operative shivering.

Higher body mass index was a protective factor for postoperative shivering. It has been demonstrated that intraoperative core temperature is higher in obese patients. The study by Eberhart et al [7] confirmed the finding that longer duration of surgery as well as pyrogenic substances released from injured tissue impaired the thermoregulatory system and induced shivering.

Similarly, Laortip Rattanapittayaporn et al [29], in their study identified higher BMI and shorter duration of surgery reduced risk of postoperative shivering. Irrigation fluid used during our study was at room temperature and thus its absorption causes perioperative hypothermia. Yue He et al [30] studied the effects of irrigation fluid temperature during flexible ureteroscopic holmium laser lithotripsy on postoperative fever and shivering and concluded that warming the irrigation fluid can reduce the incidence of postoperative fever and shivering.

The incidence of PONV has been reported to be approximately 40%–88% in patients undergoing surgery without antiemetic prophylaxis. We found that the incidence of PONV in patients receiving pre extubation paracetamol was 11.11% which is significantly less in comparison to patients receiving prophylactic preinduction paracetamol i/e/ 33.33%. This effect may be due to superior pain control in patients receiving pre-extubation paracetamol as compared to group receiving pre-induction paracetamol. Despite unclear mechanisms of analgesic and antiemetic actions of paracetamol, studies have shown that paracetamol inhibits the cyclooxygenase enzyme and affects some serotonergic pathways in the central nervous system. Serotonin is found in the brainstem vomiting center. AM404 (a metabolization product of paracetamol in the brain) inhibits the reuptake of anandamide [31]. Decreased anandamide levels were found to be associated with a high incidence of nausea and vomiting in humans [32]. This may be another explanation for the antiemetic effect of acetaminophen. In 2017, Mehmet Aksoy, et al. [33], done a prospective randomized study aimed to compare the efficacy of preoperative versus postoperative paracetamol on postoperative nausea and vomiting (PONV) in children undergoing strabismus surgery. The use of IV preoperative paracetamol reduces the incidence of PONV and postoperative antiemetic consumption during the first 6 h after strabismus surgery. The study shows paracetamol given before the onset of PONV is effective in reducing its incidence but has no effect once PONV is developed.

Table 1: Grading as per Crossley and Mahajan score

i.	No shivering
ii.	No visible muscle activity, but one or more of piloerection, peripheral vasoconstriction or peripheral cyanosis (other causes excluded)
iii.	III-Muscular activity in only one muscle group
iv.	Moderate muscular activity in more than one muscle group, but not generalised shaking
v.	Violent muscular activity that involves the entire body

Table 2: Grading as per Apfel score

i.	Nausea: No vomiting or retching.
ii.	Retching: vomiting like movements without expelling gastric content.
iii.	Vomiting: Expelling gastric content

Table 3: Core Body temperature at different time-points during PCNL

Core body Temperature	Group	N	Mean	Stdev	Independent T test	P-Value	Sig. at 5% level
Core Body Temperature (Baseline)	PI-PCM	36	36.3000	.5971	0.385	0.701	Not
	PE-PCM	36	36.2528	.4293			
Core body temperature (just before giving muscle relaxant)	PI-PCM	36	36.1972	.5624	0.125	0.901	Not
	PE-PCM	36	36.2111	.3568			
Core body temperature (30 minutes post induction)	PI-PCM	36	36.1361	.5632	0.583	0.562	Not
	PE-PCM	36	36.2000	.3389			
Core body temperature (60 minutes post induction)	PI-PCM	36	36.1694	.5595	0.051	0.960	Not
	PE-PCM	36	36.1750	.3484			
Core body temperature (90 minutes post induction)	PI-PCM	36	36.2639	.5049	0.668	0.506	Not
	PE-PCM	36	36.1972	.3211			
Core body temperature (120 minutes post induction)	PI-PCM	31	36.2710	.4887	0.595	0.554	Not
	PE-PCM	34	36.2088	.3467			
Core body temperature (150 minutes post induction)	PI-PCM	20	36.1750	.5766	0.187	0.853	Not
	PE-PCM	28	36.2000	.3496			
Core body temperature (180 minutes post induction)	PI-PCM	11	36.1727	.5711	0.294	0.771	Not
	PE-PCM	21	36.2238	.4049			
Core body temperature (210 minutes post induction)	PI-PCM	4	36.0000	.8165	1.000	0.333	Not
	PE-PCM	13	36.2385	.2256			
Core body temperature (240 minutes post induction)	PI-PCM	1	35.6000	0.000	2.005	0.101	Not
	PE-PCM	6	36.3333	.3386			
Core body temperature (AVERAGE)	PI-PCM	36	36.2481	.5137	0.305	0.761	Not
	PE-PCM	36	36.2172	.3233			

Table 4: Correlation of POS with patients age, BMI, and amount of irrigation fluid used in PI-PCM and PE-PCM groups

Post-Operative Shivering		Age	BMI	Amount of Irrigation fluid	Post-Operative Shivering
PI-PCM	Pearson Correlation	-.103	-.554**	.804**	1.000
	Sig. (2-tailed)	.551	.000	.000	.
	N	36	36	36	36
PE-PCM	Pearson Correlation	-.069	-.699**	.880**	1.000
	Sig. (2-tailed)	.688	.000	.000	.
	N	36	36	36	36

Conclusion

Prophylactic intravenous paracetamol administration prior to PCNL under GA may prevent severe post-operative shivering significantly and thereby the incidence of complications such as increased oxygen consumption, coagulopathies, delayed recovery, arterial hypoxaemia and lactic acidosis. On the other hand, PONV can be reduced significantly with administration of paracetamol before extubation.

Conflict of Interest

Not available

Financial Support

Not available

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