Section: Anaesthesiology

Original Research Article

EFFECT OF TIMING OF INTRAOPERATIVE IV PARACETAMOL ADMINISTRATION ON POSTOPERATIVE SHIVERING

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Received : 07/06/2025
Received in revised form : 03/08/2025
Accepted : 21/08/2025

Keywords:
Postoperative shivering, hypothermia, intravenous paracetamol, analgesic requirement, timing of administration.

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DOI: 10.47009/jamp.2025.7.5.6

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (5); 24-28

ABSTRACT

Background: Postoperative shivering (POS) is a common complication following general anaesthesia. Although intravenous (IV) paracetamol has been shown to reduce POS, the impact of its timing on efficacy remains unclear. This study aimed to evaluate the effect of IV paracetamol timing on POS, perioperative hypothermia, and postoperative analgesic requirement. **Materials and Methods:** This randomised controlled study was conducted on 120 patients who were admitted for elective and emergency surgeries at Government Rajaji Hospital, Madurai, for 3 months. Patients were randomly assigned to three groups of 40: Group A received IV paracetamol after induction, Group B before surgery completion, and Group C received no paracetamol. Patient details, temperatures, shivering, and analgesia requirements were recorded, with standard monitoring and core temperature measurements from pre-induction to 4 hours postoperatively. **Result:** Most patients were aged between 40 and 45 years, with the majority being males (50-55%) and ASA I category (62-68%), but the differences were not significant ($p > 0.05$). Group B had the lowest POS incidence (2.5%) compared to Group A (15%) and Group C (25%) ($p = 0.021$). Hypothermia occurred in 10% of Group B, 30% of Group A, and 37.5% of Group C ($p = 0.010$). Analgesic requirement was lowest in Group B (30%) versus Group A (45%) and Group C (50%) ($p = 0.083$). Shivering severity was minimal in Group B (one case of grade II), whereas Groups A and C had patients with severe shivering (grades III and IV). **Conclusion:** Late intraoperative IV paracetamol significantly reduced POS and perioperative hypothermia and lowered the need for analgesics.

INTRODUCTION

Postoperative shivering (POS) is a common complication following general anaesthesia, with incidence rates reported between 5% and 65%, depending on the surgical procedure and the anaesthetic method applied.[1] It involves involuntary, repetitive muscle contractions, which may result from perioperative hypothermia or may develop even when the patient's temperature remains within normal limits.[2] A study indicates that male gender, younger age, and the duration of anaesthesia or surgery are associated with a higher possibility of POS.[3] While often considered harmless, shivering can significantly raise oxygen demand by as much as 400–600% along with an increase in carbon dioxide production and lactic acidosis. This may lead to arterial hypoxaemia, variations in blood pressure, and greater strain on the heart.[4] Such effects are particularly dangerous for individuals with compromised cardiopulmonary function.[2] In addition, shivering causes discomfort and can worsen postoperative pain by stretching surgical wounds, thereby hindering accurate monitoring.[5]

The underlying aetiology of shivering is not sufficiently understood, but it is considered that mechanisms of POS involve multiple factors. The most frequent cause is hypothermia resulting from anaesthesia-induced disruption of normal temperature control combined with exposure to a cool operating room.[4] However, shivering can also occur due to non-temperature-related processes, including postoperative pain, sudden withdrawal from opioids, reduced sympathetic activity, and release of spinal reflex inhibition.[6] During anaesthesia, the temperature threshold that triggers shivering is reduced, creating a wider range between the thresholds for sweating and shivering, thereby

ISSN (O): 2687-5365; ISSN (P): 2753-6556

increasing vulnerability to hypothermia.[2,4] Surgical stress and pain can further influence the hypothalamic set-point, promoting the onset of shivering.[4]

Perioperative hypothermia, defined as a core body temperature between 33°C and 35°C, is frequently seen in surgical patients who do not receive active warming.[4] Even a slight decrease in core temperature can initiate vasoconstriction and, finally, result in shivering.[2] General anaesthesia boosts the redistribution of heat from the body's core to peripheral tissues, while the administration of large volumes of irrigation fluids, such as those used during percutaneous nephrolithotripsy, can further increase heat loss.[7] Minimising hypothermia through active warming measures and drug-based methods remains a key approach to lowering the risk of POS.[1]

Various medications have been evaluated for both the prevention and management of shivering, including meperidine, clonidine, ketanserin, and doxapram; however, their use is limited by adverse effects such as drowsiness, breathing difficulties, and unstable blood pressure.[6] Intravenous (IV) paracetamol has recently gained attention as a safer option. Its action involves centrally mediated suppression of prostaglandin production, which lowers the hypothalamic temperature set-point.[1,7] Unlike NSAIDs, paracetamol does not interfere with platelet activity or kidney blood flow and is generally well tolerated.[8] Its pain-relieving effect may also help decrease postoperative discomfort, which in turn could reduce the likelihood of shivering.[8,7]

Studies suggest that the use of IV paracetamol can significantly reduce POS. In elective caesarean deliveries performed under general anaesthesia, paracetamol administration led to a decrease in both the frequency and intensity of shivering compared with placebo.[1] In septoplasty procedures, giving paracetamol before surgery proved more effective than ketorolac for preventing both shivering and pain.8 The timing of administration can also affect the results: during percutaneous nephrolithotripsy, paracetamol given before induction reduced the prevalence of severe shivering than when given before extubation, although the late administration was associated with reduced postoperative nausea and vomiting.[7]

Although there are studies on the pharmacological profile of paracetamol and its role in POS, only a few studies have compared the association between the timing of paracetamol administration and POS. Thus, this study aimed to evaluate the effect of IV paracetamol administration timing on POS and perioperative hypothermia, along with assessing the need for postoperative analgesics.

MATERIALS AND METHODS

This randomised controlled study was conducted on 120 patients who were admitted for elective and emergency surgeries at Government Rajaji Hospital, Madurai, for 3 months. Before initiating the study, it was approved by the Institutional Ethics Committee. All data from the study were secure, and confidentiality was maintained.

Inclusion and exclusion criteria

Patients with ASA-PS I or II and a surgery duration of 1–4 hours were included, while those with ASA-PS >III, BMI >35 kg/m², liver dysfunction, paracetamol allergy, or body temperature <36 °C or >38 °C were excluded.

Methods

Patients were randomly allocated into three groups of 40 each: Group A received IV paracetamol 15 mg/kg (maximum 1 g) immediately after induction, Group B received the same dose 20-30 minutes before completion of surgery, and Group C served as the control group without paracetamol. A structured proforma was used to collect patient details, including name, age, sex, diagnosis, procedure planned, operating room temperature, patient temperature before induction, induction and intubation times, timing of paracetamol administration, extubation time, recovery room temperature, presence and grade of shivering (I–IV), need for analgesia, and time of analgesic administration. Standard monitoring (BP, ECG, and pulse oximetry) and documentation of the operating room temperature were performed. Core temperature was recorded before induction, every 15 min intraoperatively, and every 30 min postoperatively for 4 hours.

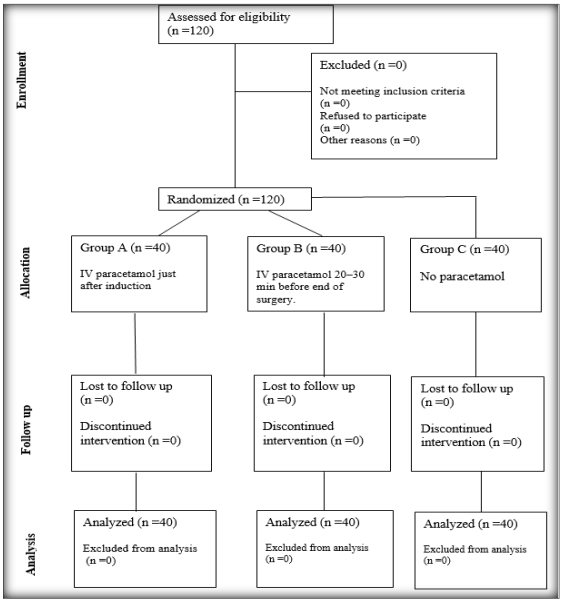

Figure 1: Consort diagram

Statistical Analysis

Data were presented as mean, standard deviation, frequency and percentage. Continuous variables were compared using the independent sample t-test. Categorical variables were compared using Pearson's chi-square test. Significance was defined as P values less than 0.05 using a two-tailed test. Data analysis

ISSN (O): 2687-5365; ISSN (P): 2753-6556

was performed using IBM-SPSS version 21.0 (IBM-SPSS Science Inc., Chicago, IL).

RESULTS

The three groups demonstrated comparable baseline characteristics, with no significant differences across any parameter ($p > 0.05$). The mean age was 42.3 ± 10.8 years in Group A 41.6 ± 9.9 years in Group B, and 43.2 ± 11.2 years in Group C. The gender distribution was balanced, with males comprising 55%, 52.5%, and 50% of Groups A, B, and C, respectively. Most patients were ASA class I (65%, 62.5%, and 67.5%), with the remainder in ASA class II. The mean surgery duration ranged from 98.5 ± 25.2 to 101.3 ± 28.7 min, and the baseline temperature was consistent across groups (36.7–36.8°C). (Table 1).

Table 1: Baseline demographic and clinical characteristics across groups

		Groups			P value
		A	B	C	
Age (years)	Mean ± SD	42.3 ± 10.8	41.6 ± 9.9	43.2 ± 11.2	0.782
Gender	Male	22 (55%)	21 (52.5%)	20 (50%)	0.835
	Female	18 (45%)	19 (47.5%)	20 (50%)	
ASA	I	26 (65%)	25 (62.5%)	27 (67.5%)	0.914
	II	14 (35%)	15 (37.5%)	13 (32.5%)	
Surgery duration (mins)	Mean ± SD	98.5 ± 25.2	101.3 ± 28.7	100.2 ± 27.1	0.882
Baseline temperature (°C)	Mean ± SD	36.8 ± 0.3	36.7 ± 0.4	36.8 ± 0.3	0.511

Shivering occurred in 15%, 2.5 %, and 25% of patients in Groups A, B, and C, respectively, with a significant difference between groups ($p = 0.021$). Hypothermia was also significantly different ($p = 0.01$), occurring in 30% of Group A, 10% of Group B, and 37.5% of Group C. The requirement for postoperative analgesia was highest in Group C (50%), followed by Group A (45%) and Group B (30%), although this difference was not significant ($P = 0.083$) (Table 2).

Table 2: Incidence of shivering, hypothermia, and analgesia requirement

		Groups			P value
		A	B	C	
Shivering	Present	6 (15.0%)	1 (2.5%)	10 (25.0%)	0.021
	Absent	34 (85.0%)	39 (97.5%)	30 (75.0%)	
Hypothermia	Present	12 (30.0%)	4 (10.0%)	15 (37.5%)	0.01
	Absent	28 (70.0%)	36 (90.0%)	25 (62.5%)	
Analgesia required	Yes	18 (45.0%)	12 (30.0%)	20 (50.0%)	0.083
	No	22 (55.0%)	28 (70.0%)	20 (50.0%)	

Shivering grades were similarly distributed across the groups, with no significant differences ($p = 0.429$). In Group A, Grade I was observed in two patients, Grade II in three, and Grade III in one. Group B had only one case of Grade II shivering. In Group C, Grade I occurred in three patients, Grade II in four, Grade III in two, and Grade IV in one patient. (Table 3).

Table 3: Comparison of shivering grade among groups

Shivering grade	Groups			P value
	A (n=6)	B (n=1)	C (n=10)	
I	2	0	3	0.429
II	3	1	4	
III	1	0	2	
IV	0	0	1	

DISCUSSION

Intravenous paracetamol, by centrally inhibiting the prostaglandin synthesis, can reduce POS, perioperative hypothermia, and postoperative pain. The timing of IV paracetamol administration during surgery can influence efficacy and alter postoperative outcomes. This study aimed to assess the effect of IV paracetamol timing on POS, hypothermia, and analgesic requirement.

In our study, most patients were aged between 40 and 45 years, with the majority being males (50-55%) and ASA I (62-68%); however, the differences were not significant ($p > 0.05$). Similarly, Wahdan et al. reported that all patients were aged between 30 and 45 years, and most belonged to the ASA I category.[9] Natapura et al. reported that all patients were aged between 30 and 50 years; in contrast to our study, most of their patients were of ASA II.[10] Further strengthening our study, Nouh et al. reported that all of their patients were aged between 30 and 45 years and equally distributed between ASA I and II.[11] In contrast, females were predominant in all these studies.

In our study, the surgery duration and baseline temperature were comparable between the groups ($p > 0.05$). Similarly, Kinjo et al. reported a comparable surgery duration in both groups (342.6 and 352.2

ISSN (O): 2687-5365; ISSN (P): 2753-6556

minutes), along with a comparable baseline temperature (37.1 and 37°C).[12] Mohta et al. reported that the surgery duration was similar in all their groups (112.7, 111.1 and 117.1 minutes), and they also observed a comparable baseline temperature (between 38 and 36°C).[13]

Group B in our study had the lowest POS (2.5%) and hypothermia (10%) among all groups, with a significant difference ($p = 0.021$ and 0.010, respectively). Similarly, Prasetyo et al. reported that the paracetamol group had the lowest POS (35.3%) compared with the control group (76.5%, $p = 0.038$). They observed that shivering onset in the paracetamol group was between 45 and 120 min, compared to 30–60 min in the control group. They also conclude that paracetamol reduces body temperature by inhibiting prostaglandins centrally.[14] Mohta et al. reported that the incidence of shivering was 12% in the late paracetamol group, compared to 29.3% in the early group and 30.6% in the control group, and this had a significant association ($p = 0.012$). They further concluded that giving paracetamol 30 minutes before the end of surgery significantly lowers the incidence of postoperative hypothermia (9.3%) compared to early administration (29.3%) or a control group (24%) ($p = 0.008$).[13] Khalil et al. reported that those patients receiving paracetamol had significantly lower core and peripheral temperatures compared to a control group ($p = 0.002$).[15]

Further strengthening our study, Shirozu et al. observed that acetaminophen was significantly associated with a decreased incidence of POS ($p = 0.005$).[16] Thus, indicating that IV paracetamol is associated with reducing POS, while IV paracetamol administration before 30 min of the end of the surgery can significantly reduce POS and hypothermia.

In our study, groups A and C had the highest analgesic requirements, with no significant difference ($p = 0.083$). Similarly, Mohta et al. reported that 48 out of 75 patients in the 'Late PCM' group required postoperative analgesia, compared to 58 in the 'Early PCM' group and 62 in the control group. They also concluded that the time to the first analgesic requirement was significantly longer in the group that received paracetamol later than in the group that received it early or the control group ($p = 0.001$).[13] Further strengthening our results, Prasetyo et al. reported that the need for rescue pethidine was significantly lower in the paracetamol group ($p = 0.04$).[14] In contrast, Greenwood et al. reported that there was no association between the timing of IV paracetamol and the need for opioid consumption, but most of their patients had a higher BMI.[17] Thus, late administration of paracetamol can significantly decrease the need for and duration of rescue analgesics, although these values may differ with an increase in BMI.

In our study, most cases in group A were of grade II and I shivering (3 and 2), while the 1 case in Group B had grade II. Only one patient in the study had grade IV shivering, which was from Group C, while most patients from Group C had grade II and I shivering (4 and 3). Supporting our findings, Mohta et al. reported that patients in the "Late PCM" group had the lowest frequency of grades 3 and 4 compared to the "Early PCM" and control groups (9.3% vs. 26.6 and 25.3%, $p = 0.013$).[13] Thus proving that late paracetamol administration not only reduces the prevalence of shivering but also its severity.

Most patients experienced some degree of POS; however, the timing of IV paracetamol administration influenced its incidence and severity. Administering paracetamol late in the surgery can significantly reduce shivering, perioperative hypothermia, and analgesic requirements.

Limitations

The study was conducted at a single centre with a limited sample size, which may affect the generalisability of the results. Factors such as differences in BMI, fluctuations in room temperature, and individual variations in temperature regulation were not considered.

CONCLUSION

Late intraoperative IV paracetamol administration can effectively reduce POS and perioperative hypothermia and lower the need for postoperative analgesics. Future multicentre studies with larger, diverse populations and standardised control of affecting factors are recommended to validate these findings and improve dosing strategies.

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