Effects of Acetaminophen on Peri-operative Shivering for Surgeries under Spinal Anaesthesia

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1.Abstract

Background

To evaluate the effect of intravenous acetaminophen on intra-operative and post operative shivering and body temperature in patients undergoing elective lower limb and lower abdominal surgeries under spinal anaesthesia.

Methods

A comparative, observational study. Patients who received intravenous acetaminophen 15mg/kg over 15 minutes (40 patients) after spinal anaesthesia were compared with patients who did not receive the drug (40 patients). We assessed intra-operative and post-operative shivering scores and body temperature before giving spinal anaesthesia intraoperatively and after shifting to the post-operative room for up to 6 hours.

Results

We included 80 patients in our study, 40 patients belonging to each group (A and C),

At the end of the measurements, we found that significantly lower severe shivering scores (≥2) were seen in Group A (10.5%) as compared to Group C (33%) at one hour intra-operative ($p=0.02$).

No patient in Group A exhibited a shivering score >2 intra-operatively.

Postoperatively, shivering scores in Group A measured immediately after shifting to PACU and one-hour post-operative were significantly lower than Group C with $p=0.040$ and $p=0.044$, respectively.

At all time intervals, intra-operative and post-operative heart rate was significantly lower in Group A. ($p<0.005$)

MAP and axillary body temperature showed no significant intergroup differences.

Conclusion

From our study, we conclude that using IV acetaminophen post spinal anaesthesia reduced the severity of intra-operative shivering and the incidence of immediate post-operative shivering post spinal anaesthesia.

Keywords: Spinal anaesthesia; Shivering; Acetaminophen; Body temperature; Intravenous; Surgery.

2. Introduction

Shivering is a very common and uncomfortable complication in patients recovering from anaesthesia and surgery [1]. Crowley et al. reviewed twenty-one studies and found that patients under neuraxial anaesthesia had an incidence of shivering ranging from 40%-64% [2].

The autonomic nervous system is responsible for maintaining core body temperature within a normal range, between 36.5 and 37.5. During regional anaesthesia, autonomic regulation is impaired, and vasodilatation occurs, which facilitates the redistribution of heat from the core body to the peripheries, decreasing core body temperature. Heat loss happens during surgery due to exposure to cold environments and administration of unwarmed fluids [3,4].

In most cases, post anaesthetic shivering is triggered by hypothermia which is usually a consequence of cold exposure and anaesthetic-induced thermoregulatory impairment [5]. Anaesthetic drugs increase the average hypothalamic set point [5,6]. This is the mechanism of hypothermia leading to shivering in general anaesthesia. This mandates that patients' body temperature is within a normal range during surgery [7]. In many cases, shivering is also seen in normothermic patients (non-thermoregulatory shivering).

Although shivering is generally considered trivial and has beneficial thermoregulatory effects, vigorous shivering increases heat production by up to six hundred per cent above the baseline [8]. It increases catecholamine levels, oxygen consumption, and carbon dioxide production and induces lactic acidosis. This, in turn, results in a rise in cardiac output, pulse rate and arterial pressure. In some patients with diminished cardiopulmonary reserve, this may prove to be harmful.

It also causes interference during monitoring of blood pressure, oxygen saturation and ECG.

Post-operative pain management and shivering are essential components of enhanced recovery after surgery and improved patient satisfaction [9].

Both pharmacological and non-pharmacological strategies are available for treating post anaesthetic shivering. Amongst the non-pharmacological measures, one of the effective interventions is active cutaneous body warming, as suggested by a systemic review performed by Park et al. [10]. However, active body warming is not always possible and might be ineffective; hence anaesthesiologists may prefer to resort to pharmacological measures to prevent post anaesthetic shivering.

Meperidine, tramadol, clonidine, ketamine, ondansetron and dexmedetomidine are a few pharmacological measures used to control post-operative shivering [11,12,13]. Dexamethasone is another studied drug used to prevention post anaesthetic shivering. It decreases the difference between skin and core body temperature and regulates immune responses [14]. However, these drugs have side effects such as nausea, vomiting, sedation, and respiratory depression [1].

Surgical stress and tissue damage are said to trigger the release of endogenous pyrogens and cytokines via mechanisms that are not understood fully. This causes a rise in the body temperatures' "set-point" and hence fever in the post-operative patient [15].

A safe and effective drug, IV acetaminophen, a non-steroidal anti-inflammatory drug, is frequently used to manage mild to moderate pain. It is usually a well-tolerated drug, has minimal side effects at therapeutic doses. Unlike opioids, they don't lead to adverse effects like sedation, respiratory depression, constipation, or vomiting [16]. Since pain has also been

implicated as a cause of post-operative shivering, its treatment prevents non-thermoregulatory tremors [17]. Rectal acetaminophen has also been shown to suppress shivering during therapeutic hypothermia [18].
Despite having proven the ill effects of post anaesthetic shivering, very little consideration is given to its treatment. Furthermore, the available pharmacological measures come with various undesirable adverse effects. Hence, this study evaluated the impact of a safe drug, IV acetaminophen, on the incidence and intensity of intra-operative and post-operative shivering body temperature changes during spinal anaesthesia.

3.Method

This study was initiated following approval from the Institutional Ethics Committee on 16/22/2020 *(IECKMCMLR-12/2020/382).* The study duration was from December 2020 to June 2022, with sampling conducted throughout the duration.

It is a comparative, observational study. Eighty patients between twenty and sixty-five years (with American Society of Anaesthesiologists physical status I and II) undergoing elective lower limb and lower abdominal surgeries under spinal anaesthesia were admitted in this study. Patients were excluded in cases of known allergy to acetaminophen, liver dysfunction (AST more than 35IU, ALT more than 35IU), body temperature greater than 38 C or less than 36 C, laparoscopic/arthroscopic surgeries as they may be an independent risk factor for shivering. Patients with any contraindication to spinal anaesthesia and height less than 150 cms and more than 170 cms were also excluded.
Detailed pre-anaesthetic evaluation and investigations were done as per protocol before the surgery. The treating anaesthesiologist obtained written informed consent at the time of pre-anaesthetic evaluation for anaesthesia. Standard monitoring was implemented throughout the procedure and included non-invasive arterial blood pressure measurement, heart rate measurement, 3-lead electrocardiography and fingertip oxyhaemoglobin saturation (SpO2) measurement. Heart rate and SpO2 were recorded continuously, whereas blood pressure was recorded every five minutes. Axillary body temperature was measured just before spinal anaesthesia and every 15 minutes intraoperatively using a reusable skin temperature probe. Intra-operative shivering scores were measured after spinal anaesthesia and every 30 minutes until the end of the procedure using the shivering score (SS) [19] "**0**: no shivering, **1**: piloerection or peripheral vasoconstriction, but no visible shivering, **2**: muscular activity in only one muscle group, **3**: muscular activity in more than one muscle group, but not generalised, **4**: shivering that involves the whole body."
Under absolute aseptic precautions, spinal anaesthesia was administered with a 25-gauge Quincke Babcock needle, injecting 2.5 of 0.5% heavy/ hyperbaric Bupivacaine in the subarachnoid space of L3-L4 or L4-L5 intervertebral space. The patient was then immediately placed supine position. All patients were covered with drapes and actively warmed using warming blankets. Group A included forty patients who received IV acetaminophen 15mg/kg over 15 minutes after spinal anaesthesia by the treating anesthesiologist. Group C included forty patients who did not receive IV acetaminophen after spinal anaesthesia. Fluid

administration (Ringers' lactate or normal saline) for maintenance was given according to body weight for both the study groups. The block level was assessed 5 min after the block with a bilateral pin prick method along the mid-clavicular line using a 26 G hypodermic needle. Once the adequate blockade was achieved, axillary body temperature was recorded every fifteen minutes till the termination of the procedure. The duration of the surgery was recorded for each patient. The patient was shifted to the post-operative room after surgery for monitoring and was covered with a blanket. Axillary body temperature was measured immediately and every hour until the patient was shifted out of the post-operative room(~6hours). Post-operative shivering was graded based on the shivering score (SS)[19]. The primary outcome variables were intraoperative and post-operative shivering scores. Secondary outcome variables were body temperature changes, intraoperative and post-operative haemodynamics (Heart rate, Mean arterial blood pressure) and incidence of adverse effects (post-operative nausea and vomiting, allergic reactions). Severe post-operative shivering (SS>/=2): was treated with 0.5 mg/kg tramadol slow IV.

4. Statistical Analysis

Data were entered into Microsoft Excel, and statistical analysis was carried out in SPSS software version 25. Qualitative variables like shivering scores and gender were presented as frequency and percentages. Quantitative variables like heart rate, axillary body temperature, and mean arterial pressure were presented as mean (standard deviation). Line diagrams were used for the graphical depiction of data.

The differences in gender between the groups and shivering scores were measured using the chi-square test. The difference in axillary body temperature, heart rate and MAP at each time point between the groups was carried out using independent t-test. P value< 0.05 was considered significant.

5.Results

A total of eighty patients were included. Forty patients were given intravenous acetaminophen after spinal anaesthesia; these patients were included in Group A. The rest were included in Group C.

The mean (SD) age of the included patients in Group A and Group C was 45(12.9) years old and 39 (12.5) years old, respectively. 26 (65%) patients were female in Group A, and 23 (57.5%) were female in Group C.

No significant differences (P>0.05) were noted between the two groups regarding age and sex.

Primary Outcomes:

Intraoperative shivering scores in Group A and Group C showed no statistical significance. (p>0.050)

However, no patient in Group A exhibited shivering scores of 3 as compared to 19 patients in group C (50%).

Postoperatively, shivering scores measured immediately after shifting to PACU (Table 1) and one-hour post-operative (Table 2) showed statistically significant differences with p=0.040 and p=0.044, respectively.
At one-hour post-operative, 95% of patients in Group A did not shiver compared to 72.5% in Group C (Table 2)

Table 1: Shivering scores immediately after shifting to PACU.

Immediately after shifting to PACU	**Group A**		**Group C**	
	n	**%**	**n**	**%**
Score 0	31	77.5	21	52.5
Score 1	6	15	10	25
Score 2	3	7.5	5	12.5
Score 3	0	0	4	10
Total	**40**	**100**	**40**	**100**
Chi-square P value:0.040 (significant)				

Table 2: Shivering scores at one hour in PACU

At one hour post-op period	**Group A**		**Group C**	
	n	**%**	**n**	**%**
Score 0	38	95	29	72.5
Score 1	2	5	8	20
Score 2	0	0	2	5
Score 3	0	0	1	2.5
Total	**40**	**100**	**40**	**100**
Chi-square P value:0.044 (significant)				

Severe shivering (SS≥2), treated with the rescue drug tramadol, was also compared between the two groups.

Table 3 and Figure 1 shows significantly lower severe shivering scores in Group A compared to Group C at one hour intraoperative (p=0.02). Only 10.5% of patients in Group A showed shivering scores of more than two compared to 33% of patients in Group C at one hour.

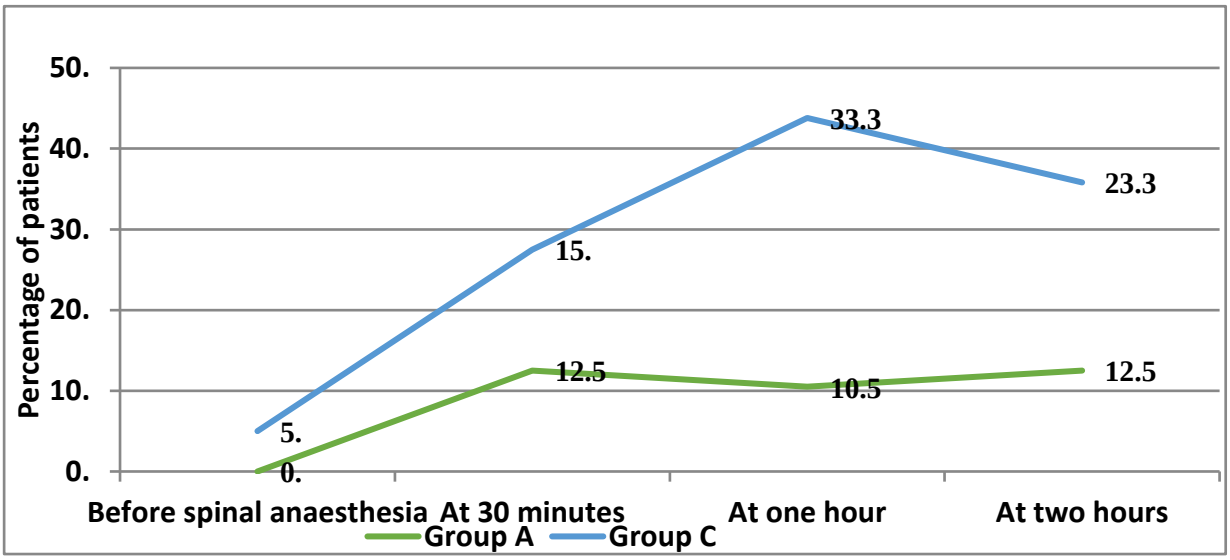

Figure 1: Comparison of Intraoperative severe shivering (≥2) between the groups

Table 3: Intraoperative severe shivering (≥2) between the groups

	Group A (% of patients)	Group C (% of patients	p-value
Before spinal anaesthesia	0	5	0.15
At 30 minutes	12.5	15	0.74
At one hour	10.5	33.3	**0.02**
At two hours	12.5	23.3	0.26

Secondary Outcomes:

The variations in pulse rate values measured throughout the study period were comparable between the two study groups (Figure 2). Both intra-operative and post-operative, were statistically significantly lower in Group A compared with Group C (P<0.005).

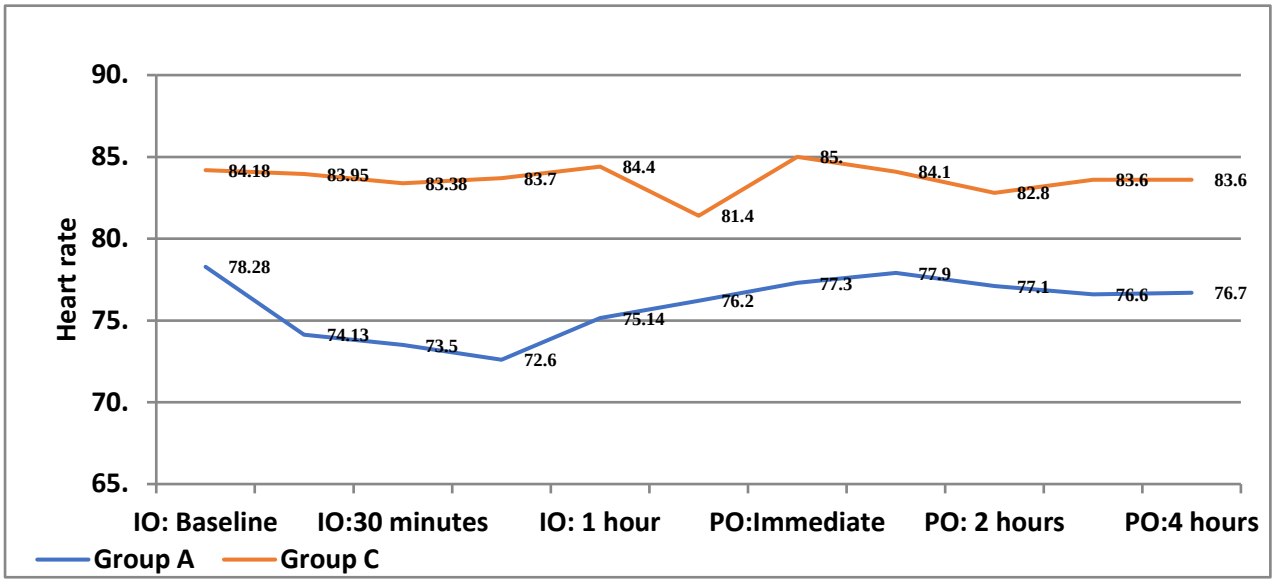

Figure 2: Heart rate changes Intraoperative and Postoperative.

No significant inter-group variations in mean arterial pressure (MAP) were present at any time point ($p>0.05$).

Axillary body temperature changes showed no significant differences between the two groups ($p>0.05$). However, there was a drop in temperature in both the groups after induction of anaesthesia at 30- and 60-minutes post spinal anaesthesia, which then returned to baseline values in the post-operative period.

No adverse effects, such as nausea, vomiting or anaphylaxis, were seen in any patient.

6. Discussion

Shivering is a widespread, notable, and harmful side effect caused by spinal anaesthesia. Besides causing hypoxia and increasing post-operative pain, it also interferes with the monitoring devices. Hence, it is vital that shivering is prevented, principally in patients with cardiopulmonary disease or elderly patients [20].

In this comparative, observational study, we tested the hypothesis that intra-operative and post-operative shivering could be treated by intravenous acetaminophen in patients undergoing surgeries under spinal anaesthesia.

The interpretation of results between the two groups by a measure of clinically significant shivering (shivering score≥2) showed statistically significant superiority of prophylactic IV acetaminophen intraoperatively. Conforming with our results, Esmat et al. recorded the lowest severe shivering scores in the acetaminophen group compared to the other two groups [21].

Rasoli et al. [22], in a similar study, measured body temperature at different intervals after administering spinal anaesthesia. The results obtained supported our observations. There were no significant differences in body temperature between the two groups (paracetamol and control groups). Thus, the effect of acetaminophen on body temperature and shivering is unclear based on current results.

In a study by Esmat et al., results show that the ninety-minute post spinal core body temperature was significantly lower in the study groups compared to pre-spinal core temperature [21]. In our study, we observed a drop in axillary body temperature in both the groups after induction of anaesthesia at 30- and 60-minutes post spinal anaesthesia, which then returned to baseline values in the post-operative period. Kinjo et al. hypothesised that acetaminophen prevented post-operative shivering by preventing the increase in the set point of core body temperature instead of lowering the threshold for shivering [19]. We could not support this inference based on our study results.

Khalili et al., in their study conducted on patients undergoing general anaesthesia, recorded significantly lower heart rates in patients receiving acetaminophen [6]. Our data revealed similar observations, but mechanisms might differ, as it was conducted in patients under spinal anaesthesia.

Time to two segments sensory blockade regression and time to first rescue analgesia are other variables that could have been studied. Different studies have shown that 1gram of paracetamol prolongs the duration of the sensory blockade and increases the time to first rescue analgesia. This effect could prove to be advantageous.

Various drugs have been considered for the management of post-spinal shivering. Amongst them, acetaminophen seems to be the safest drug with no adverse effects. The Food and Drug Association (FDA) 2010 permitted using intravenous acetaminophen to treat pain and fever [20]. The use of acetaminophen as an anti-shivering agent is yet to be evaluated further.

According to the results obtained from our study, we conclude that the use of IV acetaminophen in the lower limb and lower abdominal surgeries performed under spinal anaesthesia reduced the severity of intraoperative shivering and the incidence of immediate post-operative shivering.

7. Disclaimers

Conflicts of interest
None.
Financial disclosures
None.

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