



## Anaesthesiology

## COMPARATIVE EFFECT OF PRE-EMPTIVE INTRAVENOUS DEXMEDETOMIDINE AND PARACETAMOL ON POST-SPINAL SHIVERING: A RANDOMIZED DOUBLE-BLIND STUDY

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**ABSTRACT** **Background & Aim:** Post-spinal shivering is a common and distressing complication that impairs patient comfort and recovery. Evidence comparing prophylactic intravenous dexmedetomidine and paracetamol for preventing post-spinal shivering is limited. This prospective, randomized, double-blind study aimed to compare the effectiveness of preemptive intravenous dexmedetomidine versus paracetamol in preventing post-spinal shivering. **Method:** total of 152 patients (ASA I–II, aged 18–60 years) undergoing elective lower abdominal surgery under spinal anesthesia were enrolled and randomized into two groups (n=69). Group A received intravenous dexmedetomidine 1 µg/kg (diluted in 100 ml normal saline), while Group B received intravenous paracetamol 1 g (100 ml). Both drugs were administered 15 minutes before subarachnoid block. Shivering was graded using the Tsai and Chu scale. Duration and grade of shivering, duration of analgesia, sedation level, hemodynamic parameters, and adverse effects were recorded. **Results:** The incidence of shivering was significantly lower in Group A compared to Group B [11 (15.9%) vs. 21 (30.4%);  $p = 0.044$ ]. Group A also had a shorter mean shivering duration ( $3.45 \pm 1.23$  min vs.  $5.27 \pm 1.08$  min;  $p = 0.001$ ) and prolonged analgesia duration ( $356.3 \pm 41.2$  min vs.  $130.5 \pm 25.4$  min;  $p < 0.001$ ). However, Group A exhibited a higher incidence of adverse effects, including sedation, hypotension, bradycardia, nausea, and vomiting. **Conclusion:** Both dexmedetomidine and paracetamol effectively reduced post-spinal shivering, but dexmedetomidine demonstrated superior efficacy, albeit with a higher incidence of manageable side effects.

**KEYWORDS :** Dexmedetomidine, Paracetamol, Shivering, Spinal Anesthesia, Thermoregulation

### INTRODUCTION

Shivering is an involuntary, oscillatory muscular activity that acts as a thermoregulatory defense against hypothermia by increasing metabolic heat production to restore thermal homeostasis.<sup>1</sup> Clinically, it manifests as visible tremors involving the face, jaw, trunk, or extremities, typically lasting more than 15 seconds. The reported incidence of shivering is up to 56.7% under regional anesthesia and as high as 85% following spinal anaesthesia.<sup>2</sup>

Subarachnoid block promotes peripheral vasodilation, leading to redistribution of core heat to the periphery. This is compounded by a reduced vasoconstriction and shivering threshold, along with an elevated sweating threshold, which together shift the hypothalamic set point downward by 0.5–1.0 °C.<sup>3,4</sup> The degree of hypothermia correlates with the level and extent of spinal blockade, as well as patient factors such as advanced age.<sup>1,3</sup> Environmental factors like low ambient temperature, infusion of cold intravenous fluids, exposure of body cavities, and anesthetic-induced thermoregulatory impairment further exacerbate heat loss.

Shivering not only causes significant patient discomfort but also complicates intraoperative monitoring by interfering with ECG, non-invasive blood pressure, and pulse oximetry readings.<sup>5</sup> It can increase metabolic rate and oxygen consumption by up to 600%, posing risks of arterial hypoxemia, myocardial ischemia, elevated intracranial and intraocular pressure, lactic acidosis, delayed wound healing, and increased infection risk.<sup>1,2,6</sup>

Both non-pharmacological and pharmacological approaches have been used to prevent and manage intraoperative shivering.<sup>1,6,7</sup> Although effective, non-pharmacological strategies can be cumbersome and resource-intensive. Pharmacological agents are convenient and cost-effective but often carry adverse effects. Drugs commonly employed include tramadol, clonidine, dexmedetomidine, pethidine, ketamine, midazolam, nefopam, magnesium sulfate, dexamethasone, and ondansetron. However, many of these agents are associated with side effects such as sedation, bradycardia, hypotension, respiratory depression, nausea, and vomiting.<sup>6,7,9,11</sup>

Dexmedetomidine, a highly selective  $\alpha_2$ -adrenergic agonist, exerts anti-shivering effects by lowering thermoregulatory thresholds via central hypothalamic and spinal mechanisms, suppressing sympathetic outflow and inhibiting vasoconstriction. Paracetamol, a

centrally acting non-opioid analgesic, reduces the hypothalamic set point by inhibiting central prostaglandin E2 synthesis, thereby producing anti-shivering effects.

Although both dexmedetomidine and paracetamol are individually effective, data comparing their prophylactic use for prevention of post-spinal shivering remain limited. Therefore, this prospective, randomized, double-blind interventional study was conducted to evaluate and compare the effects of preemptive intravenous dexmedetomidine and paracetamol on post-spinal shivering. The primary objective was to assess the incidence of shivering; secondary objectives included the grade and duration of shivering, duration of analgesia, and incidence of adverse effects such as hypotension, bradycardia, desaturation, nausea, vomiting and sedation.

### METHODS

This prospective, randomized, double-blind controlled trial was conducted from June 2023 to March 2025 after approval of study protocol from the Institutional Scientific & Ethics Committee and registered with the Clinical Trials Registry of India (CTRI/2024/07/070790). A total of 152 patients were screened for eligibility. After considering exclusion criteria, 138 adults of either gender, aged 18-60 years, ASA physical status I-II, scheduled for elective lower abdominal surgery under subarachnoid block, were enrolled. Patients were excluded if they: refused participation; had an inadequate block; had comorbid conditions such as uncontrolled cardiovascular or cerebrovascular disease, renal or severe hepatic impairment, convulsions, psychiatric disorders, hypo-/hyperthyroidism, diabetes mellitus and other autonomic disorders; had known allergy to study drugs, initial nasopharyngeal temperature  $>38.0^\circ\text{C}$  or  $<35.0^\circ\text{C}$ ; sensory block above T6 and required intraoperative blood transfusion. Potential confounding variables in the study included age, gender, surgical extent, level of block, and subjective perception of shivering.

Sample size was determined based on data from a pilot study of 15 patients per group, using the difference in shivering incidence (primary outcome) as the basis. Using G\*Power software version 3.1.9.7, with a two-tailed test for difference between independent proportions, a 5% significance level, 80% power, and equal allocation ratio, the required sample size was calculated as 69 patients per group, yielding a total of 138 participants.

Pre-anesthetic evaluation was performed a day prior to surgery, and

written informed consent was obtained from all patients. As per institutional protocol, patients were kept nil per oral for at least 6 hours before surgery. Participants were randomized into two groups (N=69) using the Sequentially Numbered Opaque Sealed Envelope (SNOSE) method: **Group A** received intravenous dexmedetomidine 1 µg/kg (prepared and diluted in 100 ml normal saline) and **Group B** received intravenous paracetamol 1 g (supplied as a 100 ml bottle).

On arrival in the operating room, standard ASA monitor was attached and baseline heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SpO<sub>2</sub>), ECG and nasopharyngeal temperature were recorded. A wide-bore intravenous cannula was inserted, and patients were preloaded with Ringer's lactate at 10 ml/kg (at room temperature). Operating room temperature was maintained between 24–26 °C. Study drugs were prepared in identical coded infusion bottles by an anesthesiologist not involved in intraoperative care and administered intravenously 15 minutes prior to spinal anesthesia. Premedication included intravenous ondansetron 4 mg.

Under strict aseptic precautions, spinal anesthesia was administered at the L3–L4 or L4–L5 interspace using a 25G Quincke needle. After confirming free flow of cerebrospinal fluid, 3 ml of 0.5% hyperbaric bupivacaine was injected intrathecally. Surgery commenced once adequate sensory block was confirmed by pinprick. At the end of surgery, patients were transferred to the Post-Anesthesia Care Unit (PACU), where they were covered with a cotton blanket and monitored for vital parameters and study outcomes.

**INTRAOPERATIVE AND POSTOPERATIVE ASSESSMENT**

Hemodynamic parameters [HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), SpO<sub>2</sub>], incidence, grade and duration of shivering; degree of sedation and nasopharyngeal temperature were recorded every 2 minutes for the first 20 minutes following subarachnoid block, and then every 5 minutes until the end of surgery. Incidence of shivering, primary outcome was defined as a shivering score of ≥3 according to Tsai and Chu 5-point score (0=No shivering; 1=Piloerection, peripheral vasoconstriction but no visible shivering; 2= Muscular activity of 1 muscle group; 3= Muscular activity of more than 1 group of muscles but not generalized and 4= Shivering whole body).<sup>9</sup> Rescue therapy with intravenous tramadol 0.1 mg/kg was administered if a shivering score ≥3 persisted continuously for more than 15 minutes. Secondary outcome was grade of shivering, duration of shivering (defined as length of time in minutes from onset of ≥3 grade shivering to its cessation), duration of analgesia (defined as the time in minutes from administration of the study drug to the first request of rescue analgesic) and incidence of side effects and complications including hypotension, bradycardia, desaturation, nausea and vomiting were noted and treated. The degree of sedation was assessed using four-point Filos scale (Grade 1= Awake and alert; Grade 2= Drowsy, responsive to verbal stimuli; Grade 3= Drowsy, arousable to physical stimuli; and Grade 4= Unarousable).<sup>9</sup> Hypotension was defined as decrease in MAP of >20% from baseline value and was managed with iv mephenteramine 6mg and 250 ml fluid bolus. Bradycardia was defined as fall in HR < 60 per minute and was managed with intravenous atropine 0.6 mg. Desaturation (SpO<sub>2</sub>< 92%) was treated with supplemental oxygen via nasal cannula at 3 L/min to keep SpO<sub>2</sub>>94%. Nausea and vomiting was treated with iv ondansetron 4 mg.

**Statistical Analysis**

Data were compiled in a master chart using Microsoft Excel and subsequently analyzed using **IBM SPSS Statistics for Windows, version 22.0** (IBM Corp., Armonk, NY). Quantitative variables were presented as mean ± standard deviation (SD), and qualitative variables were summarized as frequencies and percentages. Descriptive statistics were calculated for baseline characteristics, including age, gender, ASA grade, height, weight, and body mass index (BMI). Between-group comparisons of quantitative variables such as age, height, weight, BMI, duration of surgery, HR, SBP, DBP, MBP, RR, SpO<sub>2</sub>, and nasopharyngeal temperature were performed using the **independent Student's t-test**. Categorical variables including gender, ASA grade, level of sensory block, type of surgery, incidence and grade of shivering, sedation score, and adverse effects were analyzed using the **Pearson's Chi-square test** to assess statistical significance. A *p*-value > 0.05 was considered **not significant**, < 0.05 was considered **statistically significant**, and < 0.01 was considered **highly significant**.

**RESULTS**

A total of 152 patients were screened for eligibility, and 138 patients met the inclusion criteria and were randomized into two groups (Figure 1: CONSORT diagram).

The two groups were comparable with respect to baseline demographic and clinical characteristics, including age, gender, BMI, ASA status, height, weight, type of surgery, and duration of surgery (all *p* > 0.05; Table 1). The majority of patients in both groups achieved a sensory block level of T7–T8.

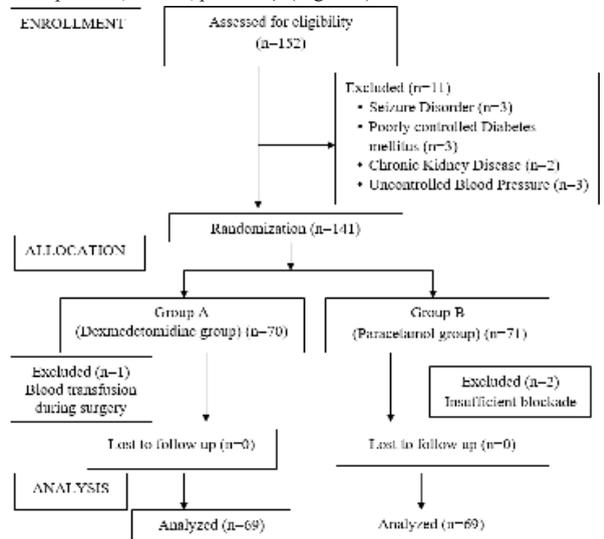
The **incidence of shivering (grade ≥ 3)** was significantly lower in **Group A (11 patients, 15.94%)** compared to **Group B (21 patients, 30.43%)** and this difference was statistically significant (*p* = **0.043**). Shivering scores were consistently lower in **Group A** throughout the observation period. Between 10–18 minutes, Group B showed a higher incidence of shivering, peaking at 14 minutes, when 17 patients experienced shivering (14 with grade 2), compared to 5 patients in Group A. The highest overall incidence was observed at 16 minutes. By 45 minutes, all patients in both groups had returned to a shivering score of 0. The mean duration of shivering was also significantly shorter in Group A compared to Group B (3.45 ± 1.23 min vs. 5.27 ± 1.08 min, *p* = 0.001; Figure 2).

Sedation (Filos grade ≥ 2) was observed in 10 patients (14.5%) in Group A and in 3 patients (4.4%) in Group B, which was statistically significant (*p* = 0.041; Figure 3). In Group B, two patients required rescue intravenous tramadol 0.1 mg/kg for persistent shivering, and one patient required intravenous midazolam 0.5 mg for anxiety.

Heart rate, SBP, DBP, and MAP were significantly lower in Group A compared to Group B throughout the study period (Figure 4). However RR, SpO<sub>2</sub>, and nasopharyngeal temperature remained comparable between the two groups at all time points, with no significant differences (*p* > 0.05). Mean respiratory rate ranged between 15–16 breaths per minute, SpO<sub>2</sub> between 98–100%, and nasopharyngeal temperature between 36.5–36.7 °C.

The **mean duration of analgesia** was markedly prolonged in Group A (**356.3 ± 41.2 minutes**) than Group B (**130.5 ± 25.4 minutes**), and this difference was **highly statistically significant** (*p* = **0.0001**).

The **incidence of hypotension, bradycardia and nausea and vomiting was higher** in Group A compared to Group B, but it was statistically significant in respect to hypotension (30 patients, **43.5%** vs 16 patients, **23.2%**; *p* = 0.011). (Figure 5).

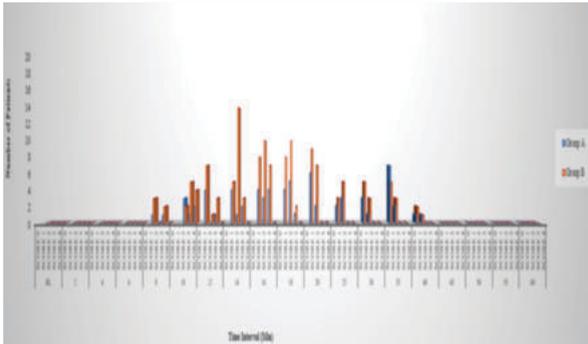


**Figure 1:** Consort Diagram

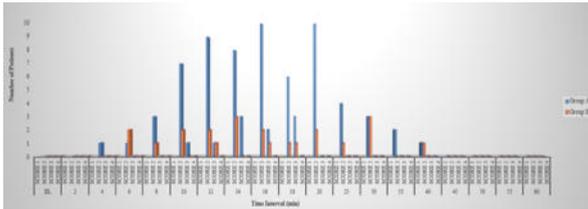
**Table 1: Patient's Demographics And Duration Of Surgery In Both The Groups**

Variable	Group A (n=69)	Group B (n=69)	p Value
Age (years)	27.96±4.17	27.03±3.84	0.177
Height (cm)	163.26±3.17	163.74±2.77	0.347
Weight (kg)	57.88±4.17	59.61±7.11	0.157

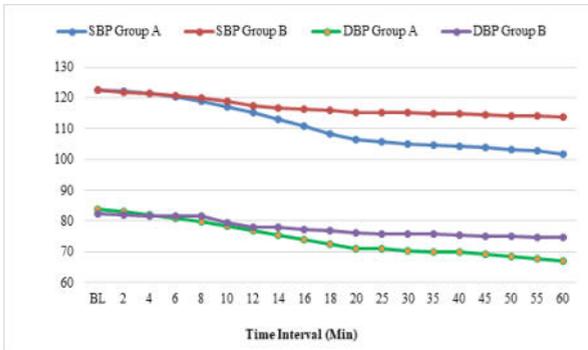
BMI (kg/m <sup>2</sup> )	21.688± 2.278	22.168± 2.356	0.226
Duration of surgery (min)	51.05±4.23	51.81±5.28	0.5891



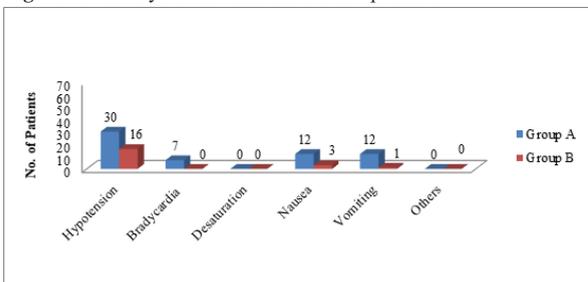
**Figure 2:** Distribution Of Patients In Various Shivering Scores At Various Time Intervals



**Figure 3:** Distribution of patients in various sedation scores at various time intervals



**Figure 4:** Mean systolic and diastolic blood pressure



**Figure 5:** Distribution of Patients According to Side effects & Complications

**DISCUSSION**

This randomized, double-blind study compared the effectiveness of pre-emptive intravenous dexmedetomidine and paracetamol in preventing post-spinal shivering. Both agents significantly reduced the incidence, severity, and duration of shivering compared to historical rates, but dexmedetomidine showed superior efficacy.

The overall incidence of shivering (grade ≥ 3) was significantly lower in the dexmedetomidine group (15.94%) compared to the paracetamol group (30.43%, *p* = 0.0437). This aligns with previous findings by Usta et al.,<sup>8</sup> who reported a 10% incidence of shivering with dexmedetomidine, and Prabhakaran et al.,<sup>10</sup> who found a 13.3% incidence in a similar cohort. Botros J M et al.<sup>11</sup> documented a 27.5% incidence of shivering following IV dexmedetomidine in patients undergoing elective surgical procedures in lower half of the body. The slightly higher incidence in our study could be attributed to patient and procedural differences. They had administered i.v bolus dexmedetomidine 1 mcg/kg diluted to a volume of 5 ml just after SAB

whereas in current study it was given as 1 mcg/kg diluted in 100 ml NS 15 min prior to SAB. The time distribution of shivering also favored dexmedetomidine: Group B showed a marked peak in shivering between 10–18 minutes, with the highest incidence at 14 minutes, while Group A had substantially fewer events during this interval. By 45 minutes, shivering had resolved completely in both groups.

The severity and duration of shivering were also lower in Group A. This reflects the robust central thermoregulatory effects of dexmedetomidine, which lowers the shivering threshold more effectively than paracetamol.

Dexmedetomidine also prolonged the duration of analgesia significantly (*p* < 0.001). This is consistent with its known analgesic-sparing properties via α<sub>2</sub>-adrenergic receptor agonism, which reduces nociceptive transmission and prolongs sensory block. Similar durations have been reported by Mohamed et al.<sup>12</sup> (356.6 minutes) in comparable settings.

Sedation was more common with dexmedetomidine (14.49% vs. 4.35%, *p* = 0.0414), but it was mild and self-limiting, consistent with findings by Prabhakaran et al.<sup>10</sup> Importantly, no patients in either group developed deep or unarousable sedation.

Hemodynamically, dexmedetomidine was associated with significantly lower HR, SBP, DBP, and MAP throughout the observation period, with a higher incidence of hypotension (43.5% vs. 23.2%, *p* = 0.011) and bradycardia (10.1% vs. 0%, *p* = 0.006), both managed effectively with standard interventions. These findings are in line with Botros et al.,<sup>11</sup> who reported 37.5% hypotension with dexmedetomidine, and Venkataraman et al.,<sup>6</sup> who observed progressive bradycardia during infusion. The higher incidence of nausea and vomiting in Group A (17.4% vs. 4.3%/1.4%) could be attributed to increased sympathetic inhibition and sedative effects.

Respiratory parameters, including respiratory rate, SpO<sub>2</sub>, and nasopharyngeal temperature, remained stable and comparable in both groups, indicating that neither drug caused clinically significant respiratory depression or hypothermia.

This study has certain limitations. As a single-center trial, its findings may not be generalizable to wider populations or varied clinical settings. The follow-up was restricted to intraoperative and immediate postoperative periods, without assessment of long-term outcomes such as patient satisfaction, functional recovery, or delayed complications. Moreover, the absence of a placebo or no-intervention control group limits the ability to determine the absolute baseline incidence of post-spinal shivering and the relative efficacy of each intervention compared to no prophylaxis.

Future research should focus on larger, multi-center studies involving diverse demographic and surgical populations to validate and generalize these findings. Studies exploring optimal dosing strategies or combination therapies, such as dexmedetomidine with paracetamol, could help achieve a better balance between efficacy and safety. Long-term outcomes, including 24-hour pain scores, quality of recovery, and patient satisfaction, should also be assessed to provide a more comprehensive evaluation of these interventions. Additionally, pharmacoeconomic analyses comparing the cost-effectiveness of dexmedetomidine and paracetamol in perioperative care could inform resource allocation decisions. Future investigations may also consider integrating non-pharmacological strategies alongside pharmacologic agents to further reduce the incidence and impact of post-spinal shivering.

**CONCLUSION**

In conclusion, pre-emptive administration of both intravenous dexmedetomidine and paracetamol effectively reduced the incidence, severity, and duration of post-spinal shivering while maintaining hemodynamic stability and overall patient safety. Dexmedetomidine demonstrated statistically significant superior efficacy than paracetamol across all evaluated parameters, including incidence and grade of shivering, duration of shivering, and duration of analgesia, albeit with a higher rate of manageable side effects such as hypotension and bradycardia. These findings highlight dexmedetomidine as a more effective option for shivering prophylaxis, with the choice of agent guided by individual patient risk profiles and clinical priorities.

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