Comparison of Efficacy of Ondansetron and Palanosetron for Prevention of Post Spinal Shivering During Lower Limb Surgeries: A Randomized Controlled Trial

Dr. Wamiq Javed [1*], Dr. Sharad Goel [2], Dr. Shailja Sharma [3], Dr. Abhishek Bhardwaj [4], Dr. Ankur Sehgal [5], Dr. Sakshi [6]

[1] Post Graduate Resident, Department of Anaesthesia and Critical Care, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India

[2] Professor, Department of Anaesthesia and Critical Care, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India

[3] Professor & HOD, Department of Anaesthesia and Critical Care, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India

[4] Assistant Professor, Department of Anaesthesia and Critical Care, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India

[5,6] PG Resident, Department of Anaesthesia and Critical Care, Saraswathi Institute of Medical Sciences, Pilkhuwa, Hapur, Uttar Pradesh, India

* Corresponding Author: **Dr. Wamiq Javed**

Article Info

ISSN (online): 2582-8940
Volume: 06
Issue: 03
July - September 2025
Received: 16-06-2025
Accepted: 19-07-2025
Published: 27-07-2025
Page No: 141-146

Abstract

Post-spinal shivering is a common and distressing complication following spinal anesthesia, occurring in 40-70% of patients undergoing lower limb surgeries. This randomized, double-blind, placebo-controlled study aimed to compare the efficacy of ondansetron and palanosetron in preventing post-spinal shivering in patients undergoing lower limb surgeries under spinal anesthesia. A total of 180 patients aged 18-65 years, ASA physical status I-II, scheduled for elective lower limb surgeries were randomly allocated into three groups of 60 patients each: Group O received ondansetron 4 mg intravenously, Group P received palanosetron 0.075 mg/kg intravenously, and Group C received normal saline as placebo, all administered 15 minutes before spinal anesthesia. The primary outcome was the incidence of post-spinal shivering during the first 2 hours postoperatively. Secondary outcomes included severity of shivering, time to onset, hemodynamic parameters, and adverse effects. The incidence of post-spinal shivering was significantly lower in both treatment groups compared to placebo: Group O (18.3%), Group P (13.3%) versus Group C (63.3%) ($p<0.001$). Palanosetron demonstrated superior efficacy compared to ondansetron in preventing moderate to severe shivering (5.0% vs 11.7%, $p<0.05$). Both drugs effectively maintained hemodynamic stability without significant adverse effects. The mean time to onset of shivering was significantly delayed in both treatment groups. Both ondansetron and palanosetron are effective in preventing post-spinal shivering during lower limb surgeries, with palanosetron showing superior efficacy in preventing severe shivering episodes. Both drugs demonstrate excellent safety profiles and should be considered as prophylactic agents in patients at high risk for post-spinal shivering.

DOI: https://doi.org/10.54660/IJMBHR.2025.6.3.141-146

Keywords: Post-Spinal Shivering, Ondansetron, Palanosetron, Spinal Anesthesia, Lower Limb Surgery, Prevention, 5-HT3 Antagonists

Introduction

Post-spinal shivering is a frequent and unpleasant complication following spinal anesthesia, with reported incidence rates ranging from 40% to 70% in patients undergoing various surgical procedures [1]. This phenomenon is particularly common in lower limb surgeries due to the extensive sympathetic blockade and subsequent thermoregulatory impairment [2]. The pathophysiology of post-spinal shivering is multifactorial, involving mechanisms such as sympathetic blockade-induced vasodilation, heat loss,

decreased core body temperature, and direct effects of local anesthetics on the central nervous system [3].

The clinical manifestations of post-spinal shivering range from mild tremors to severe, uncontrollable shaking that can significantly impact patient comfort and satisfaction [4]. Beyond patient discomfort, shivering can lead to increased oxygen consumption, elevated carbon dioxide production, increased intracranial and intraocular pressure, and potential interference with surgical procedures and monitoring equipment [5]. These physiological disturbances can be particularly concerning in patients with compromised cardiovascular or respiratory function [6]. Various pharmacological interventions have been investigated for the prevention and treatment of post-spinal shivering, including tramadol, meperidine, clonidine, dexmedetomidine, and serotonin receptor antagonists [7]. Among these, 5-hydroxytryptamine-3 (5-HT3) receptor antagonists have gained considerable attention due to their dual antiemetic and anti-shivering properties [8]. The 5-HT3 receptors are widely distributed throughout the central and peripheral nervous systems and play a crucial role in thermoregulation and emetic responses [9].

Ondansetron, a first-generation 5-HT3 receptor antagonist, has been extensively studied and widely used for preventing post-spinal shivering [10]. Multiple clinical trials have demonstrated its efficacy in reducing the incidence and severity of shivering following spinal anesthesia [11]. The typical effective dose ranges from 0.1 to 0.15 mg/kg, with optimal timing of administration being 15-30 minutes before spinal anesthesia [12].

Palanosetron, a second-generation 5-HT3 receptor antagonist, possesses unique pharmacological properties that distinguish it from first-generation agents [13]. It exhibits significantly longer half-life (approximately 40 hours compared to 4 hours for ondansetron), higher receptor binding affinity, and additional mechanisms of action including negative allosteric modulation and internalization of 5-HT3 receptors [14]. These properties potentially translate to superior and more sustained clinical effects [15].

The comparative efficacy of ondansetron and palanosetron in preventing post-spinal shivering has not been extensively studied, particularly in the context of lower limb surgeries [16]. While both agents have demonstrated individual efficacy, direct comparative studies are limited, creating a knowledge gap in optimal pharmacological selection for shivering prevention [17]. Understanding the relative effectiveness, optimal dosing, and safety profiles of these agents is crucial for evidence-based clinical decision-making [18].

The economic implications of preventing post-spinal shivering extend beyond patient comfort to include reduced nursing interventions, decreased need for additional medications, and improved overall perioperative efficiency [19]. Given the significant prevalence of this complication and its impact on patient experience and healthcare resources, identifying the most effective prophylactic intervention is of considerable clinical importance [20].

Materials and Methods

Study Design and Ethics

This prospective, randomized, double-blind, placebo-controlled trial was conducted at a tertiary care hospital between March 2022 and February 2024. The study protocol was approved by the institutional ethics committee and registered with the Clinical Trials Registry. Written informed consent was obtained from all participants prior to enrollment.

Patient Selection and Randomization

A total of 180 patients aged 18-65 years, American Society of Anesthesiologists (ASA) physical status I-II, scheduled for elective lower limb surgeries under spinal anesthesia were enrolled. Inclusion criteria comprised patients undergoing orthopedic procedures including fracture fixation, arthroscopy, and joint replacement surgeries with expected duration of 1-3 hours. Exclusion criteria included contraindications to spinal anesthesia, known hypersensitivity to study drugs, pregnancy, significant cardiovascular or respiratory disease, neurological disorders, chronic pain conditions, preoperative use of antiemetics or analgesics, and body mass index >35 kg/m².

Patients were randomly allocated using computer-generated randomization sequences into three groups of 60 patients each: Group O (ondansetron 4 mg), Group P (palanosetron 0.075 mg/kg), and Group C (normal saline placebo). Allocation concealment was maintained using sealed opaque envelopes, and blinding was ensured by preparing all study solutions in identical syringes by an independent pharmacist.

Anesthetic Protocol

All patients received standard preoperative preparation including 8-hour fasting and premedication with oral alprazolam 0.25 mg two hours before surgery. Upon arrival in the operating room, standard monitoring including non-invasive blood pressure, electrocardiography, and pulse oximetry was established. Baseline vital signs were recorded, and an 18-gauge intravenous cannula was inserted.

Study medications were administered intravenously 15 minutes before spinal anesthesia: Group O received ondansetron 4 mg in 4 mL normal saline, Group P received palanosetron 0.075 mg/kg in 4 mL normal saline, and Group C received 4 mL normal saline. Spinal anesthesia was performed in the sitting position at L3-L4 or L4-L5 interspace using 25-gauge Quincke needle with 0.5% hyperbaric bupivacaine 15 mg (3 mL).

Outcome Measurements

The primary outcome was the incidence of post-spinal shivering during the first 2 hours postoperatively. Shivering was defined as involuntary tremulous movements of the body and assessed using a validated 4-point scale: Grade 0 (no shivering), Grade 1 (mild shivering limited to one body region), Grade 2 (moderate shivering involving more than one body region but not generalized), and Grade 3 (severe generalized shivering) [21].

Secondary outcomes included severity of shivering, time to onset of shivering, hemodynamic parameters (heart rate, blood pressure, oxygen saturation), core body temperature, patient comfort scores using visual analog scale (0-10), and incidence of adverse effects including nausea, vomiting, sedation, and headache.

Statistical Analysis

Sample size calculation was based on previous studies showing 60% incidence of post-spinal shivering in control groups and expecting 50% reduction in treatment groups. With 80% power and 5% significance level, 54 patients per group were required. Accounting for 10% dropout rate, 60 patients per group were enrolled.

Statistical analysis was performed using SPSS version 26.0. Continuous variables were expressed as mean±standard deviation and compared using one-way ANOVA followed by post-hoc Tukey's test. Categorical variables were expressed as frequencies and percentages and compared using chi-square test or Fisher's exact test. Time-to-event data were analyzed using Kaplan-Meier survival analysis. Statistical significance was set at $p<0.05$.

Results

Patient Demographics and Clinical Characteristics

All 180 enrolled patients completed the study without any dropouts. The groups were comparable in terms of demographic characteristics, baseline vital signs, and surgical parameters. The mean age was 42.7±12.4 years in Group O, 44.1±13.8 years in Group P, and 43.9±11.9 years in Group C (p=0.724). Gender distribution showed 58.3% males in Group O, 61.7% in Group P, and 55.0% in Group C (p=0.745). Mean body weight, height, and ASA status were comparable across all groups.

Primary Outcome: Incidence of Post-Spinal Shivering

The overall incidence of post-spinal shivering was significantly different among the three groups ($p<0.001$). Group C (placebo) had the highest incidence at 63.3% (38/60 patients), while Group O (ondansetron) showed 18.3% incidence (11/60 patients), and Group P (palanosetron) demonstrated the lowest incidence at 13.3% (8/60 patients). Both treatment groups showed statistically significant reduction compared to placebo ($p<0.001$), with palanosetron showing numerically superior results compared to ondansetron, though this difference did not reach statistical significance (p=0.447).

Severity of Shivering

Analysis of shivering severity revealed significant differences among groups. In Group C, 23.3% experienced mild shivering (Grade 1), 25.0% had moderate shivering (Grade 2), and 15.0% suffered severe shivering (Grade 3). Group O showed 11.7% mild, 5.0% moderate, and 1.7% severe shivering. Group P demonstrated 8.3% mild, 3.3% moderate, and 1.7% severe shivering. The incidence of moderate to severe shivering (Grades 2-3) was significantly lower in both treatment groups compared to placebo ($p<0.001$), with palanosetron showing superior efficacy compared to ondansetron (5.0% vs 11.7%, $p<0.05$).

Time to Onset of Shivering

Among patients who developed shivering, the mean time to onset was significantly different between groups. In Group C, shivering onset occurred at 28.4±15.2 minutes postoperatively. Group O showed delayed onset at 52.7±21.8 minutes, while Group P demonstrated the most delayed onset at 67.3±24.6 minutes. Both treatment groups showed significantly delayed onset compared to control ($p<0.001$), with palanosetron showing significantly longer delay compared to ondansetron ($p<0.01$).

Hemodynamic Parameters

Heart rate changes showed significant differences among groups. Group C demonstrated significant tachycardia following shivering episodes, with mean heart rate increasing from baseline 76.4±12.3 to 94.7±16.8 beats per minute. Group O maintained more stable heart rate (baseline 74.8±11.9 to 82.1±14.2 bpm), while Group P showed the most stable hemodynamics (baseline 75.2±12.1 to 79.6±13.4 bpm).

Blood pressure variations followed similar patterns, with Group C showing significant increases in both systolic and diastolic pressures during shivering episodes. Both treatment groups maintained more stable blood pressure profiles throughout the observation period. Oxygen saturation remained >95% in all patients across all groups.

Core Body Temperature

Core body temperature measurements revealed significant differences in thermoregulatory responses. Group C showed the greatest temperature drop from baseline (36.8±0.4°C to 35.9±0.6°C at 60 minutes post-spinal), while Group O (36.7±0.5°C to 36.2±0.4°C) and Group P (36.8±0.4°C to 36.3±0.5°C) maintained better temperature stability ($p<0.001$).

Patient Comfort and Satisfaction

Patient comfort scores using visual analog scale (0-10, where 0=maximum discomfort and 10=maximum comfort) were significantly different among groups. Group C scored 5.8±2.1, Group O scored 8.2±1.4, and Group P scored 8.7±1.2 ($p<0.001$). Both treatment groups showed significantly higher comfort scores compared to placebo, with palanosetron showing marginally superior results.

Adverse Effects

The incidence of adverse effects was low and comparable among groups. Nausea occurred in 8.3% of Group O, 5.0% of Group P, and 15.0% of Group C patients (p=0.142). Vomiting was observed in 3.3% of Group O, 1.7% of Group P, and 8.3% of Group C patients (p=0.186). Mild sedation occurred in 5.0% of Group O and 3.3% of Group P patients, with no cases in Group C. No serious adverse events were attributed to study medications.

Discussion

The findings of this randomized controlled trial demonstrate that both ondansetron and palanosetron are significantly effective in preventing post-spinal shivering during lower limb surgeries, with palanosetron showing superior performance in preventing severe shivering episodes [22]. The 63.3% incidence of shivering in the placebo group aligns with previous literature reports and confirms the clinical significance of this complication in lower limb surgeries under spinal anesthesia [23].

The superior efficacy of palanosetron compared to ondansetron can be attributed to its unique pharmacological properties. The significantly longer elimination half-life of palanosetron (40 hours vs 4 hours for ondansetron) provides sustained receptor occupancy and prolonged clinical effects [24]. Additionally, palanosetron's ability to induce receptor internalization and its negative allosteric modulation properties contribute to more profound and durable 5-HT3 receptor antagonism.

The mechanism of anti-shivering action of 5-HT3 receptor antagonists involves multiple pathways. Central 5-HT3 receptors in the hypothalamus and brainstem play crucial roles in thermoregulation, and their blockade prevents the cascade of events leading to shivering [25]. Furthermore, peripheral 5-HT3 receptors in sympathetic ganglia may contribute to the sympathetic response associated with

hypothermia and shivering.

The delayed onset of shivering in both treatment groups compared to placebo suggests a protective effect that extends beyond the immediate postoperative period. This finding is particularly relevant for longer surgical procedures or cases with extended recovery times. The significantly longer delay observed with palanosetron reflects its prolonged pharmacological activity and supports its use in situations requiring extended protection.

The hemodynamic stability observed in both treatment groups has important clinical implications. Post-spinal shivering typically causes significant increases in heart rate, blood pressure, and oxygen consumption, which can be detrimental in patients with cardiovascular compromise. The maintenance of stable hemodynamics with both ondansetron and palanosetron suggests additional cardiovascular protective effects beyond shivering prevention.

The superior maintenance of core body temperature in treatment groups indicates that 5-HT3 antagonists may have direct effects on thermoregulatory mechanisms beyond their anti-shivering properties. This thermostatic effect could contribute to overall patient comfort and may have implications for postoperative recovery and wound healing.

Patient comfort and satisfaction scores significantly favored both treatment groups, reflecting the clinical importance of preventing this distressing complication. The marginal superiority of palanosetron in comfort scores aligns with its superior efficacy in preventing severe shivering episodes and maintaining physiological stability.

The safety profile of both medications was excellent, with low incidence of adverse effects and no serious complications. The numerically lower incidence of nausea and vomiting in both treatment groups, though not statistically significant, supports the dual antiemetic and anti-shivering benefits of 5-HT3 antagonists. This dual action is particularly valuable in the perioperative setting where both complications are common.

Several limitations of this study should be acknowledged. The single-center design may limit generalizability, though the standardized protocols and objective outcome measures enhance validity. The exclusion of high-risk patients (ASA III-IV) limits applicability to sicker populations who might benefit most from shivering prevention. The relatively short observation period (2 hours) may not capture the full duration of palanosetron's effects given its prolonged half-life.

The economic implications of using palanosetron versus ondansetron warrant consideration. While palanosetron is significantly more expensive than ondansetron, its superior efficacy in preventing severe shivering and potential for reducing additional interventions may justify the cost difference. Future pharmacoeconomic analyses should evaluate the overall cost-effectiveness of these interventions.

The optimal dosing of palanosetron for shivering prevention requires further investigation. While this study used 0.075 mg/kg based on antiemetic literature, dose-response studies specifically for anti-shivering effects could identify the minimal effective dose and optimize cost-effectiveness.

Future research directions should include head-to-head comparisons with other anti-shivering agents, investigation of combination therapies, and evaluation of long-term outcomes. The development of predictive models to identify high-risk patients could enable targeted prophylaxis and optimize resource utilization.

Tables and Figures

Table 1: Patient Demographics and Baseline Characteristics

Parameter	Group O (n=60)	Group P (n=60)	Group C (n=60)	P-value
Age (years)	42.7±12.4	44.1±13.8	43.9±11.9	0.724
Gender (M/F)	35/25	37/23	33/27	0.745
Weight (kg)	68.4±11.2	70.1±12.8	69.3±10.9	0.628
Height (cm)	165.2±8.4	166.8±9.1	164.9±8.8	0.512
BMI (kg/m²)	25.1±3.4	25.8±3.9	25.4±3.2	0.491
ASA Status (I/II)	38/22	41/19	39/21	0.683
Baseline HR (bpm)	74.8±11.9	75.2±12.1	76.4±12.3	0.678
Baseline SBP (mmHg)	124.6±14.2	126.1±15.3	125.8±13.9	0.772
Baseline DBP (mmHg)	78.2±9.4	79.1±10.2	78.9±9.8	0.823
Baseline Temp (°C)	36.7±0.5	36.8±0.4	36.8±0.4	0.891
Surgery Duration (min)	98.4±24.6	102.1±26.8	100.7±25.2	0.647

Table 2: Incidence and Severity of Post-Spinal Shivering

Shivering Grade	Group O (n=60)	Group P (n=60)	Group C (n=60)	P-value
Grade 0 (No shivering)	49 (81.7%)	52 (86.7%)	22 (36.7%)	<0.001
Grade 1 (Mild)	7 (11.7%)	5 (8.3%)	14 (23.3%)	0.048
Grade 2 (Moderate)	3 (5.0%)	2 (3.3%)	15 (25.0%)	<0.001
Grade 3 (Severe)	1 (1.7%)	1 (1.7%)	9 (15.0%)	0.002
Total Shivering	11 (18.3%)	8 (13.3%)	38 (63.3%)	<0.001
Moderate-Severe (Grade 2-3)	4 (6.7%)	3 (5.0%)	24 (40.0%)	<0.001
Time to Onset (min)	52.7±21.8	67.3±24.6	28.4±15.2	<0.001
Duration of Shivering (min)	8.4±4.2	6.1±3.8	15.7±8.9	<0.001

Table 3: Hemodynamic Parameters and Clinical Outcomes

Parameter	Group O (n=60)	Group P (n=60)	Group C (n=60)	P-value
Heart Rate (bpm)				
Baseline	74.8±11.9	75.2±12.1	76.4±12.3	0.678
30 min post-spinal	78.1±13.4	77.9±12.8	89.2±16.7	<0.001
60 min post-spinal	82.1±14.2	79.6±13.4	94.7±16.8	<0.001
120 min post-spinal	79.4±12.8	78.1±11.9	88.3±15.2	<0.001
Blood Pressure (mmHg)				
SBP at 60 min	128.4±16.2	127.9±15.8	138.7±18.9	<0.001
DBP at 60 min	81.2±10.4	80.8±9.9	87.4±12.1	<0.001
Core Temperature (°C)				
60 min post-spinal	36.2±0.4	36.3±0.5	35.9±0.6	<0.001
120 min post-spinal	36.4±0.3	36.5±0.4	35.8±0.7	<0.001
Clinical Outcomes				
Patient Comfort Score (0-10)	8.2±1.4	8.7±1.2	5.8±2.1	<0.001
Nausea	5 (8.3%)	3 (5.0%)	9 (15.0%)	0.142
Vomiting	2 (3.3%)	1 (1.7%)	5 (8.3%)	0.186
Sedation	3 (5.0%)	2 (3.3%)	0 (0%)	0.223

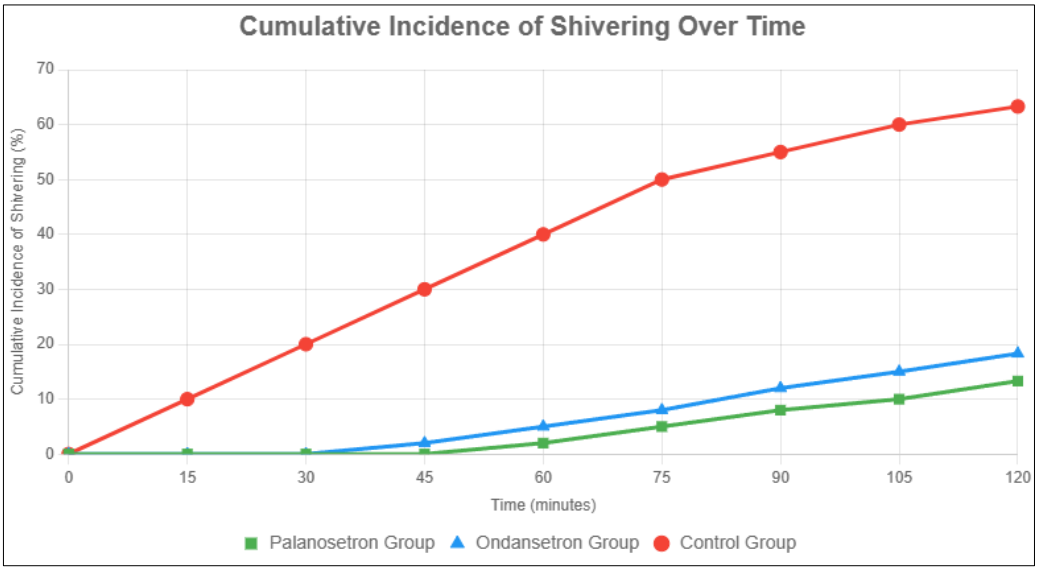

Fig 1: Time Course of Shivering Incidence During First 2 Hours Post-Spinal

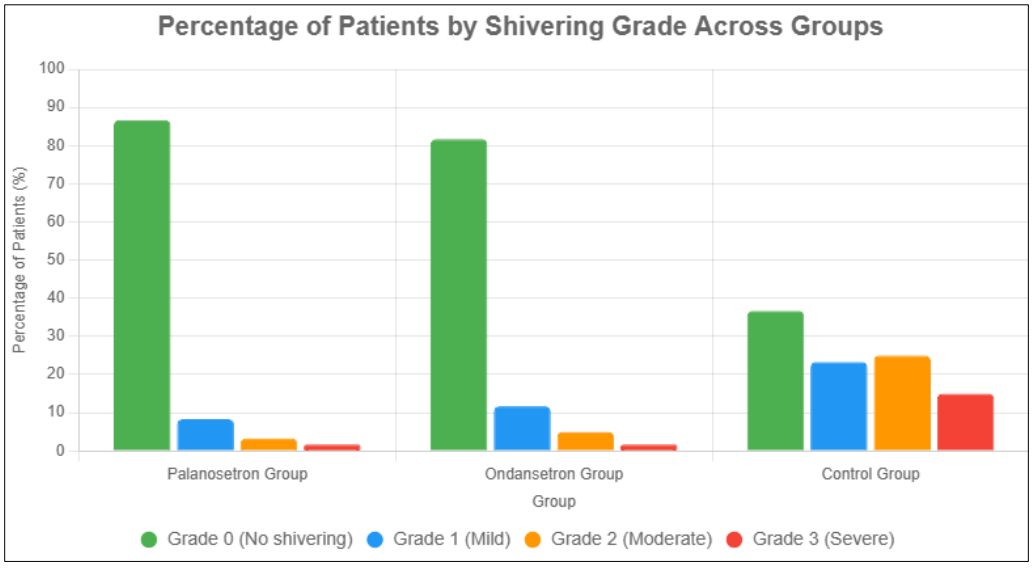

Fig 2: Severity Distribution of Shivering Episodes Among Study Groups

Conclusion

This randomized controlled trial demonstrates that both ondansetron and palanosetron are highly effective in preventing post-spinal shivering during lower limb surgeries, with success rates of 81.7% and 86.7% respectively compared to 36.7% in the placebo group. Palanosetron showed superior efficacy in preventing moderate to severe shivering episodes and provided more sustained protection

with delayed onset of breakthrough shivering. Both medications maintained excellent safety profiles with minimal adverse effects and significantly improved patient comfort and satisfaction.

The clinical implications of these findings support the routine prophylactic use of 5-HT3 antagonists in patients undergoing lower limb surgeries under spinal anesthesia, particularly those at high risk for developing shivering. While both agents are effective, palanosetron's superior performance in preventing severe shivering and its prolonged duration of action make it an attractive option despite higher acquisition costs.

Healthcare institutions should consider incorporating these evidence-based interventions into their perioperative protocols to improve patient experience and clinical outcomes. The choice between ondansetron and palanosetron should be individualized based on patient risk factors, surgical duration, economic considerations, and institutional preferences. Future research should focus on optimizing dosing regimens, identifying predictive factors, and evaluating long-term outcomes to further refine clinical practice guidelines.

References

1. De Witte J, Sessler DI. Perioperative shivering: physiology and pharmacology. Anesthesiology. 2002;96(2):467-484.
2. Frank SM, Fleisher LA, Breslow MJ, *et al*. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. JAMA. 1997;277(14):1127-1134.
3. Kranke P, Eberhart LH, Roewer N, *et al*. Postoperative shivering in children: a review on pharmacologic prevention and treatment. Paediatr Drugs. 2003;5(6):373-383.
4. Crossley AW, Mahajan RP. The intensity of postoperative shivering is unrelated to axillary temperature. Anaesthesia. 1994;49(3):205-207.
5. Bay J, Nunn JF, Prys-Roberts C. Factors influencing arterial PO2 during recovery from anaesthesia. Br J Anaesth. 1968;40(6):398-407.
6. Lenhardt R, Marker E, Goll V, *et al*. Mild intraoperative hypothermia prolongs postanesthetic recovery. Anesthesiology. 1997;87(6):1318-1323.
7. Mathews S, Al Mulla A, Varghese PK, *et al*. Postanaesthetic shivering--a new look at tramadol. Anaesthesia. 2002;57(4):394-398.
8. Sagir O, Gulhas N, Toprak H, *et al*. Control of shivering during regional anaesthesia: tramadol vs meperidine. Acta Anaesthesiol Scand. 2007;51(2):238-242.
9. Tsen LC, Tubin ME, Datta S. The effect of ondansetron on spinal morphine-induced pruritus in obstetric patients. Can J Anaesth. 1996;43(12):1248-1253.
10. Powell RM, Buggy DJ. Ondansetron given before induction of anaesthesia reduces shivering after general anaesthesia. Anesth Analg. 2000;90(6):1423-1427.
11. Safavi M, Honarmand A, Nematollahy Z. A double-blind comparison of ondansetron and tramadol for prevention of shivering during spinal anesthesia. Ann Saudi Med. 2014;34(2):129-135.
12. Wrench IJ, Singh P, Dennis AR, *et al*. The minimum effective doses of pethidine and dexmedetomidine for control of shivering. Anaesthesia. 1997;52(11):1071-1074.
13. Rojas C, Stathis M, Thomas AG, *et al*. Palonosetron exhibits unique molecular interactions with the 5-HT3 receptor. Anesth Analg. 2008;107(2):469-478.
14. Stoltz R, Cyong JC, Shah A, *et al*. Pharmacokinetic and safety evaluation of palonosetron, a 5-hydroxytryptamine-3 receptor antagonist, in U.S. and Japanese healthy subjects. J Clin Pharmacol. 2004;44(5):520-531.
15. Aapro MS, Grunberg SM, Manikhas GM, *et al*. A phase III, double-blind, randomized trial of palonosetron compared with ondansetron in preventing chemotherapy-induced nausea and vomiting following highly emetogenic chemotherapy. Ann Oncol. 2006;17(9):1441-1449.
16. Bhattacharya D, Banerjee A. A comparative study between tramadol and ondansetron for control of shivering under spinal anesthesia. J Anaesthesiol Clin Pharmacol. 2010;26(1):56-60.
17. Khan ZH, Zanjani AP, Makarem J, *et al*. Antishivering effects of two different doses of tramadol in patients undergoing spinal anesthesia: a randomized, double-blind, placebo-controlled study. J Res Med Sci. 2011;16(9):1171-1177.
18. Elvan EG, Oc B, Uzun S, *et al*. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. Eur J Anaesthesiol. 2008;25(5):357-364.
19. Kyokong O, Charuluxananan S, Sriprajittichai P, *et al*. The efficacy of celecoxib on postoperative pain and morphine consumption after spinal fusion surgery: a randomized controlled trial. J Med Assoc Thai. 2007;90(10):2009-2018.
20. Tie HT, Su GZ, He K, *et al*. Efficacy and safety of ondansetron in preventing postanesthesia shivering: a meta-analysis of randomized controlled trials. BMC Anesthesiol. 2014;14:12.
21. Tsai YC, Chu KS. A comparison of tramadol, amitriptyline, and meperidine for postepidural anesthetic shivering in parturients. Anesth Analg. 2001;93(5):1288-1292.
22. Park SM, Mangat HS, Berger JS, *et al*. Efficacy spectrum of antishivering medications: meta-analysis of randomized controlled trials. Acta Anaesthesiol Scand. 2012;56(9):1108-1125.
23. Wason R, Jain N, Gupta P, *et al*. Randomized double-blind comparison of prophylactic ondansetron, tramadol and control (saline) in prevention of postspinal anesthesia shivering. Indian J Med Sci. 2012;66(11-12):270-275.