

Antishivering effect of intrathecal versus intravenous tramadol in patients undergoing urethroscopic lithotripsy under spinal anesthesia



Manasa M¹, Jyoti Petkar², Dokku Kirtana³, Karthik GS⁴, Rangalakshmi S⁵

¹Assistant Professor, ^{2,4,5}Professor, ³Junior Resident, Department of Anesthesiology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India

Submission: 23-11-2023

Revision: 29-01-2024

Publication: 01-03-2024

ABSTRACT

Background: Shivering is the most common complication seen in the perioperative period in patients undergoing urological surgeries under spinal anesthesia. Intravenous tramadol is used for the treatment of shivering. **Aims and Objectives:** In this study, we wanted to assess the prophylactic effect of tramadol, intrathecal (IT) versus intravenous with the control group, in decreasing the incidence of shivering. **Materials and Methods:** Fifty-four eligible patients posted for urethroscopic lithotripsy (URSL) were randomly allocated into three equal groups – Group C: Received 2.5 mL 0.5% bupivacaine heavy + 0.5 mL normal saline intrathecally and 5 mL of normal saline intravenously, Group V: Received 2.5 mL of 0.5% bupivacaine heavy + 0.5 mL normal saline intrathecally and 25 mg tramadol in 5 mL of normal saline intravenously, and Group T: Received 2.5 mL of 0.5% bupivacaine heavy + 25 mg (0.5 mL) of tramadol intrathecally and 5 mL of normal saline intravenously. The incidence and severity of shivering were noted. Onset of sensory and motor block, duration of post-operative analgesia, core body temperature, and adverse effects such as nausea, vomiting, and hypotension were noted. **Results:** The incidence of intraoperative shivering was significantly lower in Group T versus C ($P=0.014$) but comparable among Group I versus C ($P=0.502$) and Group T versus I ($P=0.06$). The duration of analgesia was significantly higher in Group T compared to Groups I and C ($P<0.001$). The additional tramadol requirement was significantly lower in Group T versus I and in Group T versus C but comparable among Group I versus C. **Conclusion:** The addition of 25 mg tramadol to IT 0.5% bupivacaine heavy is effective in preventing intraoperative shivering in patients undergoing urological surgeries like URSL.

Key words: Intrathecal tramadol; Shivering; Spinal anesthesia; Urethroscopic lithotripsy

INTRODUCTION

Spinal anesthesia is most commonly performed for urological procedures like urethroscopic lithotripsy (URSL) since it helps in the early recognition of complications like bladder perforation.

Shivering is a common complication of spinal anesthesia, seen in 40–60%¹ of patients anesthetized by subarachnoid block (SAB). It can be defined as spontaneous, involuntary

and oscillatory fasciculations, or tremor-like hyperactivity of the skeletal muscles.² Shivering is attributed to peripheral vasodilatation, resulting in the peripheral distribution of heat from the core body and causing decreased core body temperature. This decrease in core body temperature is sensed by hypothalamic thermoreceptors, which try to increase heat production by shivering.³

General anesthesia impairs central thermoregulation, but spinal anesthesia affects both central and peripheral

Access this article online

Website:

<http://nepjol.info/index.php/AJMS>

DOI: 10.3126/ajms.v15i3.60133

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2024 Asian Journal of Medical Sciences



This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

Address for Correspondence:

Dr. Manasa M, Assistant Professor, Department of Anesthesiology, Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India. **Mobile:** +91-8971180007. **E-mail:** drmanasa29@gmail.com

thermoregulation by enlarging the interthreshold range through raising the sweating threshold and decreasing the vasoconstriction and shivering thresholds.⁴ Under neuraxial blockade, hypothermia may not be perceived by patients who typically feel less cold after induction of the block. The shivering threshold is consequently breached soon, and more shivering is requisite to avert further hypothermia. Other intraoperative causes of shivering include disinhibited spinal reflexes, decreased sympathetic activity, and pain.⁵ Patients undergoing URSL surgeries are furthermore at risk due to the cold irrigation fluids used throughout the surgical procedure.

Shivering-induced severe muscle movements during SAB are disturbing for the surgeon as well as for the patient. Apart from its important function of increasing core body temperature, shivering has adverse effects such as an increase in metabolic rate, oxygen consumption (300–400%), carbon dioxide production, heart rate (HR), and blood pressure.⁴ These by increasing cardiac workload are deleterious, particularly in patients with limited cardiac reserves. It also increases post-operative pain, causes delayed wound healing, and longer hospital stays. Shivering also impedes perioperative monitoring and increases intraocular and intracranial pressures. Although there are many therapeutic strategies for treating shivering, the overall quality of the antishivering guidelines is low.⁴ Thus, prophylaxis for post-anesthesia shivering needs special attention.

A number of drugs such as pethidine, tramadol, clonidine, dexmedetomidine, ondansetron, granisetron, and ketamine, acting on different receptors such as the opioid, alpha-2 adrenergic, anticholinergic, N-methyl-D-aspartate, and serotonergic receptors, have been shown to have prophylactic antishivering efficacy. Different opioids with varying receptor profiles have been shown to reduce but not completely eliminate post-spinal shivering. Respiratory depression, pruritus, nausea, vomiting, sedation, and restricted availability remain some of the problems associated with their use.⁴

Tramadol, a synthetic opioid, is unique owing to its low propensity to cause respiratory depression, pruritus, tolerance, and depression; it is easily available owing to it lying outside the realm of narcotic drugs and psychotropic substances act.⁶ Its intrathecal (IT) administration has also been found to be safe with no neural toxicity.^{7,8} Intravenous (IV) tramadol is usually used for prophylaxis and management of post-spinal shivering.

The anti-shivering mechanism of tramadol is explained by its μ receptor agonist effect. It suppresses the reuptake of serotonin, norepinephrine, and 5-hydroxytryptamine

(5-HT) at the level of the spinal cord and facilitates the release of 5-HT. It has a role in the thermoregulation process.^{4,9} IT tramadol causes suppression of sensory and motor conduction in the spinal cord.¹⁰

Previous studies compared IT tramadol in different doses, with a placebo or with other drugs, to test its anti-shivering effect. However, only one study compared the effects of the two different routes of tramadol on the prophylaxis of post-spinal shivering. Hence, this research was designed to assess the prophylactic effect of tramadol at a dose of 25 mg, IT versus intravenous with control group, in decreasing the incidence of shivering.

The primary objective of this study was to compare the incidence of post-anesthesia shivering in the three groups. Secondary objectives were to compare the severity of shivering, the onset of sensory and motor block, the duration of post-operative analgesia, and the incidence of adverse effects such as nausea, vomiting, and hypotension.

Aims and objectives

The primary objective of this study was to compare the incidence of post-anesthesia shivering in the three groups. Secondary objectives were to compare the severity of shivering, the onset of sensory and motor block, the duration of post-operative analgesia, and the incidence of adverse effects such as nausea, vomiting, and hypotension.

MATERIALS AND METHODS

This prospective double-blinded randomized control trial was conducted after obtaining institutional ethical committee approval (RRMCH-IEC/207/2023) in a 1300-bedded teaching hospital by the Department of Anesthesiology. The study proposal was registered in the clinical trial registry of India with the CTRI number: CTRI/2023/11/059583.

The American Society of Anesthesiologists (ASA) grade I and II patients undergoing elective URSL surgeries under SAB for <90 min, aged between 18 and 60 years, and weighing not more than 90 kg of either sex were included in the study. Patients with ASA grade III and higher; contraindications to SAB; allergy to tramadol; bupivacaine; significant cardiorespiratory, renal, or hepatic impairment; uncontrolled hypertension or diabetes mellitus; on chronic analgesics; vasodilators/vasoconstrictors; weight >90 kg; cerebrovascular disease; thyroid dysfunction; infection of the urinary tract; and patients not willing to participate in the study were excluded from the study. Written informed consent was obtained from all patients included in the study.

Sample size was estimated using the difference in mean shivering grade between Group A (pethidine) and Group B (tramadol) from the study by Bhatnagar et al.,¹¹ as 2.6 ± 0.2 and 2.8 ± 0.2 . Using these values, a 95% confidence limit and an 80% power sample size of 16 were obtained in each group using the MedCalc sample size software. With a 10% non-response sample size of $16 + 1.6 \approx 18$ cases were included in each group.

A pre-anesthetic evaluation was done, and routine investigations were noted. Details of the anesthetic technique and study protocol were explained to the patients during their pre-operative visit. Randomization was done using computer-generated random numbers with the opaque sealed envelope method. The study population was divided into Groups C, V, and T.

- Group C: Received 2.5 mL of 0.5% bupivacaine heavy+0.5 mL of normal saline intrathecally and 5 mL of normal saline intravenously
- Group V: Received 2.5 mL of 0.5% bupivacaine heavy+0.5 mL of normal saline intrathecally and 25 mg of tramadol in 5 mL of normal saline intravenously
- Group T: Received 2.5 mL of 0.5% bupivacaine heavy + 25 mg (0.5 mL) of tramadol intrathecally and 5 mL of normal saline intravenously.

Randomization was done using a computer-randomizing website and a randomization sequence that was concealed in closed numbered envelopes. One of the anesthesia team members who were not involved in the study opened the patient's envelope to know the group assignment, prepare the medications, and give it to the investigator to perform the spinal anesthesia. The patients and the investigator who observed the patients were blinded to the group assignment. The operating room temperature was adjusted between 22°C and 24°C. 18 G peripheral venous cannula was secured in the right or left arm, and all patients received 500 mL of Ringer's acetate as co-load. Standard intraoperative monitoring with an electrocardiogram, non-invasive arterial blood pressure, pulse oximetry (SpO₂), and axillary temperature probe was used. Then, patients received spinal anesthesia in a sitting position at L2-3 or L3-4 using a 25-gauge Quincke needle. HR, SpO₂, mean arterial pressure (MAP), and temperature were monitored every 5 min for half an hour and every 15 min till the end of surgery.

The sensory block level was assessed by the loss of pinprick sensation to the 25 G hypodermic needle in the mid-clavicle line, checked every minute until stabilization of the highest sensory block level. The motor block was assessed using the modified Bromage score:¹² 1 – complete block (unable to move feet or knees), 2 – almost complete block (able to move feet only), 3 – partial block (just able to move knees), 4 – detectable weakness of hip flexion (between scores 3

and 5), 5 – no detectable weakness of hip flexion while supine (full flexion of knees), and 6 – be able to perform a partial knee bend. The time of onset of sensory and motor block was noted. Patients with incomplete or partial block necessitating conversion to general anesthesia were excluded from the analysis.

Hypotension is defined as a systolic blood pressure 20% fall from baseline and treated with additional IV RL boluses and injection ephedrine (6 mg IV boluses). Bradycardia is defined as HR <45 beats per min and treated with an injection of atropine 0.6 mg IV. The patients were monitored for shivering intraoperatively using a five-point intensity scale:¹³

Grade 0: No shivering;

- Grade 1: One or more of the following: piloerection, peripheral vasoconstriction, and peripheral cyanosis, but without visible muscle activity
- Grade 2: Visible muscle activity confined to one muscle group
- Group 3: Visible muscle activity in more than one muscle group
- Grade 4: Gross muscle activity involving the whole body.

Injection tramadol 50 mg IV was administered if the shivering score was ≥ 2 (moderate to severe shivering). All the time periods were calculated from the time of completion of the IT injection as time 0. The time of skin incision and closure were noted to calculate the duration of surgery. The patients were monitored for pain at rest (using the VAS score) until they complained of VAS ≥ 4 . Injection paracetamol 1 g IV was administered as the rescue analgesic when the VAS was ≥ 4 . The duration of analgesia was calculated as the time from the completion of the IT injection to the time of the requirement of the first rescue analgesic. The incidence of nausea and vomiting was recorded. Injection of ondansetron (4 mg IV) was given to treat nausea or vomiting.

RESULTS

A total of 54 patients who met the inclusion criteria were enrolled in the study and were randomized with 18 patients in each group. One patient from Group T requiring conversion to general anesthesia in view of a partial block was excluded from analysis. A total of 53 patients were analyzed (Figure 1).

Statistical analysis

Data were entered into a Microsoft Excel data sheet and analyzed using the Statistical Package for the Social

Sciences (SPSS) 22 version software. Categorical data were represented in the form of frequencies and proportions. The Chi-square test was used as a test of significance for qualitative data. Fischer's exact test was used as a test of significance for qualitative data which does not fulfill the criteria for the Chi-square test (2×2 tables only). Continuous data were represented as the mean and standard deviation. The normality of the continuous data was tested by the Kolmogorov–Smirnov test and the Shapiro–Wilk test. The analysis of variance was the test of significance to identify the mean difference between more than two groups for quantitative data. A *post-hoc* Bonferroni test was used to determine the intergroup analysis. The Kruskal–Wallis test was the test of significance to identify the mean difference between more than two groups for quantitative data with a skewed distribution.

Graphical representation of data

MS Excel and MS Word were used to obtain various types of graphs, such as bar diagrams and line diagrams.

P-value (probability that the result is true) of <0.05 was considered statistically significant after assuming all the rules of statistical tests.¹⁴⁻¹⁶

Statistical software

MS Excel and SPSS version 22 (IBM SPSS Statistics, Somers, NY, USA) were used to analyze the data.

All groups were comparable with respect to the demographic profile of study participants (Table 1). The onset of sensory block was comparable in all groups. The motor block onset time was significantly earlier in Group T versus C

but comparable in Group T versus I and Group I versus C (Table 2). The duration of analgesia was significantly higher in Group T (307.53±24.67 min) compared to Groups I (200±21.42 min) and C (194.78±15.72 min).

HR and SpO₂ were comparable among all groups at nearly all time intervals. MAP was significantly lower in Group I at 5-min, 10-min, and 20-min intervals after spinal and significantly lower in Group T at a 75-min interval after spinal.

The incidence of intraoperative shivering was significantly lower in Group T versus C (P=0.014) but comparable among Group I versus C (P=0.502) and Group T versus I (P=0.06) (Table 3).

Severity of shivering: Group T had significantly less severe shivering compared to the other two groups (Figure 2).

Additional tramadol requirement was significantly lower in Group T versus I and in Group T versus C but comparable among Group I versus C (Table 2). There was a significant dip in the core body temperature in Group I at 45 min after the SAB. During other periods throughout the surgery, the core body temperature was comparable among the groups (Figure 3). The incidence of complications, nausea, vomiting, and hypotension was comparable among all groups (Figure 4).

DISCUSSION

Hypothermia is a common cause of shivering in post-spinal patients. However, shivering may also occur in normothermic patients in the perioperative period.

Table 1: Demographic profile comparison between three groups

Groups	Group T	Group I	Group C	P-value b/w 3 groups
Age (years), means±SD	45.47±11.84	45.72±13.73	52.44±17.76	0.284
Height, means±SD	168.65±4.94	168.00±6.04	165.28±4.70	0.140
Weight, means±SD	70.35±4.649	69.00±8.56	65.22±8.13	0.111
BMI, means±SD	24.75±1.670	24.50±3.35	23.94±3.19	0.686
Duration of surgery, means±SD	90.00±0.00	90.00±0.00	90.00±0.00	-
ASA 1/2	8/9	7/11	8/10	0.883
Sex				
Female, n (%)	8 (47.1)	7 (38.9)	9 (50.0%)	0.787
Male, n (%)	9 (52.9)	11 (61.1)	9 (50.0%)	

SD: Standard deviation, ASA: American Society of Anesthesiology

Table 2: Onset of sensory block, motor block, and additional tramadol requirement

Variables	Group T versus Group I	Group T versus Group C	Group I versus Group C
Intraoperative shivering	0.06	0.014*	0.502
Sensory onset time (min)	1.000	0.087	0.225
Motor onset time (min)	1.000	0.036*	0.073
Additional tramadol (50 mg)	0.042*	0.009*	0.494

*Statistically significant

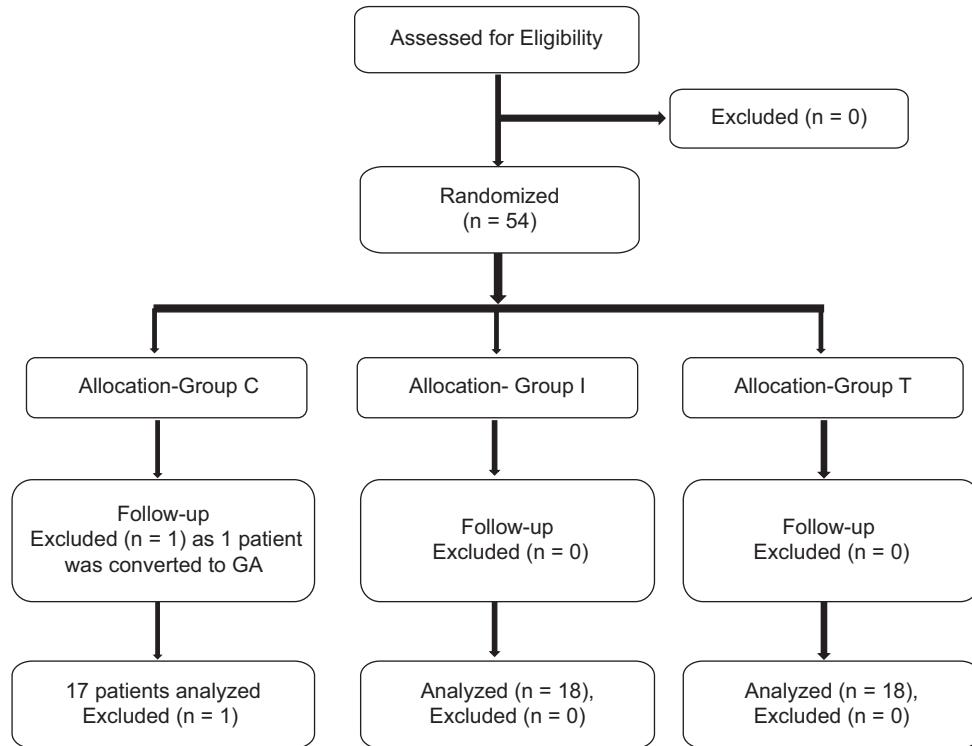


Figure 1: Consort diagram

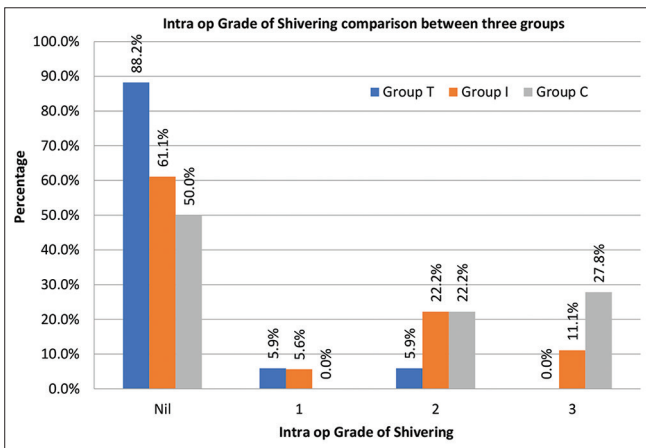


Figure 2: Grade of shivering

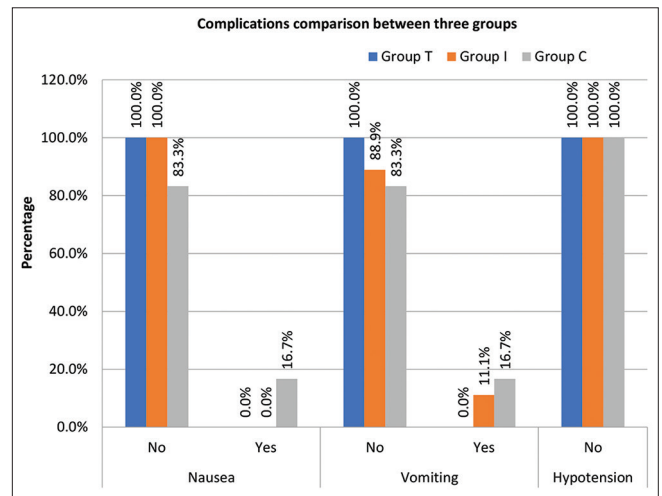


Figure 4: Adverse effects

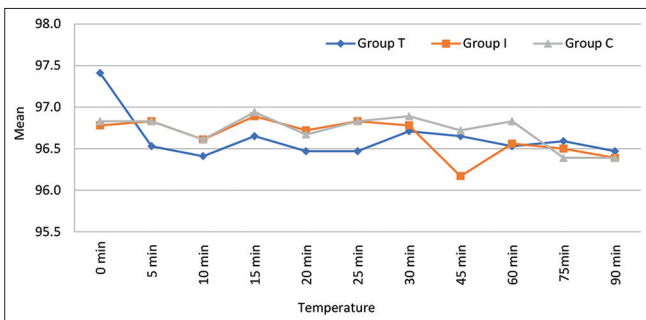


Figure 3: Temperature comparison between 3 groups intra-operatively

Groups	Group T		Group I		Group C	
	Count	%	Count	%	Count	%
Intraoperative shivering						
No	15	88.2	11	61.1	9	50.0
Yes	2	11.8	7	38.9	9	50.0

cold operating room temperatures, redistribution of heat from the core to the peripheries, pain, disinhibited spine reflexes, and decreased sympathetic activity.⁷The use of cold irrigation fluids in urological surgeries is an additional reason.

Tramadol, a synthetic opioid, acts at multiple receptors and is known to be a highly effective antishivering medication.⁷ This study was designed to evaluate and compare the antishivering efficacy and analgesia of IT tramadol (25 mg), IV tramadol (25 mg), and the control group.

Using a single IT tramadol dose alleviates the need for further systemic doses for controlling shivering tramadol is safe (no neural toxicity), quick, and relatively inexpensive. IT tramadol is commonly used as an additive to local anesthetics in doses of 10–50 mg¹⁷ to prolong the duration of sensory block, motor block, and post-operative analgesia. In our study, we opted for 25 mg of IT tramadol.¹⁸ IV tramadol is also used as prophylaxis for shivering in doses ranging from 0.25 to 1 mg/kg, showing a linear relationship with side effects. In our study, we chose to give a fixed dose of 25 mg IV tramadol.

There are previous studies comparing different doses of IT tramadol with other additives or placebo in patients undergoing cesarean sections,¹⁹ lower limb surgeries,²⁰ and shivering prophylaxis. There are only few studies done on patients undergoing urological surgeries. There is only one study comparing IT and IV tramadol⁹ conducted in patients undergoing lower-limb surgeries. Our study was designed to assess the efficacy of IT and IV tramadol in preventing post-anesthesia shivering in patients undergoing URSL.

The incidence of shivering was significantly reduced in the IT group versus the control group. The severity of shivering was significantly lower in the IT group versus the control group. Shivering requiring an additional IV dose of tramadol was significantly lower in Group T versus I and in Group T versus C. The incidence of adverse effects was comparable in all three groups.

Abd El Azeem et al.,⁹ conducted a study comparing the antishivering effects of IT tramadol (IT group) and IV tramadol (IV group) in patients undergoing lower-limb surgeries under spinal anesthesia. The IT group received 20 mg of tramadol intrathecally, and the IV group received 0.25 mg/kg of tramadol intravenously. The incidence of shivering in the IV group was higher than that of the IT group, and the severity of shivering was comparable in both groups. In our study, the incidence of shivering in the IT group was significantly lower than that in the control group but comparable with the IV group. The difference in dosage of tramadol used in both studies may be the reason for this change in the results, and we had a control group that was not taken in their study. The incidence of side effects such as nausea, vomiting, and hypotension was comparable in all three groups in our study, whereas Abd El Azeem et al., study found a lower incidence of nausea in the IT group than the IV group. This difference may be

due to the lesser dose of IT tramadol used in their study, 20 mg versus 25 mg.

Gupta and Gupta²⁰ compared the antishivering effects of 10 mg (group T10) and 20 mg (group T20) intrathecal tramadol with placebo (group C). Their results showed a significant reduction in the incidence and intensity of shivering, but they were comparable among the T10 and T20 groups. A similar significant reduction in the incidence and intensity of shivering was seen in the IT group of our study. The incidence of nausea, vomiting, and hypotension was comparable in three groups, just like in our study. The onset of sensory block was significantly earlier in group T10 versus the placebo group, whereas it was comparable in all three groups of our study. Motor block onset time was significantly earlier in group T20 versus placebo; similarly, it was significantly earlier in Group T versus C in our study. The difference may be because the total volume of spinal drugs was higher in the Gupta and Gupta studies with 3.5 mL, whereas in our study, we used a total volume of 3 mL.

Bansal et al.,¹⁹ evaluated the efficacy of IT tramadol in preventing post-spinal shivering in patients undergoing cesarean sections, in Groups T (20 mg tramadol IT) and C (control group). They found a significantly lower incidence of shivering in Group T. The result is consistent with that of our study in spite of them using 20 mg of IT tramadol compared to 25 mg in ours. Similar to our study, shivering requiring IV tramadol was significantly lower in Group T versus Group C.

Badhe et al.,²¹ compared the efficacy of IT tramadol in the prevention of shivering in patients undergoing various lower abdomen and lower-limb surgeries. Similar to our study, they found a significantly lower incidence of shivering in the IT group (IT group: 0.2 mL, 20 mg tramadol with 3 mL, 0.5% bupivacaine). In contrast to our study, they found a significantly higher incidence of nausea and vomiting in the IT group compared to the control group (3 mL of 0.5% bupivacaine with 0.2 mL of saline).

Tewari et al.,²² study was done to evaluate the efficacy of oral tramadol (50 mg 2 h before surgery) to prevent perioperative shivering in patients undergoing transurethral resection of the prostate under spinal anesthesia. They found a significant reduction in the incidence and severity of perioperative shivering in the study group. Similar to our study where we used IT or IV tramadol as prophylaxis for the prevention of shivering, they have used oral tramadol and found it effective in preventing the incidence of shivering.

In the Subedi et al.,¹⁷ study, comparing IT tramadol (10 mg) and fentanyl (10 mcg) in cesarean sections, they found a

significant reduction in the incidence of shivering and a comparable incidence of side effects (nausea and vomiting), just like in our study.

However, there were a few limitations in our study. The sample size of our study is small (54); we have included only patients of ASA I and II, aging 18–60, weighing <90 kg; therefore, further studies are required to be done in larger populations, including all other patients. We have studied only the patients undergoing URSL surgeries; hence, further studies are needed to be done in patients undergoing other surgeries under spinal anesthesia to evaluate the antishivering effect.

Limitations of the study

However there were few limitations in our study. Sample size of our study is small (54), we have included only patients of ASA I and II, aging 18 to 60 years, weighing less than 90 kgs, therefore further studies are required to be done in larger populations including all other patients. We have studied only the patients undergoing URSL surgeries, hence further studies are needed to be done in patients undergoing other surgeries in spinal anaesthesia to evaluate the antishivering effect.

CONCLUSION

The addition of 25 mg of tramadol intrathecally as prophylaxis is effective in preventing intraoperative shivering in patients undergoing urological surgeries that require cold irrigation fluids. IT tramadol also hastens the onset of motor block and prolongs the duration of analgesia, requiring lesser post-operative analgesics without increasing the incidence of side effects such as nausea, vomiting, and hypotension.

ACKNOWLEDGMENT

The authors would like to express their gratitude to Dr. Suresh for the sample size calculation and statistical analysis report. We would also like to thank the urologists who have been cooperative in our study.

REFERENCES

- Shakya S, Chaturvedi A and Sah BP. Prophylactic low dose ketamine and ondansetron for prevention of shivering during spinal anaesthesia. *J Anaesthesiol Clin Pharmacol*. 2010;26(4):465-469.
- Prasad RB, Joel CJ and Zachariah VK. Effectiveness of addition of intrathecal tramadol with hyperbaric bupivacaine in prevention of shivering in parturients undergoing caesarean section under spinal anaesthesia: A randomized placebo-controlled study. *Karnataka Anaesth J*. 2015;1(3):123-127.
- Hynson JM, Sessler DI, Glosten B and McGuire J. Thermal balance and tremor patterns during epidural anesthesia. *Anesthesiology*. 1991;74(4):680-690. <https://doi.org/10.1097/0000542-199104000-00011>
- Lopez MB. Postanaesthetic shivering-from pathophysiology to prevention. *Rom J Anaesth Intensive Care*. 2018;25(1):73-81. <https://doi.org/10.21454/rjaic.7518.251.xum>
- Sessler DI. Temperature monitoring. In: Millar RD, editor. *Textbook of Anaesthesia*. 5th ed. New York: Churchill Livingstone Inc.; 1994. p. 1367-1389.
- Wason R, Jain N, Gupta P and Gogia AR. Randomized double-blind comparison of prophylactic ketamine, clonidine and tramadol for the control of shivering under neuraxial anaesthesia. *Indian J Anaesth*. 2012;56(4):370-375. <https://doi.org/10.4103/0019-5049.100821>
- Tsai YC, Chang PJ and Jou IM. Direct tramadol application on sciatic nerve inhibits spinal somatosensory evoked potentials in rats. *Anesth Analg*. 2001;92(6):1547-1551. <https://doi.org/10.1097/0000539-200106000-00040>
- Chakraborty S, Chakrabarti J and Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. *Indian J Pharmacol*. 2008;40(4):180-182. <https://doi.org/10.4103/0253-7613.43166>
- Abd El Azeem EM, Abdel-Ghaffar ME and Al-Touny SA. Anti-shivering effect of intrathecal tramadol versus intravenous tramadol in patients received spinal anesthesia for lower limb surgery. A randomized controlled clinical trial. *Egypt J Anaesth*. 2023;39(1):50-55. <https://doi.org/10.1080/11101849.2023.2167300>
- Jou IM, Chu KS, Chen HH, Chang PJ and Tsai YC. The effects of intrathecal tramadol on spinal somatosensory-evoked potentials and motor-evoked responses in rats. *Anesth Analg*. 2003;96(3):783-788. <https://doi.org/10.1213/01.ANE.0000049683.58980.30>
- Bhatnagar S, Saxena A, Kannan TR, Punj J, Panigrahi M and Mishra S. Tramadol for postoperative shivering. A double-blind comparison with pethidine. *Anaesth Intensive Care*. 2001;61(15):2193-2205.
- Breen TW, Shapiro T, Glass B, Foster-Payne D and Oriol NE. Epidural anesthesia for labor in an ambulatory patient. *Anesth Analg*. 1993;77(5):919-924. <https://doi.org/10.1213/0000539-199311000-00008>
- Wrench IJ, Singh P, Dennis AR, Mahajan RP and Crossley AW. The minimum effective doses of pethidine and doxapram in the treatment of post-anaesthetic shivering. *Anaesthesia*. 1997;52(1):32-36. <https://doi.org/10.1111/j.1365-2044.1997.006-az006.x>
- Dakhale GN, Hiware SK, Shinde AT and Mahatme MS. Basic biostatistics for post-graduate students. *Indian J Pharmacol*. 2012;44(4):435-442. <https://doi.org/10.4103/0253-7613.99297>
- Sunder Rao PS and Richard J. *An Introduction to Biostatistics, A Manual for Students in Health Sciences*. 4th ed. New Delhi: Prentice Hall of India; 2006. p. 86-160.
- Elenbaas RM, Elenbaas JK and Cuddy PG. Evaluating the medical literature. Part II: Statistical analysis. *Ann Emerg Med*. 1983;12(10):610-620. [https://doi.org/10.1016/s0196-0644\(83\)80205-4](https://doi.org/10.1016/s0196-0644(83)80205-4)
- Subedi A, Biswas BK, Tripathi M, Bhattarai BK and Pokharel K. Analgesic effects of intrathecal tramadol in patients undergoing caesarean section: A randomised, double-blind study. *Int J*

- Obstet Anesth. 2013;22(4):316-321.
<https://doi.org/10.1016/j.jjoa.2013.05.009>
18. Alhashemi JA and Kaki AM. Effect of intrathecal tramadol administration on postoperative pain after transurethral resection of prostate. *Br J Anaesth.* 2003;91(4):536-540.
<https://doi.org/10.1093/bja/aeg213>
19. Bansal AP, Chakole V, Singam A and Latwal BS. Evaluation of efficacy of intra thecal tramadol for prevention of shivering post spinal anaesthesia in patients undergoing caesarian section. *Biomed Pharmacol J.* 2020;13(3):1305-1310.
<https://doi.org/10.13005/bpj/1999>
20. Gupta P and Gupta M. Intrathecal tramadol for prevention of postanesthesia shivering after subarachnoid block: A prospective randomized placebo-controlled comparison of two different doses (10 and 20 mg). *Anesth Essays Res.* 2018;12(2):495-500.
https://doi.org/10.4103/aer.AER_75_18
21. Badhe VK, Swami NR, Gore SK, Badhe VK and Vinayak SR. Comparative study of efficacy of intrathecal tramadol added to bupivacaine in prevention of intraoperative shivering. *Pravara Med Rev.* 2019;11(2):10.
22. Tewari A, Dhawan I, Mahendru V, Katyal S, Singh A and Garg S. Use of oral tramadol to prevent perianesthetic shivering in patients undergoing transurethral resection of prostate under subarachnoid blockade. *Saudi J Anaesth.* 2014;8(1):11-16.
<https://doi.org/10.4103/1658-354X.125898>

Authors Contribution:

MM- Prepared first draft of manuscript, implementation of study protocol, data analysis, manuscript preparation, editing and submission of article; **JP**-Design of study, statistical analysis and interpretation, literature survey, concept, design, clinical protocol, and manuscript revision; **KP**- Data collection, preparation of Figures; **KGS**- Review manuscript; **RS**- Review manuscript, coordination and manuscript revision.

Work attributed to:

Rajarajeswari Medical College and Hospital, Bengaluru, Karnataka, India.

Orcid ID:

Manasa M - <https://orcid.org/0000-0003-0348-4250>
Jyoti Petkar - <https://orcid.org/0000-0002-4595-6781>
Dokku Kirtana - <https://orcid.org/0009-0003-4189-5322>
Karthik GS - <https://orcid.org/0000-0001-5102-1133>
Rangalakshmi S - <https://orcid.org/0000-0003-0051-4266>

Source of Support: Nil, **Conflicts of Interest:** None declared.