ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 04 | April - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EFFECT OF NALBUPHINE AND TRAMADOL IN POST-SPINAL ANAESTHESIA SHIVERING: A COMPARATIVE STUDY

Anaesthesiology

Manmeet Kour* Department of Anesthesiology and Intensive Care, Government Medical College Jammu, J&K. *Corresponding Author

Hitesha Gurtoo Department of Anesthesiology and Intensive Care, Government Medical College Jammu, J&K.

Ashwani Kumar Department of Anesthesiology and Intensive Care, Government Medical College Jammu, J&K.

ABSTRACT

Background: In Spinal anaesthesia, a consequence of impaired thermoregulatory control, shivering is one of the most frequently reported complications of central neuraxial blockade, affecting 40–70% of patients. Nalbuphine is a mixed opioid agonist–antagonist with high affinity for the opioid receptor that functions as both a competitive opioid antagonist and a partial opioid agonist. Theoretically, nalbuphine could have significant anti-shivering effects on post-anaesthetic shivering. **Methods:** This prospective randomised (computer-generated) double-blinded study was conducted at Department of Anaesthesiology and Intensive Care, Government Medical College Jammu J&K, after obtaining approval from hospital ethical committee. Randomisation was done using a computer-generated number where patients were randomly allocated into two groups: Group-N and Group-T. We confined our investigation to 84 patients divided into two equal groups of 42 people. **Results:** The non-significant difference was observed in age, gender, BMI, ASA physical status, duration of surgery, and duration of spinal anesthesia between the groups. The drug was found to significantly reduce SBP, increase DBP, and increase MAP in the group given the drug compared to the nalbuphine group. The time taken to control shivering was significantly shorter in the group-T. The group-T also had a lower Ramsay Sedation Scale score, indicating less sedation compared to the group-N group. The drug did not cause any adverse effects, while sedation, hypotension, and bradycardia were observed in the group-N. Nausea, vomiting, and dizziness were reported in the group-T, but not in the group-N. There was no significant difference in the effectiveness of shivering control between the two groups. **Conclusion:** Both intravenous nalbuphine 0.05 mg/kg and tramadol 1 mg/kg are effective in managing post-spinal anesthesia shivering. However, tramadol had a shorter time to control shivering than nalbuphine. Both drugs had minimal effects on blood pressure and heart rate, and the side effects observed were minor and treatable.

KEYWORDS

Tramadol, Nalbuphine, Post spinal anaesthesia shivering

INTRODUCTION

Spinal anaesthesia is commonly used for both elective and emergency surgical procedures. As a result of impaired thermoregulatory control, shivering is one of the most frequently reported complications of central neuraxial blockade, occurring in 40–70% of patients undergoing surgery under spinal anaesthesia. Postanaesthetic shuddering is defined as involuntary, rhythmic, oscillating muscle hyperactivity that increases metabolic heat production by up to 600%. [2] During neuraxial anaesthesia, shivering is a frequent occurrence that may have adverse effects, including increased oxygen consumption, carbon dioxide production, lung ventilation, and cardiac activity, as well as decreased mixed venous oxygen saturation. Spinal anaesthesia hinders the thermoregulatory system by inhibiting tonic vasoconstriction, which plays a crucial role in temperature regulation. [3] To control shivering during anaesthesia, both nonpharmacological and pharmacological methods employing drugs with anti-shivering characteristics play a crucial role.

However, equipment-based nonpharmacological methods are effective but costly and impractical. [4] The most common method of treating trembling is still the use of pharmaceuticals. Meperidine, doxa pram, dexamethasone, tramadol, nefopam, ketanserin, clonidine, propofol, physostigmine, magnesium sulphate, and fentanyl have all been used to alleviate postoperative trembling. [5,6,7] As μ-opioid receptor agonist, −1 −1 tramadol hydrochloride has a modulatory effect on central monoaminergic pathways, repressing the neuronal absorption of noradrenaline/ serotonin and stimulating 5HT3 discharge, which resets the body's temperature regulating centre. Nalbuphine is a mixed agonist– antagonist opioid with high affinity for the opioid receptor that functions as both a competitive opioid antagonist and a partial opioid agonist. Theoretically, nalbuphine may have significant anti-trembling effects on post-aesthetic shivering. The aim of this study was to compare the efficacy of and haemodynamic changes related to nalbuphine and tramadol when used for the control of post-spinal anaesthesia shivering, as per Wrench shivering grades.

MATERIALS AND METHOD

This study was conducted among 84 patients of either sex with the American Society of anaesthesiologists (ASA) physical status class I/II who were scheduled to undergo elective surgeries like lower limb surgeries and percutaneous nephrolithotomy under spinal anaesthesia administered by the Department of Anaesthesiology and Intensive Care, Government Medical College Jammu J&K, after obtaining approval from hospital ethical committee. Randomisation was done using a computer-generated number where patients were randomly allocated into two groups: Group N and Group T. We confined our investigation to 84 patients divided into two equal groups of 42 people. Patients of aged between 21 and 60 years of both genders with ASA I and II status who were scheduled for elective surgeries under spinal anaesthesia were included in our study. However, Patients aged less than 20 years and more than 60 years, patients with a history of uncontrolled comorbidities, cardiac, respiratory, renal, or hepatic diseases or those who had a history of allergy to any of the test drugs, patients with contraindications to spinal anaesthesia (coagulation disorder, infection at the puncture site, raised intracranial tension, preexisting neurological deficits in lower extremities or any spine deformity), and patients with initial body temperature >38°C or <36°C were excluded from our study.

On the day before the scheduled surgery, a thorough pre-anaesthetic evaluation was done for all the patients. Patients were explained about the study procedure. All patients were kept nil by mouth for at least six hours prior to surgery. On the day of surgery, in the preoperative room, intravenous access was secured with a 20-gauge cannula, and patients were preloaded with 15-ml/kg Ringer's lactate fluid and maintained on intravenous fluids throughout the surgery. In the operation room, minimum mandatory monitoring was carried out using a multiparameter monitor. Continuous monitoring of heart rate (HR), blood pressure (BP), peripheral oxygen saturation (SpO2), ECG, and axillary temperature monitoring was carried out throughout the procedure.

Under all aseptic precautions, and with patients in the sitting position, spinal anaesthesia was given at L3-L4 intervertebral space using 26-G Quincke Babcock spinal needle; after confirming free and clear flow of cerebrospinal fluid, 0.5% bupivacaine heavy (3/3.5 ml) was given to achieve the desired level according to the surgical procedure. An optimum temperature of around 22-24 °C was maintained in the operation theatres, and patients were covered with drapes but not actively warmed. Intravenous fluids and drugs were administered at room temperature.

After the induction of spinal anaesthesia, patients were observed for any occurrence of shivering until the postoperative period. Shivering

was graded according to the Wrench shivering grade system.

Patients who developed either Grade 3 or 4 shivering were included in the study. Injection tramadol 1 mg/kg or injection nalbuphine 0.05 mg/kg were diluted to a volume of 10 ml in a 10-ml syringe. And the syringe was assigned as coded syringes as per the randomisation list by an anaesthesiologist who was unaware of the group allocation. This was then administered to the patient as a slow intravenous injection over a period of 10 minutes. The attending anaesthesiologist recorded in minutes the time of the onset of shivering after spinal anaesthesia, the time of the administration of the test drug, and the time to the cessation of shivering.

Shivering control was defined as "complete" when the shivering grade declined to 0; "incomplete" when the scores decreased but the shivering did not stop completely; and "failed" if no change in scores were observed. All the parameters were recorded at 0, 1, 5, 10, 15, and 30 minutes. In case there was a recurrence of shivering, patients were treated with an additional dose of intravenous tramadol (0.5 mg/kg) or intravenous nalbuphine (0.025 mg/kg IV), as per the respective groups, and/or active warming measures using convection heaters or infusing moderately warm intravenous fluids. Adverse effects were recorded, treated, and monitored. Sedation was assessed as per the Modified Ramsay Sedation Scale. A sedation score of more than 3 was termed sedation as a side effect.

Statistical Analysis

The data collected were tabulated using Microsoft Excel software and analyzed using SPSS v 26.0 version for Windows (IBM, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to assess sample distributions. The results are presented as the mean± SD and median. Student t-test and chi-square test are used to compare two independent samples and to compare proportions respectively. The P value < 0.05 was considered significant.

RESULTS

The mean age of patients in group-T is 39.16±10.49 and in group-N is 38.62±9.64. Male had predominancy in group-T while female had in group-N. The mean BMI of patients in group-T is 24.97±3.48 and in group-N is 24.61±4.36. The percentage of patients classified as ASA physical status I in Group-T is 57.14%, while in Group-N, it is 70.73%. Regarding other factors, the study found that age, gender, BMI, ASA physical status classification, duration of surgery and duration of spinal anaesthesia were not significant factors in the comparison of the two groups. **[TABLE-1]**

In SBP, there was no significant difference between the two groups at baseline (p=0.0554). However, there were significant differences in SBP between the two groups at 1, 2, 5, and 10 minutes after giving the drug, with the group given the drug having lower mean SBP values than the group not given the drug (p<0.05). At 15 and 30 minutes after giving the drug, there was no significant difference between the two groups. **[TABLE-2; FIGURE-1]** In DBP, there was no significant difference between the two groups at baseline (p=0.9294). However, there were significant differences in DBP between the two groups at 2, and 5 minutes after giving the drug, with the group given the drug having higher mean SBP values than the group not given the drug. At 0,1,10,15 and 30 minutes after giving the drug, there was no significant difference between the two groups. **[TABLE-3; FIGURE-2]** The mean MAP was significantly higher in Group-T compared to Group-N at all time points except for baseline and 0 min after giving drug. The p-values were statistically significant for all time points except for baseline and 0 minutes after giving the drug, indicating that drug caused a significant increase in MAP compared to control group. **[TABLE-4; FIGURE-3]**

Six patients in group-N and 3 patients in group-T exhibited uncontrolled shuddering; 37 patients in group-T and 35 patients in group-N exhibited effective control; and 2 patients and 1 patient in both groups exhibited partial control. However, among the group, a non-significant difference was observed.

Sedation, hypotension, and bradycardia were observed in Group N, with 9.52%, 11.90%, and 4.76% of patients experiencing these side effects, respectively. However, no patient in Group T experienced these adverse effects. On the other hand, nausea, nausea and vomiting, and dizziness were reported in Group T, with 14.29%, 7.14%, and 4.76% of patients experiencing these side effects, respectively. None of the patients in Group N experienced nausea or vomiting. Respiratory depression or itching were not reported in either group. Time taken to control shivering (min): Group-T had a significantly shorter time taken to control shivering (3.64 ± 1.29) compared to Group-N (4.93 ± 1.57) with a significant difference among the groups. **[TABLE-5]** Ramsay Sedation Scale Score: Group-T had a significantly lower mean score (1.39 ± 0.23) compared to Group-N (2.74 ± 0.63) with a statistically significant difference among the groups. **[TABLE-6]**

Table-1: Clinico-demographical Parameters Of The Enrolled Patients Among The Groups.

		GROUP-T [N=42]		GROUP-N [n=42]		P-Value
		N	%	N	%	
AGE(YEARS)		39.16±10.49		38.62±9.64		t=0.2456 p=0.8066
GENDER	Male	25	59.52%	20	47.62%	X=1.197
	Female	17	40.48%	22	52.38%	p=0.2740
BMI (kg/m^2)		24.97±3.48		24.61±4.36		t=0.4182 p=0.6769
ASA	I	24	57.14%	29	70.73%	X=1.660
	II	18	42.86%	12	29.27%	p=0.1976
Duration Of Surgery (min)		90.69±19.98		85.47±11.28		t=1.474 p=0.1442
Duration Of Spinal Anaesthesia (min)		218.62±19.67		232.11±18.35		t=1.564 p=0.1218
The Onset of Shivering (min)		30.45±6.48		29.74±4.32		t=0.5908 p=0.5563

Table-2: Systolic Blood Pressure Of The Enrolled Patients Among The Groups.

SBP (mmHg)	GROUP-T [n=42]		GROUP-N [n=42]		P-VALUE
	MEAN	SD	MEAN	SD	
Baseline	112.67	11.74	117.68	11.89	t=1.943 p=0.0554
0 Min After Giving the Drug	114.65	10.49	112.35	10.47	t=1.006 p=0.3175
1 Min After Giving the Drug	116.07	9.21	111.29	10.06	t=2.271 p=0.0258*
2 Min After Giving the Drug	117.41	9.26	109.67	11.93	t=3.321 p=0.0013*
5 Min After Giving the Drug	116.22	9.02	109.52	11.38	t=2.990 p=0.0037*
10 Min After Giving the Drug	115.39	9.31	109.42	10.56	t=2.748 p=0.0074*
15 Min After Giving the Drug	113.24	9.28	109.58	10.14	t=1.726 p=0.0882*
30 Min After Giving the Drug	112.67	9.52	109.72	10.32	t=1.362 p=0.1770*

Table-3: Diastolic Blood Pressure Of The Enrolled Patients Among The Groups.

DBP (mmHg)	GROUP-T [n=42]		GROUP-N [N=42]		P-VALUE
	MEAN	SD	MEAN	SD	
Baseline	77.46	9.12	77.62	7.29	t=0.08881 p=0.9294
0 Min After Giving the Drug	77.28	9.61	74.05	6.54	t=1.801 p=0.0754
1 Min After Giving the Drug	77.16	9.47	73.68	7.61	t=1.856 p=0.0670
2 Min After Giving the Drug	77.36	9.14	73.12	7.35	t=2.343 p=0.0216*
5 Min After Giving the Drug	78.57	8.31	72.48	7.81	t=3.461 p=0.0009*
10 Min After Giving the Drug	72.76	8.66	72.39	7.24	t=0.2124 p=0.8323
15 Min After Giving the Drug	73.64	9.26	73.32	7.81	t=0.1712 p=0.8645
30 Min After Giving the Drug	73.81	9.58	73.86	6.57	t=0.0279 p=0.9778

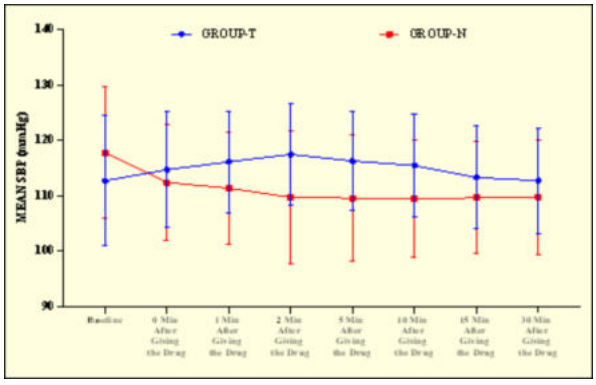

Figure-1: Graphical representation of the Systolic blood pressure of the enrolled patients among the groups.

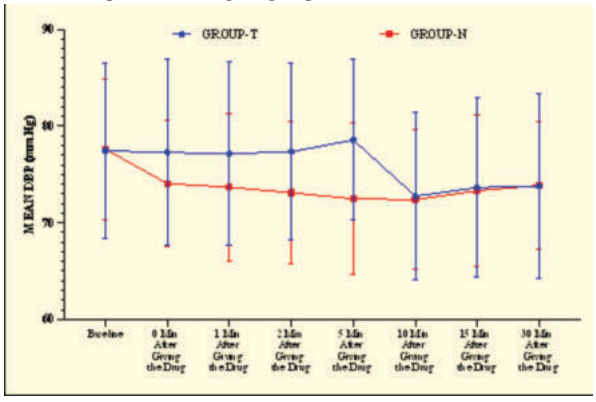

Figure-2: Graphical representation of the Diastolic blood pressure of the enrolled patients among the groups.

Table-4: Mean Arterial Pressure Of The Enrolled Patients Among The Groups.

MAP (mmHg)	GROUP-T [n=42]		GROUP-N [n=42]		P-VALUE
	MEAN	SD	MEAN	SD	
Baseline	89.63	9.14	90.63	8.97	t=0.5061 p=0.6142
0 Min After Giving the Drug	89.26	9.06	87.26	7.39	t=1.109 p=0.2708
1 Min After Giving the Drug	90.18	9.53	86.74	7.28	t=1.859 p=0.0662*
2 Min After Giving the Drug	91.02	9.38	85.68	7.12	t=2.939 p=0.0043*
5 Min After Giving the Drug	91.65	8.96	84.23	7.26	t=4.170 p<0.0001*
10 Min After Giving the Drug	90.28	8.74	84.51	7.34	t=3.276 p=0.0015*
15 Min After Giving the Drug	89.71	9.05	85.77	7.59	t=2.162 p=0.0335*
30 Min After Giving the Drug	88.64	8.59	85.34	7.67	t=1.857 p=0.0669*

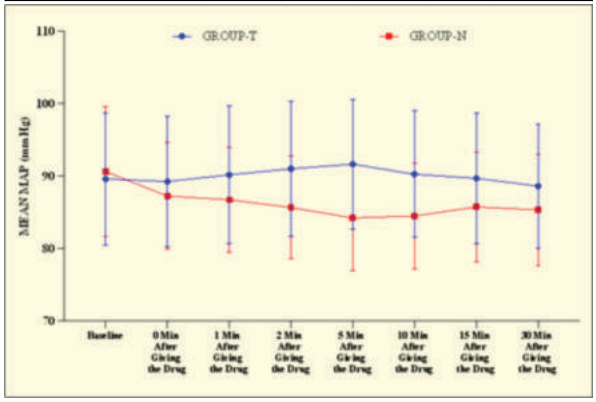

Figure-3: Graphical Representation Of The Mean Arterial Pressure Of The Enrolled Patients Among The Groups.

Table-5: Mean Time Taken To Control Shivering Of The Enrolled Patients Among The Groups

TIME TAKEN TO CONTROL SHIVERING (min)	GROUP-T [n=42]		GROUP-N [n=42]		P-VALUE
	MEAN	SD	MEAN	SD	
	3.64	1.29	4.93	1.57	t=4.114 p<0.0001*

Table-6: Mean Ramsay Sedation Score Of The Enrolled Patients Among The Groups

RAMSAY SEDATION SCORE	GROUP-T [n=42]		GROUP-N [n=42]		P-VALUE
	MEAN	SD	MEAN	SD	
	1.39	0.23	2.74	0.63	t=13.05 p<0.0001*

DISCUSSION

In the present study, there were no statistically significant difference in gender, age, BMI, or ASA grade between Group-N and Group-T (p>0.05). Similarly, **Sonalika Tudimilla et al. [8]** found that the differences between Group-N and Group-T in terms of gender, mean age, BMI, and ASA classification were not statistically significant (p>0.05). In our study, the duration of surgery [90.69±19.98 vs.85.47±11.28], spinal anaesthesia, [218.62±19.67 vs. 232.11±18.35] and the onset of shivering [30.45±6.48 vs. 29.74±4.32] did not differ statistically significant between group-T and group-N. Similarly, In a study conducted by **Sonalika Tudimilla et al.,[8]** the durations of surgery, spinal anaesthesia, and the onset of shivering were recorded and statistically analysed for both study groups. The lack of statistical significance between the groups indicates that nalbuphine and tramadol have no influence on these parameters.

In our study, the wrench shivering grade was also comparable in both groups and difference was statistically significant. Similarly, according to **Sonalika Tudimilla et al.,** [8] the shivering grades were subjected to statistical analysis, which revealed that the difference at various intervals was not statistically significant (p>0.05). In 2011, **Shukla et al. [9]** compared the effects of intravenous clonidine 0.5 mcg/kg (Group-C) and intravenous tramadol 0.5 mg/kg (Group-T) on shivering and found that the severity of shivering grade in Group-T was 2.9±1.2 while it was 3.1±0.7 in Group-C. In a 2020 study comparing tramadol (1 mg/kg) (Group-T) and nalbuphine (0.06 mg/kg) (Group-N) for shivering, a Wrench shivering grade of three was observed in 29 patients and grade four in 16 patients in group T, whereas in group N, grade three was observed in 31 patients and grade four in 14 patients, which was not statistically significant (p>0.05). **[10]** Both nalbuphine and tramadol were found to have anti-shivering properties.

We observed that the mean value of time taken for control of shivering in Group-N was 4.93±1.57 and in Group-T was 3.64±1.29 and the difference was statistically significant between the groups. Similarly in **Sonalika Tudimilla et al.,[8]** the mean value of time taken for control of shivering in the nalbuphine group was 4.692 ± 1.643 minutes and it was 3.633 ± 1.572 minutes in the tramadol group, and this difference was statistically significant (p=0.02). Hence, shivering was controlled significantly earlier in the tramadol group. Reddy et al., in 2011, **[11]** compared tramadol (50 mg) (Group-T) and clonidine (50 mcg) (Group-C) for shivering, and the time taken to control shivering in Group-T was 2.2 ± 0.41 minutes with a response rate of 95.56%, whereas in Group-C, it was 3.17 ± 0.03 minutes with a response rate of 86.67%. They observed that tramadol was more effective than clonidine in controlling shivering. In the above-mentioned study by Nirala et al.,**[12]** the time taken for cessation of shivering in Group-T was 4.84 ± 1.23 minutes, while it was 3.84 ± 1.23 minutes Group-N, which led them to conclude that the time taken to control shivering was significantly lower in Group-N when compared to Group-T. In study conducted by **Sonalika Tudimilla et al.,[8]** lower time was required to control shivering with tramadol than nalbuphine when compared with the mentioned studies. Similarly, in our study the result was same. Our study results are consistent with that of a few studies.

In our study, 6 patients in group-N and 3 patients in group-T exhibited uncontrolled shuddering; 37 patients in group-T and 35 patients in group-N exhibited effective control; and 2 patients and 1 patient in both groups exhibited partial control. However, among the group, a non-significant difference was observed. Similarly, **Sonalika**

Tudimilla et al. [8] observed that shivering was not under control in four patients in Group N and three patients in Group-T; 25 patients (83.3%) had effective control in Group-T whereas 23 patients (76.67%) had effective control in Group-N; three patients (10%) and two patients (6.67%) had partial control in both Groups T and N, respectively. On the basis of the effectiveness of medications in preventing shivering, the difference between the groups was not statistically significant. None of our study groups experienced a recurrence of trembling. In 2019, **Taneja et al. [12]** conducted a study on tramadol (0.25 mg/kg) (Group 2) and nalbuphine (0.28 mg/kg) (Group 1), observing a response rate of 85% in Group 2 and a response rate of 90% in Group 1, along with a recurrence rate of 25% in Group 2 and 20% in Group 2. They came to the conclusion that nalbuphine is marginally more effective than tramadol. Tramadol is more effective than other medications at controlling trembling, which is likely due to the higher dose used in our study compared to another research.

In our study, in mean HR, SBP, DBP, MAP, and oxygen saturation a significant difference was observed at various interval and the haemodynamic parameters were significantly high in patients treated with tramadol as compared to nalbuphine treated patients at some interval. **Sonalika Tudimilla et al., [8]** there was no appreciable change in mean HR, SBP, DBP, MAP, and oxygen saturation. It was noted that there were no significant differences in all these parameters at all intervals of time. However, there was a gradual fall in BP subsequent to the administration of drugs in both groups when compared to the baseline, but this did not reach statistical significance ($p>0.05$).

In our study, Sedation, hypotension, and bradycardia were observed in Group N, with 9.52%, 11.90%, and 4.76% of patients experiencing these side effects, respectively. However, no patient in Group T experienced these adverse effects. On the other hand, nausea, nausea and vomiting, and dizziness were reported in Group T, with 14.29%, 7.14%, and 4.76% of patients experiencing these side effects, respectively. None of the patients in Group N experienced nausea or vomiting. Respiratory depression or itching were not reported in either group. Similarly, to our findings the **Sonalika Tudimilla et al., [8]** observed a different set of side effects was seen in each group. In Group N, out of 30 patients, five (16.67%) patients were sedated, four (13.33%) had hypotension, and two (6.67%) had bradycardia, whereas, in Group T, none of the patients had sedation, hypotension, or bradycardia. In Group T, out of 30 patients, five (16.67%) patients had nausea, four (13.33%) had nausea and vomiting, and two (16.67%) had dizziness following the administration of the drug. In group N, none of the patients experienced nausea or vomiting. Respiratory depression or itching was not seen in either of the group. **Kyokong et al., in 2007, [13]** conducted a study to compare the efficacy of tramadol and nalbuphine and found that only 1.4% of patients had severe nausea in the tramadol group and 4.3% of patients were sedated in the nalbuphine group. However, these side effects were few, minor, and treatable.

CONCLUSION

According to the findings of the research, intravenous nalbuphine at a dose of 0.05 mg/kg and tramadol at a dose of 1 mg/kg are both effective in treating shivering that occurs after spinal anaesthesia. However, the time it took for tramadol to regulate shivering was significantly less than that of nalbuphine. Both medications had only a modest impact on patients' blood pressure and heart rates, and those patients who did experience adverse effects did so in a way that was manageable.

Conflict Of Interest:

The authors have no conflict of interests in this article.

Acknowledgements:

This study was supported by Department of Anesthesiology and Intensive Care, Government Medical College Jammu, J&K

REFERENCES

1. De Witte J, Sessler DI. Perioperative shivering: Physiology and pharmacology. Anesthesiology. 2002; 96:467–84.
2. Giesbrecht GG, Sessler DI, Mekjavić IB, Schroeder M, Bristow GK. Treatment of mild immersion hypothermia by direct body-to-body contact. J Appl Physiol (1985) 1994;76:2373–9.
3. Glosten B, Sessler DI, Faure EA, Karl L, Thisted RA. Central temperature changes are poorly perceived during epidural anesthesia. Anesthesiology. 1992; 77:10–6.
4. Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. Indian J Anaesth. 2011;55:242–6.
5. Rosa G, Pinto G, Orsi P, de Blasi RA, Conti G, Sanitá R, et al. Control of post anaesthetic shivering with nefopam hydrochloride in mildly hypothermic patients after neurosurgery. Acta Anaesthesiol Scand. 1995;39:90–5.
6. Yared JP, Starr NJ, Hoffmann-Hogg L, Bashour CA, Insler SR, O'Connor M, et al. Dexamethasone decreases the incidence of shivering after cardiac surgery: A randomized, double-blind, placebo-controlled study. Anesth Analg. 1998;87:795–9.
7. Pauca AL, Savage RT, Simpson S, Roy RC. Effect of pethidine, fentanyl and morphine on post-operative shivering in man. Acta Anaesthesiol Scand. 1984;28:138–43
8. Tudimilla S, Suryawanshi C, SaravanKumar K (December 17, 2021) A Comparative Evaluation of Nalbuphine and Tramadol for the Control of Post- Spinal Anaesthesia Shivering. Cureus 13(12): e20481.
9. Shukla U, Malhotra K, Prabhakar T: A comparative study of the effect of clonidine and tramadol on postspinal anaesthesia shivering. Indian J Anaesth. 2011, 55:242-6.
10. Nirala DK, Prakash J, Ram B, Kumar V, Bhattacharya PK, Priye S: Randomized double-blinded comparative study of intravenous nalbuphine and tramadol for the treatment of postspinal anesthesia shivering. Anesth Essays Res. 2021, 14:510-4.
11. Reddy VS, Chiruvella S: Clonidine versus tramadol for post spinal shivering during caesarean section: a randomized double blind clinical study. J Obstet Anesth Crit Care. 2011, 1:26-9.
12. Taneja P, Bansal Y, Sharma N, Banotra KK: A randomized control trial for comparison among Nalbuphine, Tramadol and placebo for treating post anesthetic shivering undergoing spinal anesthesia in Cesarian section. J Pharm Sci Rev Res. 2019, 11:2095-8.
13. Kyokong O, Tamdee D, Charuluxananan S: Comparison of the efficacy of nalbuphine, tramadol, ondansetron and placebo in the treatment of postanesthetic shivering after spinal anesthesia for caesarean delivery. Asian Biomed. 2007, 1:189-94.