Original Article

Efficacy of Intravenous Nalbuphine for Managing Post-Anesthesia Shivering

Amjid Ali, Jawad Hameed, Abid Haleem Khattak, Muhammad Sheharyar Ashraf, Haseeba Naeem and Ahmad Ali

ABSTRACT

Objective: To investigate the efficacy of intravenous nalbuphine in managing post anesthesia shivering.
Study Design: Cross sectional
Place and Duration of Study: This study was conducted at the Anesthesia department of Lady Reading Hospital, Peshawar from January 2022 to December 2022.
Methods: A total of 60 patients who were planned for surgery under anesthesia were enrolled. Patients were divided into two groups. Group Nalbuphine: Patients in this group received nalbuphine at a dose of 0.08 mg/kg, administered via the intravenous (IV) route. The nalbuphine was mixed with 5 mL of saline. Group placebo: This is the control group, where patients received only saline (5 mL) via the IV route.
Results: After 5 minutes of treatment, nalbuphine was effective more than placebo, 70.0% and 10.0%, respectively. ($p<0.001$). After 15 minutes of treatment, nalbuphine was more effective than placebo, 70.0% and 6.7%, respectively. ($p<0.001$). Similarly, after 30 minutes of treatment, nalbuphine was most effective than placebo 80.0% and 20.0%, respectively. ($p<0.001$).
Conclusion: The intravenous administration of nalbuphine, a kappa-receptor agonist provides potent antishivering effect on the peripheral nervous system. Nalbuphine can be used in post anesthesia shivering in different surgeries.

Key Words: Anesthesia, Efficacy, Nalbuphine, Placebo, Shivering

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INTRODUCTION

Post-anesthesia shivering (PAS) refers to the involuntary shaking or shivering that occurs in some patients after they undergo anesthesia[1]. This phenomenon is common and can occur during the recovery period in the post-anesthetic care unit (PACU) or in the operating room[2]. Several factors contribute to post-anesthesia shivering, including temperature regulation disruption, peripheral vasodilation, loss of heat from surgical exposure, drug induced and longer duration of surgery[3].

Research studies have reported varying incidence rates of post-anesthesia shivering. Generally, it is estimated that the overall incidence ranges from 20% to 70%, with some studies suggesting rates as high as 80% in certain patient populations[4].

Department of Anesthesia, Lady Reading Hospital, Peshawar.

Correspondence: Dr. Jawad Hameed, Assistant Professor of Anesthesia, Lady Reading Hospital, Peshawar.
Contact No: 0333 9202031
Email: drjawadhameed@gmail.com

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The variability in reported incidence can be attributed to differences in study populations, anesthesia techniques, and definitions of shivering. Severe or prolonged shivering can lead to various complications[5]. Some potential complications associated with post-anesthesia shivering include increase oxygen consumption, cardiovascular stress, pain and discomfort, delayed recovery, compromised wound healing, fluid imbalance and patient's anxiety[6].

Management of post-anesthesia shivering typically involves addressing its underlying causes and providing interventions to increase the patient's core temperature[7]. This may include warming blankets, warm intravenous fluids, and adjusting the ambient temperature in the recovery room. Medications such as meperidine, clonidine, and nefopam may also be used to control shivering[8]. Among these medications nalbuphine is a mixed agonist-antagonist opioid that exhibits both agonist and antagonist activity at opioid receptors[9]. It has a high affinity for the kappa-opioid receptors and a lower affinity for the mu-opioid receptors. Theoretically, its kappa-opioid receptor agonism could contribute to certain effects, including potential anti-shivering effects[10].

The findings of this study may inform clinical practice by providing evidence-based recommendations for the incorporation of intravenous nalbuphine into post-operative care protocols.

METHODS

Study was conducted at Anesthesia department of Lady reading hospital, Peshawar from January 2022 to December 2022 after approval from hospital ethical board. Informed written consent was taken from all patients after detailed description of study to all patients. Patients at low risk, ASA status I and II, age 20-45 years, planned surgery under general anesthesia and who developed shivering within 10 minutes after shifting to recovery room were included. Patients with neuromuscular disorder, cardiopulmonary illness, contraindication of nalbuphine and hyperthyroidism were excluded from the study. A scale used to grade postoperative shivering (PS), grading system validated by Crossley and Mahajan. The scale ranges from 0 to 4, with each grade describing different levels of shivering severity based on observed muscular activity. No shiering was graded as "0", no visible shivering but vasoconstriction and piloerection was graded as "1", if only one muscle group involved in muscular activity it was graded as "2". Not generalized shivering but more than one muscle group were involved means "3" grade shivering and whole body shivering graded as "4". The study focused on patients who experienced grade 3 or 4 shivering for at least 3 minutes in the recovery room. This indicates a specific threshold for shivering severity and duration that was used to select participants for further investigation or analysis in the study. Recovery room temperature was Maintained at 21±23°C: This indicates that the recovery room is kept at a temperature between 21 degrees Celsius, with a possible variation of ±23 degrees Celsius and humidity of approximately 55%±65%.

Heat reflective blankets were used for to cover patients, this is likely done to help maintain the patient's body temperature and prevent heat loss after surgery. Patients receive oxygen at a rate of 5 liters per minute via a Hudson face mask. This is a common practice to ensure patients receive adequate oxygenation during the recovery period. Random numbering tables were used for allocation of patients in groups. This is a common method to ensure that the assignment of patients to different treatment groups is unbiased.

Group Nalbuphine: Patients in this group received nalbuphine at a dose of 0.08 mg/kg, administered via the intravenous (IV) route. The nalbuphine was mixed with 5 mL of saline. Group placebo: This is the control group, where patients received only saline (5 mL) via the IV route. This group is often included to compare the effects of the active treatments against a placebo or no-treatment condition.

Response of shivering treatment drugs was assessed at specific time points: 0, 5, 15, and 30 minutes after treatments. Shivering response was categorized as follows: Not change in shivering status labelled as Null, decrease in shivering labelled as improvement and stop of shivering labelled as successful treatment.

Body temperature (tympanic temperature) was assessed upon entry into the study using an ear thermometer (Insta-Temp 9000; WelchAllyn, San Diego, CA). Throughout a 30-minute observation period, vital signs, including respiratory rate, heart rate and blood pressure were regularly monitored at 5-minute intervals. Additionally, arterial oxygen saturation was continuously monitored using pulse oximetry.

A study population comprising 30 patients in each group was determined to yield 90% statistical power at a significance level of 0.05 (two-tailed) for detecting a 25% difference in success rates compared to the saline group in response to nalbuphine treatment for PS (presumably referring to a medical condition).

RESULTS

Sixty patients were included in this study, both genders. Half of the patients treated by nalbuphine and half of the patients treated by placebo. The distribution of age, sex, weight, duration of surgery, tympanic temperature and shivering grade were almost equal, and differences were statistically insignificant, ($p>0.050$). (Table. I).

After 5 minutes of treatment, nalbuphine was effective more than placebo, 21 (70.0%) and 3 (10.0%), respectively. ($p<0.001$). After 15 minutes of treatment, nalbuphine was more effective than placebo, 21 (70.0%) and 2 (6.7%), respectively. ($p<0.001$). Similarly, after 30 minutes of treatment, nalbuphine was most effective than placebo 24 (80.0%) and 6 (20.0%), respectively. ($p<0.001$). (Table. 2).

Nalbuphine had a strong effect to produce anti-shivering than the placebo. After 5 minutes of treatment, arterial blood pressure and heart rate were lower for nalbuphine than the placebo, ($p<0.001$). After 15 minutes of treatment, arterial blood pressure and heart rate were lower for nalbuphine than the placebo, ($p<0.001$). After 30 minutes of treatment, arterial blood pressure was lower for nalbuphine than the placebo, ($p<0.001$). (Table. 3).

Table. No. 1: Demographic and baseline characteristics of the study groups

Characteristic	Nalbuphine 30 (50.0%)	Placebo 30 (50.0%)	p-value
Age (years)	37.16±3.35	36.13±3.74	0.263
Sex			
Male	19 (63.3)	15 (50.0)	0.297
Female	11 (36.7)	15 (50.0)	
Weight (kg)	65.74±4.55	65.81±3.98	0.952
Duration of surgery (min)	100.0±9.79	101.01±11.46	0.962
Tympanic temperature (°C)	35.14±1.5	36.60±0.94	0.073
Shivering grade			
3	20 (66.7)	18 (60.0)	0.592
4	10 (33.3)	12 (40.0)	

Table No. 2: Post anesthetic shivering response after treatment of the study groups

Response	Nalbuphine 30 (50.0%)	Placebo 30 (50.0%)	p-value
5 minutes			
Null effect	5 (16.7)	22 (73.3)	<0.001
Improvement	4 (13.3)	5 (16.7)	
Success	21 (70.0)	3 (10.0)	
15 minutes			
Null effect	3 (10.0)	23 (76.6)	<0.001
Improvement	6 (20.0)	5 (16.7)	
Success	21 (70.0)	2 (6.7)	
30 minutes			
Null effect	1 (3.3)	12 (40.0)	<0.001
Improvement	5 (16.7)	12 (40.0)	
Success	24 (80.0)	6 (20.0)	

Table. No. 3:Vital signs at different time interval of the study groups

Vital sign	Nalbuphine 30 (50.0%)	Placebo 30 (50.0%)	p-value
5 minutes			
Arterial blood pressure (mm Hg)	132.54±5.76	138.33±5.08	<0.001
Heart rate (bpm)	105.31±2.85	111.06±2.16	<0.001
Respiratory rate (breath/min)	20.13±0.93	20.54±1.19	0.155
Oxygen saturation	96.14±2.52	95.81±2.12	0.582
15 minutes			
Arterial blood pressure (mm Hg)	130.60±4.39	135.06±4.81	<0.001
Heart rate (bpm)	99.86±1.11	93.03±2.26	<0.001
Respiratory rate (breath/min)	15.10±1.82	15.04±1.48	0.938
Oxygen saturation	98.01±1.25	97.86±1.33	0.692
30 minutes			
Arterial blood pressure (mm Hg)	125.66±3.79	134.50±2.01	<0.001
Heart rate (bpm)	90.01±1.05	92.04±1.03	0.902
Respiratory rate (breath/min)	14.36±1.38	13.93±1.34	0.221
Oxygen saturation	98.04±2.11	98.02±1.98	0.900

DISCUSSION

Positive pressure ventilation leads to heightened oxygen consumption and elevated carbon dioxide production. Additionally, it results in an augmented intracranial pressure, disrupts electrocardiographic monitoring, and induces a general sense of discomfort, often accompanied by a perception of coldness[11,12].

After 30 minutes of treatment, nalbuphine was most effective than placebo 80.0% and 6 20.0%, respectively. ($p<0.001$). In a study Megalla et al[13] observed a mean response time for shivering control in the nalbuphine group to be 3.56±0.82 minutes, with a success rate of 92% and a relapse rate of 8.7% in patients after spinal anesthesia. Taneja P et al[14] administered nalbuphine at a dose of 0.3 mg/kg for managing shivering following spinal anesthesia in cesarean sections, achieving a 90% response rate to shivering with a 20% recurrence of shivering observed in patients. In our study we used nalbuphine dose 0.08 mg/kg.

Another study by Nirala et al[15] reported that nalbuphine resulted in a significantly shorter time for the cessation of shivering compared to tramadol ($P < 0.05$). This suggests that nalbuphine may be more effective in stopping shivering in a quicker time frame. A study conducted by Sun et al[16] regarding the use of nalbuphine for the treatment of shivering. According to this study the mean time to cessation of shivering with 0.07 mg.kg−1 nalbuphine was 3.5 ± 2.7 with use of 0.06 mg.kg−1.

In another study, found that the administration of 10 mg nalbuphine effectively reduced postoperative shivering, demonstrating a comparable and prompt efficacy to meperidine. The suppression of shivering was achieved within an average time of 4.6 ± 4.1 minutes following the injection of nalbuphine. Author demonstrated that nalbuphine exhibited a swift and efficient antishivering effect on postanesthetic shivering, achieving high response rates of 80% and 90% at 5 minutes and 30 minutes after treatment, respectively.

A study was conducted by Tudimilla et al[17] in 2021 and reported both intravenous nalbuphine (at a dose of 0.05 mg/kg) and intravenous tramadol (at a dose of 1 mg/kg) are effective in treating shivering that occurs after spinal anesthesia. Tramadol is reported to have a quicker onset of action in controlling shivering compared to nalbuphine. Our findings are also in agreement with Eskandr et al[18], who observed that intrathecal nalbuphine demonstrated effective and safe prevention of shivering in patients undergoing knee arthroscopy during spinal anesthesia.

CONCLUSION

The intravenous administration of nalbuphine, a kappa-receptor agonist provides potent antishivering effect on the peripheral nervous system. Nalbuphine can be used in post anesthesia shivering in different surgeries.

Author's Contribution:

Concept & Design of Study:	Amjid Ali
Drafting:	Jawad Hameed, Abid Haleem Khattak
Data Analysis:	Muhammad Sheharyar Ashraf, Haseeba Naeem, Ahmad Ali
Revisiting Critically:	Amjid Ali, Jawad Hameed
Final Approval of version:	Amjid Ali

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