ORIGINAL ARTICLE

NALBUPHINE AND TRAMADOL IN THE TREATMENT OF POST SPINAL ANAESTHESIA SHIVERING: A RANDOMIZED CONTROL STUDY

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Background: Post-spinal anaesthesia shivering is a frequent problem which can lead to certain hazardous complications like lactic acidosis and hypoxemia. Tramadol and nalbuphine are commonly used for the treatment of post-spinal shivering, and are readily obtainable. The aim of this study was to determine and compare the effectiveness of these two drugs in the treatment of post-spinal anaesthesia shivering. **Methods:** This randomized controlled study was conducted in Ayub Teaching Hospital, Abbottabad from July 2018 to March 2019. It was conducted on 156 patients who developed post-shivering after caesarean section. These patients were randomly divided into two equal groups. Group 1 patients were given tramadol while Group 2 patients were given nalbuphine, both in a dose of 0.5 mg/Kg. First baseline shivering score of both groups of patients was noted down and then reassessed after 15 minutes of drug administration. Data was analysed on SPSS-16 using Chi-square test, and $p \leq 0.05$ was considered statistically significant. **Results:** Tramadol was found effective in 58 (74.4%) and not effective in 20 (25.6%) patients of Group-1. Nalbuphine was found effective in 63 (80.8%) patients and not effective in 15 (19.2%) of Group-2. The differences between the two groups were found to be statistically non-significant. **Conclusion:** Tramadol and nalbuphine were found equally effective in the treatment of shivering after spinal anaesthesia.

Keywords: shivering; nalbuphine; tramadol; spinal anaesthesia; effectiveness

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INTRODUCTION

Healthy humans have a core body temperature ranging between 36.5 °C and 37.5 °C. In regulation of the body temperature, inputs from the thermo-receptors reach the hypothalamus where comparison of these details is done with a predetermined point. When the core temperature exceeds this set point adjustments are made to lower the temperature of body and *vice versa*.[1] Anaesthesia, either general or local, can affect this process and lead to different degrees of hypothermia both during and after the surgery. There is a 0.5 °C reduction in this threshold above the level of block when regional anaesthesia is used which results in vasoconstriction and shivering.[2] In spinal anaesthesia the local anaesthetic agents, mostly bupivacaine, is introduced into the subarachnoid space by penetrating the lower back area of the patient.[3,4] Out of the many reported complications, shivering occurs commonly in about 40–70% of patients who are operated under regional anaesthesia.[5,6] Shivering is defined as 'readily detectable tremors of face, jaw, head, trunk and extremities lasting longer than 15 seconds'.[7]

Post spinal shivering may further deteriorate the patient's condition after surgery like post-op pain may aggravate due to incision stretching. It can lead to rise in intracranial and intraocular pressure. The oxygen demand of the body tissues also increases by 500% in addition to raised cardiac output and amount of air breathed per minute for the maintenance of aerobic metabolism. Further deleterious effects can result in patients who already have a low cardiac reserve or who have an impaired breathing. Shivering causes difficulty in monitoring of the patients due to artefacts in pulse oximetry, ECG, and blood pressure.[8]

The true process how shivering develops after regional anaesthesia is still not clearly known. The cause may be temporary improper functioning and temperature regulation by hypothalamus leading to hypothermia. Other mechanisms like un-inhibited spinal reflexes, pain after the surgery, reduced activity of the sympathetic system, pyrogens release, respiratory alkalosis, and adrenal suppression may be involved.[9] Due to this, proper and vigorous treatment of shivering during the operation is necessary to decrease the problems in the patients.[10]

Many interventions are available for the treatment of post-anaesthesia shivering. It can be treated by raising the room temperature. Body can be kept warm and heat loss can be prevented by using warming blankets and humidifiers. Intravenous fluid can also be warmed before infusion. To treat shivering after anaesthesia, different drugs have been used like morphine, tramadol, ketamine, fentanyl, pethidine, nalbuphine, and meperidine.[11]

Tramadol is a pain killer which is a μ-opioid agonist and acts centrally. It is quite effective in management of post spinal shivering including its prevention. It has the advantage of having lesser adverse effects as compared to other such drugs.[12] Tramadol is

used commonly for pain relief before and after surgery. In addition to this, it is also efficient in management of shivering after surgical operation. The success rate of this drug in case of management of shivering ranges from 53.3% to 55%.[13] Tramadol increases the release of hydroxyl tryptophan which is an important contributor in regulation of temperature at hypothalamus level. It is interesting to note that nalaxone principally reverses action of tramadol on shivering while partly on temperature regulation.[14]

Nalbuphine is a well-known analgesic agent. It is a semisynthetic opioid with both agonistic and antagonistic actions. Similar to meperidine, nalbuphine binds strongly to K-opioid receptors.[15] This agonistic action of nalbuphine might probably be responsible for its role in the treatment of shivering; however, the exact mechanism is not clear. Another mechanism for anti-shivering property of nalbuphine may be that it reduces the threshold for vasoconstriction and shivering.[16] Its antagonistic action resembles nalaxone as it is a μ-opioid receptor (MOR) antagonist which reverses the effects of opioid agents.[17]

The success rate in the treatment of post spinal shivering was found to be 81% for nalbuphine and 88% for tramadol in a study.[18] On the other hand, the efficacy in the management of shivering after anaesthesia was found to be 79% for tramadol and 74% for nalbuphine in a systematic review.[19]

Post spinal shivering is a frequently occurring phenomenon and tramadol and nalbuphine are used commonly for its treatment. No data about the effectiveness of both tramadol and nalbuphine is available at our local level. The aim of our study was to determine the effectiveness of these two drugs and compare it when used for the treatment of shivering developed after regional anaesthesia.

MATERIAL AND METHODS

This randomized control trial (RCT) was carried out at Anaesthesia Department of Ayub Teaching Hospital, Abbottabad from July 2018 to March 2019 after approval of ethical review committee. The sample size was calculated by using WHO software for sample size calculation. A total of 156 patients, 78 patients in each group were included using 55%[13] efficacy of tramadol and 74%[18] efficacy of nalbuphine in the control of post spinal anaesthesia shivering. After fully informed consent from the patients, all the ASA II women between 20–40 years of age who were undergoing elective caesarean section under spinal anaesthesia and developed shivering after the surgery were selected in the study using consecutive sampling technique while the women undergoing elective caesarean section under general anaesthesia or those who declined to participate, patients with zero grade shivering or not meeting the inclusion criteria were excluded.

All women who met the inclusion criteria were chosen from Obstetrics and Out-patient Department. Complete assessment of all patients for spinal anaesthesia was done prior to surgery. For random allocation of the patients who experienced shivering after spinal anaesthesia into two groups, lottery method was used. Group-1 patients were given intravenous tramadol while group-2 patients were given nalbuphine for control of shivering. Both drugs were introduced slowly over 5 minutes in a dose of 0.5 mg/Kg.[20] To prevent shivering from other causes, intravenous fluids were warmed before injecting; blankets were used to cover the patients and Operation Theatre (OT) temperature was controlled at 24–26 °C according to weather conditions. Blood loss was monitored and the patient was kept calm during the surgery. To determine the effectiveness of the drugs, all the patients of both groups were reassessed after 15 minutes of giving intravenous tramadol and nalbuphine.

Shivering was graded by using a scale similar to that validated by Tsai and Chu[21] where:

0= No shivering,

1= Piloerection or peripheral vasoconstriction but no visible shivering.

2= Muscular activity in only one muscle group.

3= Muscular activity in more than one muscle group but not generalized.

4= Shivering all over the body.

All information was recorded on pro forma. Efficacy of the medicines was determined by improvement in the grades of shivering as mentioned above. Data was entered on and analysed using SPSS-16. For comparison of effectiveness of the two drugs, Chi-square test was employed and $p \leq 0.05$ was considered significant. To see the effect modifications, age stratification of efficacy was done in both groups.

RESULTS

In this study, total 156 patients participated with 78 patients in each group. Group-1 was given tramadol while Group-2 was given nalbuphine.

The mean age of Group-1 patients were 26.84±6.03 years ranging between 20–38 years while the mean age of the patients in Group-2 was 25.88±5.93 years ranging between 20–37 years. Mean weight of Group-1 patients was 80.19±4.14 Kg while mean weight of the patients in Group-2 was 79.20±3.83 Kg. Frequencies and percentages of age stratification of both groups are shown in Table-1.

Tramadol was found to be effective among 58 (74.4%) patients in Group-1 while nalbuphine was found to be effective in 63 (80.8%) patients of Group-2. However the difference between the two groups was not found to be statistically significant ($p>0.05$). Frequencies and percentages of shivering grades in both groups with *p*-value are also shown in the Table-2.

Table-1: Age and weight distribution [n (%)]

Age groups	Group-1	Group-2
20–25	36 (46.2)	41 (52.6)
26–30	24 (30.8)	22 (28.2)
31–35	15 (19.2)	13 (16.7)
36–40	3 (3.8)	2 (2.5)
Age (Year) (Mean±SD)	26.84±6.03	25.8±5.93
Age Range	20–38	20–37
Weight (Kg) (Mean±SD)	80.19±4.14	79.20±3.83
Weight Range	70–90	70–87

Table-2: Distribution of patients by effectiveness and grades of shivering [n (%)]

	Group-1	Group-2	*p*
Effective	58 (74.4)	63 (80.8)	0.337
Not effective	20 (25.6)	15 (19.2)	
Shivering grade 1	0 (0)	0 (0)	0.692
Shivering grade 2	6 (42.9)	8 (57.1)	
Shivering grade 3	24 (47.1)	27 (52.9)	
Shivering grade 4	48 (52.7)	43 (47.3)	

DISCUSSION

The process through which shivering develops when surgeries are performed under spinal anaesthesia is complex. The factors that may possibly contribute include peripheral vasodilatation with a resultant increase in blood flow to the skin and more loss of heat due to sympathetic blockade; the rapid intravenous fluids infusions at lower temperature; action of cold agents used for anaesthesia directly on our temperature control centre located in the spinal cord.[7]

This RCT was conducted for determining the difference in the effectiveness of two drugs (tramadol and nalbuphine) used for spinal anaesthesia in attempt to standardize the protocols in the treatment of post spinal shivering. In this study, no statistically significant difference was observed between the effectiveness of tramadol and nalbuphine in treatment of shivering although the effectiveness of nalbuphine was found to be higher 63 (80.8%) in contrast to tramadol 58 (74.4%) given patients. Similar results were obtained in a study carried out by Kyokong *et al* which also showed insignificant difference between tramadol and nalbuphine in the post spinal shivering control. Out of the total 290 patients, tramadol stopped shivering in 88.7% cases and nalbuphine in 81.4% cases but this study also showed both of these drugs to be better than placebo. The results are similar however in our study frequency of effectiveness of nalbuphine was more in contrast to tramadol. The research of Kyokong *et al* also studied the difference in symptoms recurrence and found it to be insignificant. It was found to be 14.3% with tramadol while 15.8% with nalbuphine.[18] However, both tramadol and nalbuphine have few side effects like tramadol can cause more nausea and vomiting while nalbuphine has a mild sedating effect.[22]

Another study which was a systemic review on comparison of effectiveness of tramadol and nalbuphine also strengthens our study results because of observation of non-significant difference between the two drugs with almost similar outcome, i.e., 79% in tramadol and 74% in nalbuphine.[19] Although some studies show lesser effectiveness of tramadol, i.e., 53.3% in contrast to our and other studies like research by Mohta *et al*.[13]

In this research, we used a simple scale for grading of shivering similar to as validated by Tsai and Chu.[21] This can be easily used by health professionals on bed side. However similar grading scales for shivering are also present for use like those used by Kyokong *et al*.[18]

There are some limitations of our study like it was conducted in only one hospital on a limited population. Randomization was done in this study, however, it could have been better if it was a double blind study. The expertise of the anaesthetist was not taken into account which might have affected the results in the assessment of shivering due to causes other than the spinal anaesthesia.

CONCLUSION

Effectiveness of both tramadol and nalbuphine is similar in the control of post-spinal anaesthesia shivering with no statistically significant difference. Studies at multiple centres with large sample size will determine better option between these two regional anaesthetic agents.

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