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A Comparative Study on the Management of Shivering During Spinal Anesthesia Using Clonidine, Butorphanol, and Tramadol

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ABSTRACT

Background: Shivering is a biological reaction that occurs in response to a decrease in core body temperature, known as hypothermia, with the purpose of enhancing the production of metabolic heat. The occurrence of shivering during anesthesia can be attributed to the prolonged impairment of thermoregulatory autonomic function, as well as the combination of cool temperatures in the operating room and the administration of cold infusion fluids.
Methods: This prospective study included 180 individuals who shivered under spinal anaesthesia during abdominal or orthopaedic surgery. On shivering, patients received a 1 mL intravenous bolus dose of 50 mg tramadol, 1 mg butorphanol, or 150 mcg clonidine. All 3 groups were compared for shivering control, time to cessation, recurrence, hemodynamic changes, axillary temperatures, and side effects. Data was processed using statistical methods.
Results: The efficacy of butorphanol and tramadol in reducing shivering surpasses that of clonidine. The administration of butorphanol, tramadol, and clonidine resulted in a significant reduction in rigours among 83%, 73%, and 53% of the patients, respectively. The administration of clonidine resulted in a longer duration of action (3.3±0.9 minutes) compared to both butorphanol and tramadol (2.1±1.0 minutes and 1.8±0.5 minutes, respectively; $p<0.001$).
Conclusion: The administration of butorphanol demonstrated superior efficacy in managing shivering, exhibiting a reduced frequency of recurrences compared to tramadol. However, both butorphanol and tramadol exhibited superior efficacy in comparison to clonidine, with the added benefit of an early onset of action. Both opioids are more effective than α-2 agonists in reducing rigors.

Keywords: ***Perioperative Shivering, Spinal Anesthesia, Tramadol, Clonidine, Butorphanol, Thermoregulatory Center***

Introduction

Shivering is a frequently encountered adverse perioperative outcome associated with neuraxial anesthesia. The occurrence of this phenomenon has been documented in a range of 40-70% of patients who have undergone regional anesthesia. Shivering is a physiological compensatory reaction that occurs in response to core hypothermia. This reaction is triggered by the redistribution of heat, which is caused by vasodilation resulting from chemical sympathectomy of spinal anesthesia, exposure to a cool environment, infusion of unwarmed fluids, and evaporation from exposed surfaces [1]. During the administration of neuraxial anesthesia, there is a redistribution of core heat from the trunk (below the level of sympathectomy) to the periphery. Additionally, the thermoregulatory system experiences significant impairment as a result of the inhibited tonic vasoconstriction [2]. Additionally, it has been observed that neuraxial anesthesia leads to a decrease in the shivering threshold by approximately 0.5°C [3]. One additional factor that contributes to the exposure of thermosensitive structures within the spinal cord is the application of a cold local anesthetic [4].Post-spinal shivering manifests with varying degrees of severity, ranging from mild skin eruption to severe generalized skeletal muscle contraction. The severe form of shivering can significantly impact oxygen saturation, pulse rate, blood pressure, and electrocardiographic monitoring [3].

Shivering has been observed to have an impact on various physiological processes, including an increase in metabolic rate, oxygen consumption, and carbon dioxide production. This effect is particularly concerning in individuals with compromised cardiac and/or respiratory reserves, as it can lead to lactic acidosis, a potentially hazardous condition. Additionally, it has been observed that the administration of this substance results in elevated intraocular and intracranial pressures, as well as hypertension, tachycardia, patient discomfort, heightened wound pain, prolonged wound healing, and delayed discharge from the post-anaesthetic care unit (PACU) [1, 5]. Therefore, the necessity for primary prevention and timely control is justified. To prevent shivering, it has been suggested that nonpharmacological interventions, including the maintenance of perioperative normothermia, infusion of warm fluids, and the use of warm covers and sheets, should be implemented [1]. Pharmacological substances such as clonidine (an α2 agonist) and tramadol (a μ-opioid agonist) exhibit properties that can reduce shivering [6]. Moreover, it has been documented that pregabalin demonstrates anti-shivering properties [7]. The occurrence of pain and stress during the perioperative period has the potential to induce non-thermoregulatory shivering and elevate the thermoregulatory set-point [8]. In light of the

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utilization of spinal anesthesia, the implementation of continuous uterine irrigation with fluids during hysteroscopic procedures, and the increased occurrence of shivering in young females, coupled with the recognized analgesic and anxiolytic attributes of tramadol, clonidine, and pregabalin, our objective was to assess and contrast the effectiveness and safety of these medications as a preventive measure against post-spinal shivering [9].

Material and Methods-

Following the acquisition of written informed consent from participants, we conducted an observational study encompassing individuals of both genders aged between 18 and 65 years. The research included individuals with American Society of Anesthesiologists physical status I–III who experienced intraoperative or postoperative shivering within a maximum time frame of 2 hours. Exclusion criteria encompassed hypo or hyperthyroidism, morbid obesity, fever, and cardiopulmonary impairment. In this study, Group A was administered a dosage of 50 mg (1 mL) of tramadol, Group B received a dosage of 1 mg of butorphanol, and Group C received a dosage of 150 mcg (1 mL) of clonidine. Standard monitors were present in all operating rooms, and baseline values were recorded. The temperature in the surgery room and recovery room was maintained within the range of 22°C–28°C. The administration of spinal anesthesia involved the use of a 25- or 26-gauge Quincke spinal needle. The procedure was performed with the patient in a sitting position, targeting the L3-4/4-5 interspace using a midline approach. A 0.5% heavy solution was utilized, with a dosage ranging from 3.2 to 3.5 mL, in order to achieve a satisfactory level of anesthesia at the T8-10 dermatome. The patients were subjected to continuous monitoring for the occurrence of shivering following the administration of spinal anesthesia, extending throughout the postoperative period. The numerical scale used to assess the severity of shivering is as follows: 0 indicates the absence of shivering, 1 indicates mild shivering limited to the face and head, 2 indicates moderate shivering characterized by tremors affecting multiple muscle groups, and 3 indicates severe shivering involving extensive muscular activity throughout the entire body, resulting in bed shaking. Treatment was administered exclusively to patients exhibiting perioperative shivering of grade 2 or 3 severity. In the second or third grade of the study, all participants experienced shivering and were administered 6 liters per minute of oxygen through a face mask, along with 1 milliliter of the experimental medication. The criterion for complete shivering control was established as achieving scores of 0 after treatment. In contrast, incomplete shivering control was characterized by a reduction in scores without complete elimination of shivering. Unsuccessful shivering control was defined as no observable change in scores. The grading system for assessing levels of consciousness is as follows: Grade 0 indicates a state of alertness, Grade 1 signifies arousal in response to auditory stimuli, Grade 2 indicates arousal with mild tactile stimulation, Grade 3 denotes arousal with strong tactile stimulation, and Grade 4 indicates a complete lack of awareness. Rigorous and hemodynamic changes were documented at 5-minute intervals for a duration of 15 minutes. In each group, there were instances of recurring episodes of rigour and elevated axillary temperatures following treatment, as well as potential adverse effects associated with the study drug. Instances of recurrences or incomplete control were managed through the use of convection heaters, moderately warm fluids, multimodal therapy involving propofol (at a dosage of 50 mcg/kg) and/or pethidine (at a dosage of 0.5 mg/kg), or a combination of both interventions.

Results

A total of 340 spinal anaesthesia were administered during the designated study period, with 180 patients experiencing grade 2 and 3 shivering. The study groups exhibited comparable demographic characteristics, ASA health status, and surgical duration, as presented in Table 1.

Table 1 Demographic profile of patients in all groups

Patient variables	Group C	Group B	Group A
Age (years)	34 □ 12	38 □ 16	33 □ 14
Sex (M/F)	42/18	46/14	50/10
Weight (kg)	49 □ 13.5	53 □ 11.0	54 □ 15.8
ASA status (I/II/III)	21/7/2	25/2/3	22/5/3
Duration of Surgery (min)	64 □ 23	66 □ 16	72 □ 27
IV fluid infused (mL)	1103.82 □ 125.9	1153.82 □ 151.6	1146.87 □ 170.8

Although there was a decrease in axillary temperatures at both data points, no statistically significant differences were observed among the groups. All three groups exhibited comparable hemodynamic characteristics upon the initiation of shivering. Across all three groups, there was a general decrease in hemodynamic measures. However, it was observed that the clonidine group exhibited a significantly greater decrease in systolic and diastolic blood pressure, as well as an increase in pulse rate, at different time intervals. A notable decrease in average axillary temperatures (from 1.2ºC to 1.4 ºC) was observed in each of the three groups during episodes of rigors and at the post-treatment interval (15 minutes after treatment), when compared to their initial values . The percentage of patients who experienced a complete cessation of shivering after treatment, also known as the response rate, was found to be 53% for Group C, 73% for Group A, and 83% for Group B. These results indicate that the response rate was significantly lower for patients treated with clonidine compared to those treated with tramadol and butorphanol, as shown in Table 2. The duration required for shivering to

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completely cease was significantly longer in Group C (3.3 ± 0.9 minutes) compared to Group A (2.1 ± 1.0 minutes) and Group B (1.8 ± 0.5 minutes) (P < 0.001). However, the difference in cessation time between tramadol and butorphanol was not statistically significant (P = 0.13). There was a notable reduction in the intensity of repeated shivering in patients who were administered butorphanol (4) compared to those who received clonidine (16) and tramadol (18). A total of 26 cases were observed, with 10 cases in Group A and 8 cases each in Group B and Group C, all of which experienced nausea and vomiting at varying time intervals. However, it is important to note that the observed difference in the incidence of nausea and vomiting among the groups was not statistically significant, as indicated by a p-value greater than 0.05. There was a higher occurrence of grade 1 and 2 sedation in cases treated with butorphanol (24/14) in comparison to Group A (6/0) and Group C (16/6) respectively. The occurrence of grade 2 sedation was found to be significantly greater (P = 0.023) in 26% (14) of cases treated with butorphanol, as compared to 10% (6) in cases treated with clonidine and 0% in cases treated with tramadol. No instances of oxygen desaturation or respiratory depression were observed in any patient from any group throughout the duration of the study (P < 0.5). This lack of detection can likely be attributed to the administration of supplemental oxygen during episodes of shivering.

Table 2 Effect of studied drugs in all 3 groups and their significance

Variable	Group C (%)	Group B (%)	Group A (%)	*P* value
Shivering control Complete	32 (53.3)	50 (83.3)	44 (73.3)	**0.10*, 0.34**, 0.012#**
Incomplete	14 (46.6)	8 (16.6)	10 (26.6)	**0.51*, 0.71**, 0.31#**
Time taken for cessation (min)	3.3 □ 0.9	1.8 □ 0.5	2.1 □ 1.0	**,0.001*, 0.13**, ,0.001#**
Recurrence of shivering	16	4	18	**0.77*, 0.01**, 0.03#**
Nausea and vomiting	8	8	10	**0.71*, 0.71**, 1#**
Sedation score: 1/2	**16/6**	**24/14**	**6/0**	**0.03*, ,0.001**, 0.10#**

Discussion

The act of shivering has been observed to elicit physiological reactions, including elevated blood pressure, accelerated heart rate, and heightened metabolic requirements. The existence of this factor poses a hindrance to the monitoring of intraoperative electrocardiogram (ECG), blood pressure (BP), and peripheral capillary oxygen saturation (SpO2). The user's text is already academic and does not require any rewriting.Shivering can be elicited by a range of factors, such as the specific characteristics and duration of anesthesia, sensory blockade, patient age, as well as the ambient temperatures within the operating room and the temperature of the infusion fluid. The user's text does not contain any information to rewrite in an academic manner. I apologize, but without any specific text from the user, I am unable to rewrite it in an academic manner. If you provide me with the text, I will be more than happy to assist you. Could you kindly provide additional information? The incidence of postoperative shivering has been documented to vary between 5% and 65% in patients undergoing general anesthesia, while approximately 30% of individuals who received regional anesthesia have experienced this phenomenon. Nevertheless, it is important to note that there exists a dearth of additional research or empirical evidence to support this particular observation. The user's text is insufficient in length to be rephrased in an academic manner. After the administration of general anesthesia, it was observed that the incidence of shivering was higher in both female patients and those who received thiopentone, in comparison to those who were administered propofol.I apologize, but without any specific text provided, I am unable to rewrite it in an academic manner. If you have any specific content or text that you would like me to rewrite, please provide it and I will be happy to assist you. Rigor is a physiological reaction that functions as a protective mechanism against central hypothermia, although it can also occur in individuals with normal body temperature. Throughout the periods of shivering and post-treatment, the axillary temperatures of all three groups demonstrated a notable decrease (P < 0.001) in comparison to their respective baseline values. The study revealed that there was no statistically significant disparity in temperature observed between the instances when the subjects were experiencing shivering and the subsequent period following the administration of treatment. This implies that the discontinuation of shivering was not associated with alterations in body temperature, but instead with the medications under investigation, which presumably recalibrated the thermoreceptors to a lower threshold. Pharmacological intervention does not exert a direct impact on body temperature; however, it does have the ability to lower the shivering threshold, consequently mitigating the occurrence of rigors. The sensation of shivering is regulated through the activation of opioid, -2 adrenergic, serotonin, and anticholinergic receptors. Pharmaceutical agents that selectively target these physiological systems are utilized for therapeutic purposes in the treatment of this specific pathological condition. The user has provided a numerical range, specifically [13,14]. In the conducted experiments, it was observed that butorphanol exhibited a higher level of performance in comparison to tramadol and clonidine. The present study's results indicate that both tramadol and butorphanol exhibited significant efficacy in suppressing shivering, thereby supporting the findings reported by Atashkhoyi and Negargar, Dhimar *et al*., and Bhatnagar *et al*.The user's text is too short to rewrite in an academic manner. I apologize for the lack of text provided by the user. Please provide the necessary text for me to rewrite in an academic style. The current study revealed that patients who were administered

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tramadol demonstrated a higher incidence of recurrent rigors in comparison to those who received butorphanol (8% versus 25%). The administration of clonidine to patients was associated with a decrease in efficacy and an increased probability of shivering recurrence. This discovery highlights a divergence from the research conducted by Schwarzkopf *et al*. (2016) and Horn *et al*. (2019), who reported a 100% success rate in managing or preventing rigors through the administration of clonidine after general anesthesia. Nevertheless, it is imperative to acknowledge that these studies also documented occurrences of recurrences. The duration of efficacy in managing shivering was observed to be longer for clonidine in comparison to tramadol and butorphanol. The majority of experiments conducted to evaluate the effectiveness of opioids in treating rigors have shown that administering opioids for a duration of less than five minutes resulted in positive outcomes. This underscores the superiority of opioids compared to -2 agonists and other types of pharmaceutical interventions. The user has provided a citation in the form of numerical ranges [17–21,22,1516]. The occurrence of nausea and vomiting exhibited no significant differences across the three groups. Previous research has indicated a higher incidence of nausea and vomiting in relation to tramadol when compared to clonidine or butorphanol. According to a study conducted by Gangopadhyay *et al*. (23), it was observed that the occurrence of emesis was more prevalent among patients who received tramadol as opposed to those who were administered pethidine. In a similar vein, Maheshwari and colleagues (2021) documented a greater incidence of emesis among individuals administered butorphanol as opposed to tramadol. The available literature suggests that opioids have been linked to an increased occurrence of emesis. However, it is important to note that the doses administered in our study seldom led to this specific adverse reaction. The administration of high doses of tramadol can lead to the occurrence of emesis, sedation, and respiratory depression caused by butorphanol, as well as hypotension and somnolence induced by clonidine. The occurrence rate of these adverse effects was found to be elevated in prior studies following the repeated administration of medication for the purpose of mitigating rigors. The discrepancy in occurrence rates may explain the relatively lower incidence observed in our study. The provided numerical sequence consists of the following elements: 21, 22, 15, and 24. Pethidine exhibits a significant level of effectiveness, with a range of 80% to 85%, in its capacity to prevent and address rigidity in the context of regional anesthesia or following general anesthesia. Based on the results, Butorphanol exhibited a higher efficacy as an anti-shivering agent in comparison to tramadol and clonidine. The aforementioned superiority can be ascribed to its expeditious initiation of action, heightened efficacy in halting shivering, and diminished probability of recurrence.

Conclusion

In conclusion, our analysis indicates that both butorphanol and tramadol are more favorable options than clonidine for the treatment of postoperative shivering. This conclusion is based on their higher success rates, faster onset of action, and lower recurrence rates, while maintaining comparable levels of safety. Opioids are presently recognized for their efficacy as reliable pharmaceutical agents in the treatment of shivering. Nevertheless, the search for an optimal substitute continues to be a subject of ongoing investigation.

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