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Effectiveness of Prophylactic Ketamine on Shivering in Cesarean Section after Spinal Anesthesia

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ABSTRACT

Background: Regional anesthesia, including spinal or epidural techniques, can disrupt the body's ability to regulate temperature, leading to a heightened risk of shivering. Studies have indicated that shivering occurs in up to 55% of patients undergoing procedures under regional anesthesia. To address this issue, numerous medications have been explored for their potential to prevent post-anesthetic shivering. **Objective:** To assess the effectiveness of prophylactic ketamine on shivering in cesarean section after spinal anesthesia. **Study Design:** Prospective, randomized, double blind, clinical trial. **Settings:** Department of Anesthesiology, Surgical Intensive Care Unit and Pain Management, Civil Hospital Karachi Pakistan. **Duration:** Six months from August 2019 to January 2020. **Methods:** A total of 60 patients undergoing spinal anesthesia for elective cesarean section were included in this study. Two groups A and B were formed and patients were equally divided into these groups by lottery method. Group A were treated with ketamine 0.5 mg/kg I/V and group B treated with normal saline 0.05ml/kg/I/V. Grade 0-1 shivering was labeled as effective and shivering grade 2, 3 or 4 at 15 minutes after administration of the drug, was considered ineffective. **Results:** The average age of the patients was 28.33 ± 5.67 Years. Rate of shivering was significantly high in patients who were treated with normal saline than ketamine in which shivering was not observed (53.3 *vs.* 0% respectively; *P* value of 0.0005). This implies that effectiveness was significantly high in groups A than group B (100% vs. 46.7%). **Conclusion:** Ketamine observed to be the effective drug for the treatment of postanesthetic shivering. It should be considered prophylactically in any patient undergoing spinal anesthesia.

Keywords: *Ketamine, shivering, spinal anesthesia, shivering.*

INTRODUCTION

Shivering frequently occurs as an adverse outcome following spinal anesthesia in women undergoing cesarean section. This type of anesthesia disrupts the central thermoregulatory system and alters blood flow distribution within the body.[1,2] Hypothermia often accompanies neuraxial block because it involves the redistribution of blood among various body compartments and disrupts central thermoregulatory control.[1,3] Postoperative shivering can cause significant discomfort for patients and may disrupt the monitoring of vital signs such as electrocardiogram, blood pressure, and pulse oxygen saturation. Its occurrence has been documented to range from 50% to 60% in various studies.[4,5] The origin of shivering likely encompasses several mechanisms. Pregnant women typically have elevated levels of progesterone in circulation, which could contribute to lowered shivering thresholds.[5] The sympathetic blockade induced by spinal anesthesia might disrupt thermoregulation, resulting in peripheral vasodilation. This process facilitates the movement of heat from the core to the periphery, increasing heat loss through the skin. Furthermore, at the central nervous system level, there are heightened thresholds for sweating and reduced vasoconstriction.[5,6] According to

other studies spinal anesthesia (SA) is generally regarded as safe, it is not without its risks. Shivering stands out as the foremost and distressing complication of anesthesia, occurring up to 70.7% of cesarean sections conducted under spinal anesthesia. Its presence correlates with cardiovascular and respiratory complications.[7,8] Shivering can be prevented or addressed through both non-pharmacological and pharmacological approaches. Non-pharmacological interventions encompass the use of forced-air warmers, active and passive cutaneous warming techniques, blankets, core body warming, electro-acupuncture, fluid warming, and adjusting the operating room temperature to deter shivering.[7,9,10]

Neglected shivering can lead to heightened wound pain, elevated metabolic requirements, increased oxygen consumption, and impaired blood clotting function. Numerous studies have investigated the efficacy of preventing post-spinal shivering through the administration of ketamine and other medications.[11,12] Ketamine functions as a noncompetitive antagonist of the N-methyl-D-aspartate (NMDA) receptor. Its involvement in thermoregulation stems from its inhibition of norepinephrine uptake, which in turn reduces the transfer of heat from the body's core to its periphery.[11,13] Different international studies observed that the Ketamine reduces the occurrence of hypotension and shivering in individuals undergoing spinal anesthesia for cesarean delivery.[11,12,14] Despite advancements in medical literature, there remains a scarcity of data at the local level regarding the effectiveness of prophylactic ketamine in mitigating shivering among patients undergoing cesarean sections. Therefore, this study aims to investigate the use of prophylactic ketamine as a preventive measure against shivering and its associated complications in individuals undergoing spinal anesthesia for cesarean delivery. By conducting this research, we seek to contribute valuable insights at the local level, which can potentially benefit patients by offering effective strategies to alleviate this uncomfortable condition.

METHODS

It was is a prospective, randomized, double blind, clinical trial, was conducted in Department of Anesthesiology, Surgical Intensive Care Unit and Pain Management, Dow University of Hea1th Sciences, Civil Hospital Karachi, during a period of 6 months from August 2019 to January 2020. Non probability consecutive sampling technique was used. Patients undergoing spinal anesthesia for elective cesarean section and patients with ASA physical status I and II were included. Patient having temperature >100^{o}F or <97^{o}F, patients with increased intracranial pressures and hypertension and patients receiving other drugs to control shivering like meperidine and tramadol were excluded. After assessment for the inclusion and exclusion criteria, 60 patients undergoing spinal anesthesia for elective cesarean section will be included in the study. Following informed consent, these 60 patients were randomized into two equal groups through lottery method by an anesthetist technician who is not involved in the study. Patients undergoing spinal anesthesia for cesearean section were applied standard monitoring of noninvasive blood pressure, ECG and pulse oximetry. Intravenous line was maintained and crystalloid solution was administered at room temperature. After injecting bupivacaine 0.75% at L3-L4 or L4-L5 interspace, the patients were placed supine and covered with cotton sheets. Supplement oxygen was given by Hudson mask. Just after receiving spinal anesthesia and on the basis of lottery results, the patients were randomly allocated to receive intravenous ketamine (0.5 mg/kg i.v.) or normal saline (0.05 ml/kg i.v.). The anesthetist technician noted the drug group (A or B) in front of each patient's identification number in a given record register. Ketamine and normal saline were administered in the same volume via a 10-cc syringe. For a 60 kg woman, the volume of required dose of both normal saline (0.05 ml/kg) and ketamine (0.5 mg/kg) was 3 ml. Finally, the anesthetist conducting the study was monitor and assess the response of the given drug at 0 (baseline) up to 15 minutes. Patient's shivering grades were assessed and recorded. If the patient shows grade 0-1 shivering, it was labeled as effective. If the patient shivers with grade 2, 3 or 4 at 15 minutes after administration of the study drug, the prophylaxis against shivering was considered ineffective and the emergency drug to control the shivering was given to manage as per hospital protocol. Data were fed and analyzed by using statistical software SPSS-Version 26.

RESULTS

A total of 60 patients undergoing spinal anesthesia for elective cesarean section were studied in this study. The average age of the patients was 28.33 ± 5.67 Years. Average weight and height of the patients were 67.90±9.22 kg and 157.38±6.79 cm respectively. Out of 60 patients, 54(90%) were ASA I and 6(10%) were in ASA II. Significant difference was observed between groups (p=0.01). According to the comparison of shivering between groups within 15 minutes, the overall rate of shivering rate was 26.7% (16/60). Rate of shivering was significantly high in patients who were treated with normal saline than ketamine in which shivering was not observed (53.3 *vs.* 0% respectively; *P* value of 0.0001). This implies that effectiveness was significantly high in groups A than group B (100% vs. 46.7%) as shown in table 1.

According to the effectiveness with respect to age, weight and height stratification, the shivering was significantly

high in group B than group A in all age groups (p=<0.05), as shown in table 2.

Table 1: Comparison of shivering between groups within 15 minutes (n=60)

Shivering	Group A n=30	Group B n=30	Total n=60	P-Value
Yes (Shivering Grade 2 to 4)	0(0%)	16(53.3%)	**16(26.7%)**	0.0005
No (Shivering Grade 0 & 1)	30(100%)	14(46.7%)	**44(73.3%)**	

Group A = Ketamine 0.5 mg/kg I/V, Group B = Normal saline 0.05ml/kg/ I/V

Table 2: Comparison of shivering according to age and weight between groups within 15 minutes (n=60)

Variables	Shivering	Group A n=18	Group B n=13	Total	P-Value
Age < 27 Years	Yes	0(0%)	7(53.8%)	7(22.6%)	0.003
	No	18(100%)	6(46.2%)	24(77.4%)	
Age ≥27 Years	Yes	0(0%)	9(52.9%)	9(31%)	0.0005
	No	12(100%)	8(47.1%)	20(69%)	
Weight < 70 Kg	Yes	0(0%)	8(50%)	8(20.5%)	0.018
	No	23(100%)	8(50%)	31(79.5%)	
Weight > 70 Kg	Yes	0(0%)	8(57.1%)	8(38.1%)	0.0005
	No	7(100%)	6(42.9%)	13(61.9%)	

Group A = Ketamine 0.5 mg/kg I/V, Group B = Normal saline 0.05ml/kg/ I/V

DISCUSSION

Shivering, a common complication after anesthesia, is influenced by various factors. It can occur either due to core hypothermia or even in cases of normothermia at the end of surgery. Heating solutions can decrease both the frequency and severity of shivering in women scheduled for cesarean delivery under spinal anesthesia. Addition of various opioids extramurally also reduced the incidence of shivering. However, this study was designed to evaluate the effectiveness of prophylactic ketamine on shivering in cesarean section after spinal anaesthesia. A total of 60 patients undergoing spinal anesthesia for elective cesarean section were studied in this study and the average age of the patients was 28.33 ± 5.67 years. In the comparison of this study Zoengmawia *et al*[15] reported that the mean age of the patients was 42.6 ± 11.174 years in ketamine group and 38.00 ± 11.84 years was in normal saline group. Consistently Aboelsuod MA *et al*[14] also reported that the mean age of the women undergone c-sections was 29.12±2.9 years in ketamine group and 27.25±3.16 years was in normal saline group.

In this study, the comparison of shivering between groups within 15 minutes revealed an overall shivering rate of 26.7% (16/60). The incidence of shivering was significantly higher in patients treated with normal saline compared to those treated with ketamine, where shivering was not observed (53.3% vs. 0% respectively; p = 0.0001). These results were corroborated by previous studies, including the one conducted by Aboelsuod MA *et al*[14] who observed that the Ketamine reduced the occurrence of hypotension and shivering in patients undergoing spinal anesthesia for cesarean delivery. Moreover, it led to enhanced sedation for the mother and prolonged postoperative pain relief without adverse effects on the newborn. In alignment with our study, Kapi M *et al*,[17] conducted a comparative study and they found that intravenous tramadol and ketamine effectively decreased the frequency and intensity of intraoperative shivering in patients undergoing cesarean section under spinal anesthesia. However, an Indian study indicated that prophylactic ketamine exhibited comparable effectiveness to tramadol in preventing shivering during spinal anesthesia for elective surgeries of the lower limb. According to the findings of the study by the Lema GF *et al*,[12] administering low-dose intravenous ketamine or tramadol prophylactically effectively reduces both the frequency and severity of shivering. They suggest considering prophylactic administration of low-dose intravenous ketamine or tramadol for women undergoing cesarean section following by the spinal anesthesia. However, inconsistently, Kumar RA *et al*[19] found that dexmedetomidine at a dose of 0.5 µg/kg effectively reduced the occurrence of intraoperative shivering among cases undergoing surgery under subarachnoid blockade when compared to ketamine and tramadol. The results of studies involving surgeries other than cesarean sections displayed slightly varying outcomes, which could be attributed to differences in patient demographics or surgical techniques. While equipment designed to maintain normothermia effectively prevents shivering, its widespread use is hindered by its high cost and impracticality in certain settings. Moreover, the adverse cardiac events associated with mild perioperative hypothermia may not solely be attributable to shivering but could also involve other mechanisms, such as the notable increase in plasma catecholamine concentrations. However, it is important to acknowledge several limitations of this study, including the absence of comparison with alternative medications like tramadol and dexmedetomidine, as well as its limited sample size. Therefore, larger-scale multicenter studies are warranted to confirm and validate these findings.

CONCLUSION

In conclusion, ketamine in a dose of 0.5 mg/kg is the effective drug for the treatment of postanesthetic shivering, and it is not associated with hemodynamic disturbances, excessive sedation or other side-effects. It should be considered prophylactically in any patient undergoing spinal anesthesia.

LIMITATIONS

Limited study sample size and absence of comparison with alternative medications

SUGGESTIONS / RECOMMENDATIONS

It is recommended to conduct larger-scale multicenter studies to confirm and validate these findings

CONFLICT OF INTEREST / DISCLOSURE

None.

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