The Effect of Different Doses of Ketamine on Reducing Shivering after Elective Cesarean Section

Hasan Zabetian\textsuperscript{1,2}, Navid Kalani\textsuperscript{3*}, Mohammad Sadegh Sanei\textsuperscript{1,2}, Mansour Deylami\textsuperscript{4}, Hossein Kargar Jahromi\textsuperscript{5} and Farzad Poorgholami\textsuperscript{2}.

\textsuperscript{1}Research center for Social Determinants of Health, Jahrom University of Medical Sciences, Jahrom, Iran.
\textsuperscript{2}Department of Anaesthesiology, Jahrom University of Medical Sciences, Jahrom, Iran.
\textsuperscript{3}Medical Ethic Research Center, Jahrom University of Medical Sciences, Jahrom, Iran
\textsuperscript{4}Department of Anaesthesiology, Golestan University of Medical Sciences, Golestan, Iran.
\textsuperscript{5}Research center for non-Communicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran.

Correspondence email: navidkalani@ymail.com

ABSTRACT

Introduction: Shivering is a protective reaction. It increases the production of body temperature by muscular contraction. Post-surgery shivering is one of the prevalent side effects of anesthesia. This is usually accompanied with other problems such as oxygen consumption increase, intracranial pressure increase, and other complications. Hence, this study compared the effect of various doses of ketamine on reducing selective post-cesarean section shivering.

Materials and Methods: It was a double-blinded, randomized clinical trial. Thirty pregnant women undergoing selective cesarean section under spinal anesthesia at Motahari Hospital, Jahrom participated in this study. They received ketamine (0.3mg/kg and 0.15mg/kg) in two groups of 15. Data was analyzed by T-test, Mann-Whitney test, and Chi square using SPSS16. The level of significance was considered below 0.05 (P<0.05).

Results: Patients’ mean age was 27.18±4.38. Mean operation time was 43±16min in ketamine 0.15mg/kg and 40.67±7min in ketamine 0.3mg/kg. No significant difference was observed in this respect. Regarding shivering intensity, most patients had no shivering. The prevalence of ketamine 0.3mg/kg and 0.15mg/kg shivering intensity was not significant in recovery in 5min, 10min, 15min, 30min and 45min (P-value>0.05).

Conclusion: Ketamine 0.3mg/kg is more effective in controlling shivering and other post-surgery side effects as compared to ketamine 0.15mg/kg.

Keywords: Cesarean Section, Ketamine, Shivering

INTRODUCTION:

Shivering is a protective reaction. It increases the production of body temperature by muscular contraction. Post-surgery shivering etiology has not perfectly understood, yet (1). Factors like the reduction of core body temperature, hindered spinal reflexes, post-surgery pain, the reduction of sympathetic system activity, the secretion of fever-bearing substances, suppressing metabolic alkalosis and adrenal are probably involved (2). Today, post-surgery shivering is one of the
commonplace side effects of anesthesia. It appears after general anesthesia in almost %50-%65 of patients and %33 during regional anesthesia (3). The incidence of shivering in regional anesthesia is not less prevalent than in general anesthesia. Patients’ hypothermia continues under block level until the removal of block effects. This is because the submission of sensory messages from lower limbs to nervous centers is disrupted in regional anesthesia. Again, due to lower limbs muscles’ paralysis, temperature production is also reduced. As a result, the time needed to patient to warm again is twice the times in regional anesthesia as compared to general anesthesia (4). Spinal anesthesia hinders the thermal messages (mainly, cold messages) of the blocked region. It is caused by the reduction of vascular contraction and shivering threshold. Inducing vasodilation resulting from the sympathetic block, spinal anesthesia also decreases body temperature. Then, patient gets susceptible to hypothermia and shivering. This increases oxygen consumption, CO₂ production, and hypoxia. It also results in high blood pressure, high intracranial pressure, ocular hypertension, pain intensification in surgery area, and undoing ulcer stitch (5-7). The interference of oxymetry pulse monitoring, measuring blood pressure, and ECG are among other side effects of shivering. It also increases oxygen consumption up to %500. It in turn increases the need for further heart output and respiratory ventilation. It induces cardio-respiratory failure in older patients and (or) in patients with cardio-respiratory ground diseases (4). Today, cesarean section is among widely common operations. Based on statistics, cesarean section percentage is three times the world standard (%15 of labors) in Iran. It even includes between %26 and %60 of labors. Mean shivering for this group is reported between %36 and %71 by respective studies (8-9). Pregnant women’s shivering after spinal anesthesia is a cause of stress during cesarean section (10). Non-

medicinal and medicinal techniques are suggested for the treatment and prevention of post-operation shivering. Keeping operation room warm during cesarean section is among the non-medicinal actions (11). Concerning the fact that total skin surface controls about %20 of the body temperature. Hence, this method is not adequate for controlling core hypothermia. Thus, it seems necessary to take medicinal actions (12). Ketamine is among anesthetics. It is an antagonist. It can alleviate pain in doses below anesthesia level. It regulates temperature in several stages. Doing so, it prevents from shivering (13). Through blocking N Methyl D Aspartate (NMDA) receptors, it can hinder postsurgery shivering both centrally and influencing the center of temperature regulation (14). In this study, we intend to examine a low ketamine dose in preventing from shivering during and after spinal anesthesia in cesarean section.

**MATERIALS AND METHODS:**

Thirty pregnant women participated in this double-blinded, randomized clinical trial. They underwent anesthesia Class I and II based on American Society of Anesthesia (ASA) scale. The participants aged between 18 and 35. They were admitted at Shahid Motahari Hospital of Jahrom for selective cesarean section under spinal anesthesia. After obtaining the permission of the university ethics committee and patients’ informed consent for entering the design, they were randomly divided into two groups of 15. Group A (15 patients) received ketamine 0.3mg/kg IV and group B (15 patients) ketamine 0.15mg/kg IV. Entrance criteria included lack of hallucination and delirium, lack of drug sensitivity, lack of hart problem history, lack of blood pressure history, lack high ocular pressure, and lack of heart palpitation history. Again, patients would be omitted from the study, in case of any unpredicted incidence during cesarean section needed the injection of other medicines and (or) put patient’s life at risk and affect her
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All patients received adequate serum before cesarean section. During operation, 5l oxygen was administered by facial mask. When entered the operation room, patients’ BP (Blood Pressure), respiration rate, and HR (Heart Rate) were recorded. All of them underwent spinal anesthesia by a certain method using lidocaine 5%. Spinal anesthesia was conducted in spinal space L3-L4 or L4-L5 under sterilized condition using 25G Quincke spinal needle. The patients were immediately positioned in supine status.

Anesthesia level was kept at T4-T6 by pinprick test. Patients did not receive any pre-anesthetics. Operation room temperature was kept between 21°C and 22°C. Intravenous liquids received were also at room temperature. During operation, standard monitoring was done including BP, arterial blood oxygen saturation, HR, and electrocardiogram. Before spinal anesthesia, patients’ tympanic temperature was measured by tympanic thermometer in 5min, 10min, 15min, 30min, and 45min. Patients’ vital signs were recorded in 5min, 10min, 15min, 30min, and 45min from the beginning to the end of the operation. Side effects (including shivering, nausea and vomiting, hypotension, and bradycardia) were recorded, if occurred. In case of arterial hypotension over %22 of the basic level and in case of nausea and vomiting, the patients were removed from the study.

Immediately after labor, the patients were randomly received ketamine 0.15mg/kg with midazolam 0.03mg/kg or ketamine 0.3mg/kg with midazolam 0.03mg/kg. In the end of surgery and in recovery during 45min, the presence or absence of shivering and its degree were set based on Matthews et al. shivering scale, as follows: no shivering = 0 (Do not have shivering), mild face and neck fasciculation and electrocardiogram disruption in the lack of arms’ conscious activity = 1 (mild shivering), evident shivering of more than a group of muscles = 2 (average shivering), whole body intensive muscular activity = 3 (severe shivering). Besides examining the presence or absence of shivering in recovery, BP, HR, and arterial blood oxygen saturation was also monitored before operation and in recovery room (in 5min, 10min, 15min, 30min, and 45min). Ketamine side effects (including hallucination and eyes subconscious movements and abnormal sleepiness, vomiting, and too much sleepiness) were also recorded.

Data was analyzed using SPSS16. Quantitative dependent variables were examined by t-test (normal data distribution) and (or) non-parametric Mann-Whitney test (non-normal data distribution). Nominal quantitative variables were examined by Chi square test. Ordinal qualitative variables were examined using Mann-Whitney test. P-value was considered below 0.05. All through the study, Helsinki Statement principles and Committee of Medical Ethics of Jahrom Medical School were followed.

RESULTS:

All patients were randomly divided into two groups of 15. Group A (15 patients) received ketamine 0.3mg/kg IV and group B (15 patients) ketamine 0.15mg/kg IV. Mean operation time was 43±16min in ketamine 0.15mg/kg and 40.67±7min in ketamine 0.3mg/kg. No significant difference was observed in this respect (Table 1).

| Table 1: A comparison of the average action time between ketamine (%3) and ketamine (%15) in 5min, 10min, 15min, 30min, and 45min using T-test |
|---|---|---|---|---|
| dose | N  | Mean±SD | T   | p-value |
| 0.15 | 15 | 43±16   | 0.512 | 0.612 |
| 0.3  | 15 | 40.67±7 |       |        |

Based on Chi square results, there is no significant differences between ketamine 0.3mg/kg and 0.15mg/kg regarding shivering intensity in 5min, 10min, 15min, 30min and
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45min (P-value>0.05). Most patients did not have shivering. With ketamine 0.15, %6.7 of the patients had severe shivering and %6.7 had average shivering in 15min. With ketamine 0.3, %6.7 had mild shivering in 15min and %13.3 had mild shivering in 30min (Table 2).

Based on Chi square results, there is no significant differences between ketamine 0.3mg/kg and 0.15mg/kg regarding shivering intensity in 5min, 10min, 15min, 30min and 45min (P-value>0.05, Table 3). Most patients did not have shivering.

Systolic blood pressure was normal in recovery in 5min, 10min, 15min, 30min, and 45min. Results from T-test showed that there was a significant difference between ketamine 0.3mg/kg and 0.15mg/kg regarding systolic BP in recovery in 5min, 10min, 15min (P-value<0.05). Yet, it was not significant in 30min and 45min (P-value>0.05). Diastolic BP was normal in recovery in 5min, 10min, 15min, 30min, and 45min. Results from T-test showed that there was no significant difference between ketamine 0.3mg/kg and 0.15mg/kg regarding diastolic BP in recovery in 5min, 10min, 15min, 30min, and 45min (P-value>0.05). Heart rate was normal in recovery in 5min, 10min, 15min, 30min, and 45min. Results from T-test showed that there was a significant difference between ketamine 0.3mg/kg and 0.15mg/kg regarding HR in recovery in 30min, and 45min (P-value<0.05). Yet, it was not significant in 5min, 10min, and 15min. Results from Chi square showed no significant difference between ketamine 0.3mg/kg and 0.15mg/kg regarding hallucination, nausea, and vomiting in recovery in 5min, 10min, 15min, 30min, and 45min (P-value>0.05). Most patients lacked hallucination, nausea, and vomiting in ketamine 0.3mg/kg and 0.15mg/kg groups.

**DISCUSSION:**
Post-surgery shivering prevention and treatment form the main part of post-operation care. It is
due to the possibility of serious injuries resulted from sympathetic stimulation, oxygen consumption increase, and (or) Co2 production increase in patient (15). In this study, we examined a low ketamine dose in preventing from shivering during and after spinal anesthesia in cesarean section.

Ketamine is an anesthetic and analgesic drug with sympathetic stimulation effects. It is effective in spinal anesthesia due to increasing BP and creating hemodynamic stability. It controls shivering probably through regulating temperature via hypothalamus and (or) the beta adrenergic effect of norepinephrine. It has an analgesic effect due to its antagonistic impact on NMDA receptor (N Methyl D Aspartate). Thus, it is effective in the non-thermoregulatory control of shivering (16).

In some studies, ketamine 0.75mg/kg led to the reduction of shivering more effectively than meperidine. Yet, side effects like nystagmus and lightheadedness were also reported (17 & 18). Of other inadvertent side effects of ketamine are nausea, vomiting, hallucination and delirium, respiratory channel secretion increase, urinary retention, intracranial pressure increase, stomach pressure increase, and ocular pressure increase (19, 20, 21). In the present study, lower doses were applied to reduce inadvertent side effects. In a study by Mahuri et al., ketamine significantly decreased shivering in patients. In this study, ketamine 0.5mg/kg was injected intravenously to prevent from shivering (22). In some other studies, ketamine decreased shivering even further than granisetron and the mixture of granisetron and ketamine (23).

In a study by Heidari et al., patients’ body temperature in pethidine group was lower than ketamine and dexamethasone groups when entering into recovery. Although body temperature increased during recovery in all groups, it was again higher in 60min in dexamethasone group as compared to ketamine and pethidine groups. The incidence of shivering was less in pethidine group as compared to other groups (24).

In another study, 90 ASA I and II patients with shivering degrees 3 and 4 were grouped after general anesthesia to intravenously receive meperidine 25mg/kg, ketamine 0.5mg/kg or ketamine 0.75mg/kg. It was concluded that shivering degree was lower in ketamine groups during the first 4min. Yet, there was nystagmus and a feeling of loosely walking in the space in both doses of ketamine (25).

Another study compared the application of midazolam and (or) ketamine with midazolam prophylaxis regarding shivering in topical anesthesia. Here, 120 ASA I and II patients underwent orthopedic surgery under epidural analgesia by bupivacaine. It was demonstrated that the incidence of shivering was respectively %60, %50, and %32.3 in normal saline, midazolam, and ketamine + midazolam groups 15min after the surgery. There was a difference between these three groups. In ketamine + midazolam group, shivering was evidently lower than the other groups (23).

In 2008, the effect of intramuscular ketamine on post-surgery shivering decrease was compared to pethidine and placebo in Arabia. About 120 children between 5 and 12 years of age were examined. Shivering was observed in 3 patients in ketamine group and 38 in placebo group when reaching recovery room in 10min and 20min after operation. No shivering was seen in patients receiving pethidine. Thus, this study showed that using a lower preventive dose of ketamine is effective in hindering post-anesthesia shivering in children undergoing tonsil surgery or, at least, it theoretically has better effects on respiratory failure, nausea, and vomiting, for instance, as compared to pethidine (25).

**CONCLUSION:**

Ketamine (0.3mg/kg) is more effective in controlling post-cesarean section shivering as compared to ketamine (0.15mg/kg). Small
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variations in ketamine dose induce different side effects in different people. Hence, further studies are required to determine a desirable ketamine dose for post-cesarean section shivering control.

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REFERENCES:
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