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EFFECT OF INTRAVENOUS GRANISETRON ON CONTROL OF SHIVERING OF PARTURIENTS UNDERGOING ELECTIVE CESAREAN SECTION

Siavash Jabarzadeh[1], Sussan soltani Mohammadi[2]

1. *Anesthesiologist , Department of Anesthesia and Intensive Care Medicine Shahid Rasi hospital, Urmia University of Medical Sciences, Urmia, Iran.*
2. *Associate professor, Department of Anesthesia and Intensive Care and Pain Medicine ,Dr Shari-ati Hospital,Tehran University of Medical Sciences.*

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ABSTRACT

Background and Objective: Shivering is one of the common problems during spinal anesthesia and may lead to numerous complications. Shivering may reduce oxygen supply to the pregnant mother or increase the amount of oxygen consumption, which leads to significant decrease in arterial oxygen and dangerous side effects in the fetus.
Materials and Methods: In an interventional double blinded clinical trial, a total of 100 ASA I and II pregnant women were enrolled. Patients were randomly assigned into two groups. Inter-vention group or G group (n=50) received 3 mg intravenous granisetron immediately after spinal anesthesia. Control group (n=50) received 3 ml intravenous normal saline immediately after spinal anesthesia. Then, patients were categorized in 5 degrees from zero to 4 scores in terms of shivering rate during and after surgery and compared between two groups.
Results: there were no significant differences between intervention and control groups in terms of demographic data (age, weight, duration of anesthesia, duration of surgery and central temperature (P>0.05). There was a significant difference between intervention and control groups in terms of shivering frequency (P=0.001).
Discussion and Conclusion: The results showed that intravenous granisetron decreased shiver-ing in parturients undergoing caesarean section with spinal anesthesia.

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Introduction

Spinal anesthesia is usually used as the preferred anesthetic method for elective cesarean section (1, 2). Caesarean section surgery is one of the most common and important operations. Maternal and fetal health during surgery is one of the most important concerns in this type of delivery. It is very important to maintain hemodynamic and oxygenation status of the mother and the fetus in desirable conditions (3). Since shivering during and after surgery often occurs in the field of spinal anesthesia in cesarean sectional operations, it is defined as involuntary movement of one or more muscles which occurs in the first stages after general or local anesthesia (4, 5). Local anesthesia significantly impair the regulation of temperature in patients who are prone to hypothermia, which reduces the threshold for vasoconstriction and shivering (6). A number of potential mechanisms associated with shivering include reduction in central body temperature, which usually decreases from 0.5 to 1.5°C in the first hour after anesthesia induction. Anesthesia significantly changes the temperature control center and distribution of body heat (7). Anesthetic shivering is usually stressful, lasting for 20 to 60 minutes and its main reason is not exactly known. However, this will be more intense if duration of anesthesia is prolonged. In recent years, anesthetic shiver has been attributed to the following reasons: 1) no inhibition of spinal reflex, 2) reduced body temperature during surgery, 3) pain, 4) reduced sympa-

Corresponding Author: Siavash Jabarzadeh, Departement of Anesthesia and Intensive Care Medicine Shahid Rasi hospital, Urmia University of Medical Sciences, Urmia, Iran

thetic system activity (8). In cesarean section, shivering is a stressor for anesthetist and mother (1, 4). During operation, shivering can increase oxygen consumption by up to 500% and also increase carbon dioxide emissions; this causes an increase in cardiac output, which in turn can increase myocardial oxygen requirement and cause hypoxic leukemia. In addition, it may cause lactic acidosis following hypoxia in older patients (4, 9, 10). Obviously, the risk of hypoxia will increase by 4 to 5 times in the mother and consequently in the fetus. Due to increased sympathetic tone, tachycardia, and increased maternal hypertension and maternal and fetal complications particularly in the long term as ischemic myocardial infarction, it increases the risk of heart attack in the mother (1, 4). Therefore, shivering control during cesarean section significantly reduces these complications, particularly complications of maternal and fetal hypoxia, followed by healthy and uncomplicated childbirth, which will significantly reduce the burden of diseases caused by complicated childbirth and reduce economic costs of treating postnatal disease neonates (1). Meperidine (pethidine), tramadol and clonidine are known and useful in prevention and control of anesthetic shivering. Different side effects associated with medications include nausea, heart rate, and hypotension, which limit their use in many cases. An anesthetist may not be reluctant to use narcotic drugs on the mother and the fetus due to concerns about their unwanted side effects (11). 5-HT_3 antagonists are commonly used as anti-vomiting in gynecological, obstetric and surgical procedures. A number of studies have confirmed their anti-shivering properties both in general anesthesia and during spinal anesthesia (12, 13). Granisetron is a 5-HT_3 antagonist, which often has anti-nausea and anti-vomiting and anti-pruritus activity in cesarean under spinal anesthesia with the advantage of very low levels of sleepiness, cardiovascular side effects, or risk to the baby (1). Considering the lack of research in this field, it has been suggested that intravenous graniticrosterone with twice half-life of ondansetron as a preventive agent to prevent shivering significantly reduces the incidence or severity of shivering as the primary objective of research and reduces nausea and vomiting as a secondary objective in women undergoing cesarean sectional surgery with spinal anesthesia.

Materials and Methods

This is an interventional study or double-blind clinical trial. After receiving approval from the Ethics Committee of Tehran University of Medical Sciences, pregnant mothers undergoing cesarean section provided their informed consent about receiving the drugs used for them. The studied population included mothers who were candidates for spinal cesarean section aged 18 to 40 years. Participants had no cardiovascular, thyroid and psychosocial diseases and no contraindication for spinal anesthesia and no need for blood transfusion. Their central temperature measured by pre-operative tympanometry was less than 38°C and more than 36.5°C. Participants did not receive any shiver-intervening drug such as phenobarbital and effective drugs on liver metabolism such as erythromycin or cimetidine. Sample size of each group was estimated at 47; considering 5% exclusion from the study based on determined criteria, sample size was set at 50 per group; totally, 100 patients with ASA II and I were included in the study. Patients were randomly assigned to two groups. Intervention group or G group (n=50) received 15 mg bupivacaine 0.5% for spinal anesthesia and underwent cesarean section and received 3 mg intravenous granisternone immediately after spinal anesthesia. Control group (n=50) received 3 cc intravenous normal saline immediately after spinal anesthesia. Patients in both groups were monitored for heart rate, non-invasive blood pressure, pulse oximetry and electrocardiography after entering the operating room, and two IV lines were inserted with angioutica 18. In all patients, two groups experienced cold fever, postoperative nausea and vomiting, and seizure sensation during and after surgery, which were recorded in the checklist. After monitoring, patients received 5 cc/kg lactate ringer solution, which was heated to 37°C for 15 min before spinal anesthesia through angioutica 18. Temperature of all injectable fluids was kept at 37°C; OR and recovery room temperatures were kept at 24 ± 0.6°C. Immediately after the onset of spinal anesthesia, 3 mg granistorrone and 3 cc normal saline were injected by anesthetized technicians without anesthetist's knowledge. For spinal anesthesia, the patient was placed in a sitting position and received 15 mg Bupivacaine 0.5% under sterile conditions in L_4-L_5 vertebral space by spinal quincke needle 25 into subarachnoid space. The patient's sensory level was raised to T_4-T_6 level in the supine position. In case of hypotension below 25% of the patient's blood pressure from baseline, 50 µg intravenous phenylephrine was used. In the case of bradycardia (HR<60 bpm), 0.5 mg atropine was administered intravenously. After performing the above procedures and starting the surgery, observations of patients showed shivering at 5 degrees from 0 to 4, including 0) no shivering, 1) peripheral vasoconstriction but no visible shivering, 2) muscle activity in only one muscle group, 3) muscular activity in more than one muscle group but not generalized, 4) shivering including the whole body, nausea and vomiting during the operation. Patients with zero to 2 degrees were considered without shivering and patients with 3-4 degrees were considered with shivering. Questionnaire was used to collect data. Demographic data and the received code of the patient given to each group specifically were recorded. Data was analyzed by SPSS[18]. Mann-Whitney test was used to measure shivering; Chi-square test was used for quality variables of nausea and vomiting.

Results

According to results obtained from descriptive and inferential statistics, Table 1 shows mean of age, weight, minimum and maximum block levels in intervention and control groups. There was no significant difference between intervention and control groups.

Table 1: mean of age, weight, minimum and maximum block level in intervention and control groups

P-Value	Group	Variable

	Control	Intervention	
0.3	30.2 ± 4.5	31.2 ± 5.3	Age
0.4	61.8 ± 6.5	63.1 ± 7.4	Weight
1	T_4	T_4	Maximum block level
1	T_8	T_8	Minimum block level

Table 2 compares central temperature during anesthesia in intervention and control groups. There was no significant difference between intervention and control groups (P>0.05).

Table 2: comparison of central temperature in intervention and control groups

P Value	Group		Variable
	Control	Intervention	
0.4	37.2 ± 0.41	37.6 ± 0.5	Central temperature (°C)

Table 3 compares duration of anesthesia and duration of surgery in intervention and control groups. The average duration of anesthesia was considered from the onset of spinal anesthesia to reduction of block level to 4 dermatomes. There was no significant difference between intervention and control groups (P>0.05).

Table 3: duration of anesthesia and duration of surgery in intervention and control groups

P Value	Group		Variable
	Control	Intervention	
0.2	111.2 ± 18.0	116.1 ± 26.6	Duration of anesthesia (min)
0.2	57.7 ± 13	56.7 ± 9.7	Duration of surgery (min)

Table 4 compares mean of shivering degrees between two groups at the initial minutes less than 15 minutes from administration of Granisetron. The median degree of shivering during the first 15 minutes from administration of Granisetron and normal saline was 10 patients (20%) with degree 2 and 17 controls (34%) with degree 3. The degrees 0-2 were considered as absence of shivering and degrees 3-4 were considered as presence of shivering. There was a significant difference between intervention and control groups in terms of presence or absence of shivering (P=0.001).

Table 4: frequency of shivering during the first 15 min from administration of granisetron and normal saline in intervention and control groups

P Value	Total	Shivering		Variable
		No	Yes	
0.001	50	40	10	Intervention (granisetron)
	100%	80%	20%	
	50	33	17	Control (normal saline)
	100%	66%	34%	

Table 5 compares mean of shivering degrees between two groups after 15 minutes from administration of Granisetron. Shivering remained only in 4 patients (8%), while it remained in 10 controls (20%). This difference was significant (P=0.004). All patients with continued shivering were treated with pethidine.

Table 5: frequency of shivering after 15 min from administration of granisetron and normal saline in intervention and control groups

P Value	Total	Shivering		Variable
		No	Yes	
0.004	50	46	4	Intervention (granisetron)
	100%	92%	8%	
	50	40	10	Control (normal saline)
	100%	80%	20%	

According to Table 6, frequency of intra- and post-operative vomiting was significantly lower in intervention group than control group; 3 patients (6%) and 10 controls (20%) experienced vomiting during and after the surgery. This difference was significant (P=0.003).

Table 6: frequency of vomiting in intervention and control groups

P Value	Total	Vomiting	Variable

		No	Yes	
0.003	50	47	3	Intervention (granisetron)
	100%	94%	6%	
	50	40	10	Control (normal saline)
	100%	80%	20%	

According to Table 7, frequency of intra- and post-operative nausea was significantly lower in intervention group than control group; 15 patients (30%) and 30 controls (60%) experienced nausea during and after the surgery. This difference was significant (P=0.002).

Table 7: frequency of nausea in intervention and control groups

P Value	Total	Nausea		Variable
		No	Yes	
0.002	50	35	15	Intervention (granisetron)
	100%	70%	30%	
	50	20	30	Control (normal saline)
	100%	40%	60%	

Discussion and Conclusion

This study tended to evaluate the effect of venous granitometry on shivering control during cesarean section under spinal anesthesia. First, intervention and control groups were evaluated in terms of demographic data. There was no significant difference in mean age, weight, mean anesthesia duration, mean duration of surgery and mean central temperature (P>0.05), while there was a significant difference between two groups in terms of frequency and rate of shivering; in the intervention group, shivering was lower than the control group (P=0.001). In the first 15 minutes of administration of Granisetron, 10 patients (20%) experienced shivering; after 15 minutes of Granisetron administration, 4 patients (8%) experienced shivering. In the first 15 minutes of administration of Granisetron, 17 controls (34%) experienced shivering; after 15 minutes of Granisetron administration, 10 controls (20%) experienced shivering. Vomiting was lower in the intervention group than control group (P=0.003) and nausea was lower in the intervention group than the control group (P=0.002); this difference was significant. Studying 132 patients, Sajedi et al (2008) showed that no patients in Granisetron group and 6 controls experienced shivering, which was a significant difference. This is consistent with the current study (14). Studying 90 patients, Iqbal et al (2009) showed that intervention group (Granisetrone) significantly decreased shivering compared to control group, which is consistent with current study (15). Umar and Shayma (2014) studied 117 patients (58 interventions and 59 controls). They found no significant difference in shivering rate and degree between two groups (P>0.05). Moreover, vomiting and nausea decreased in 6 patients (10.3%) and 16 controls (27.1%) 12 hours after surgery (1). Sagir et al. (2009) showed that 22 controls and 6 patients receiving granisetron and 7 patients receiving graniestrone and ketamine and no patients receiving ketamine experienced shivering; this is consistent with current study (16). Eldaba et al. (2012) compared children aged 2-5 years in intervention group receiving 10 μg/kg intravenous granitometry and control group receiving 10 ml intravenous normal saline after spinal anesthesia. No shivering was observed in the intervention group, which is consistent with current study (17). Kim et al. (2010) examined the effect of Ramestrone, a 5-HT_3 antagonist, in patients undergoing knee arthroscopy. In the intervention group, 2 patients and 9 controls receiving normal saline experienced shivering; this difference was significant (P = 0.038) (13). Mohammadi et al. (2015) showed no significant difference in mean central body temperature; moreover, there was a significant difference in 4 patients in the intervention group (Granisetron) (8%) and 27 patients in the normal saline group (54%) during the postoperative period treated with pethidine (P = 0.002). Nausea was lower in 10 patients (20%) and 30 controls (60%); this difference was significant (6). Through a double-blind random study, Mandira et al (2012) administered intravenous 40 μg/kg Granisetron and placebo to 80 patients and 40 controls. Immediately after closing the embryo's umbilical cord, nausea and vomiting were observed after 24 hours of spinal anesthesia. During 0-4 hours, no nausea and vomiting were observed in 80% of the intervention group and 45% of the patients in the control group (18).

The results of this study showed that administration of Granisetron is associated with a significant reduction in incidence of shivering in candidate mothers for cesarean section. Therefore, shivering prevention reduces the rate of disease, which is one of the main advantages of treatment with granistron. Other advantages of Granisetron treatment include a reduction in frequency of vomiting in patients; reducing the frequency of vomiting during or after surgery reduces its complications, including hemodynamic changes and aspiration. It is recommended to conduct more studies with larger sample size to support the results and evaluate long-term exposure of patients with granisetron and marlenale saline.

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