

## EFFECTS OF TRAMADOL ON SHIVERING POST SPINAL ANESTHESIA IN ELECTIVE CESAREAN SECTION

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### ABSTRACT

**Background and Objective:** Post operative shivering is a complication commonly observed in post spinal anesthesia. For prevention and treatment of this complication different drugs are used. This study evaluated the effects of tramadol for post operative shivering prevention in parturients carried out by help of spinal anesthesia (SA) for cesarean section.

**Methodology:** In this randomized double blind cross-sectional study, 90 patients who were candidates for cesarean section with American Society of Anesthesiologist (ASA) I or II, from April 2005 until February 2006 were randomly allocated to one of two groups (study and control). All patients underwent spinal anesthesia. Near the end of operation, 1mg/kg tramadol in 20ml (diluted by normal saline) to study group and 20ml of normal saline to control group was slowly injected intravenously. Patients were evaluated regarding their hemodynamic signs, arterial oxygen saturation percentage, oral temperature, presence and intensity of shivering and nausea and vomiting. Collected data was analysed by using of Chi-square test.

**Results:** Thirty nine patients (86.6%) in control group had shivering, while only four patients (8.8%) in study group had shivering. Thirty three patients (73.3%) of control group experienced moderate shivering and six patients (13.3%) experienced mild shivering. In study group two patients (50%) had moderate shivering and two patients (50%) experienced mild shivering. Neither group experienced severe shivering. Therefore between the two groups a significant difference ( $P < 0.001$ ) was seen. There were no significant differences between the two groups according to heart rate, systolic and diastolic blood pressure, oxygen saturation percentage, nausea and vomiting and body temperature of the patients.

**Conclusions:** Tramadol is an effective drug in prevention of post spinal anesthesia shivering. In addition, this does not lead to any hemodynamic complications. As such drug is safe and effective for prevention of post spinal anesthesia shivering.

**KEY WORDS:** Tramadol, Spinal anesthesia, Post spinal anesthesia, Shivering.

Pak J Med Sci January - March 2009 Vol. 25 No. 1 12-17

### How to cite this article:

Javaherforoosh F, Akhondzadeh R, Aein KB, Olapour A, Samimi M. Effects of Tramadol on shivering post spinal anesthesia in elective cesarean section. Pak J Med Sci 2009;25(1):12-17.

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- \* Received for Publication: April 15, 2008
- \* Revision Received: October 15, 2008
- \* Revision Accepted: October 16, 2008

### INTRODUCTION

Post operative shivering is very uncomfortable for patients and may interfere with monitoring of electrocardiogram, blood pressure, and pulse oxygen saturation. Its incidence has been reported 50%-60% in different reports.<sup>1,2</sup> This complication generally occurs following unwanted hypothermia during operation.<sup>3,4</sup> It

increases oxygen consumption, heart rate, cardiac output, lactic acidosis, and carbon dioxide production, hemodynamic changes and increased pain in site of operation;<sup>5</sup> thus, it may cause distress to patients with a low cardiac pulmonary reserve.

To prevent and treat this complication, warming of the operative room and patient, administration of warm IV liquids, moist and warm gases can be used.<sup>1,2</sup> In addition a variety of medications are used which include meperidine,<sup>4</sup> clonidine, ketanserin,<sup>6</sup> anticholinergics,<sup>7</sup> opiate agonists, dexamethasone and finally tramadol.<sup>8-16</sup>

Tramadol hydrochloride, a centrally-acting analgesic drug, is effective in the treatment of shivering after spinal anesthesia (SA) in parturients.<sup>9</sup> In addition to a  $\mu$ -opioid agonist effect, it exerts a modulatory effect on central monoaminergic pathways, inhibiting the neuronal uptake of noradrenalin (pain stimulant) and serotonin in spinal cord and encourages hydroxytryptamine secretion which effects on body temperature regulation center.<sup>12,17,18</sup> It has less side effects (especially respiratory depression and nausea and vomiting) than other  $\mu$  receptor agonists.<sup>12</sup>

Chan et al.,<sup>12</sup> compared 0.25 and 0.50 mg/kg of tramadol for prevention of shivering in pregnant women who had undergone spinal anesthesia.<sup>9</sup> Dewitt et al.,<sup>12</sup> studied 2mg/kg and Mathew et al.,<sup>1</sup> studied 1mg/kg of tramadol for prevention and treatment of shivering. This prospective, double-blind, randomized clinical study was performed to evaluate one mg/kg of tramadol in prevention of shivering in post spinal anesthesia in patients who had undergone cesarean section.

## METHODOLOGY

After obtaining approval from the Ahwaz University of medical sciences research committee, this study was carried out as a randomized double blind cross-sectional study. Ninety obstetric patients (ASA physical status I or II, aged 18-40 years) scheduled for cesarean delivery under spinal anesthesia with no prior

medication in Imam Khomeini hospital, from April 2005 until February 2006 were included in this study. Parturients with hyperthyroidism and cardiopulmonary were excluded. Shivering was graded as: 0=no shivering, 1=shivering in face and head (mild), 2=shivering in face and head and upper extremity (moderate), 3=shivering in face, head, upper and lower extremities (severe).<sup>19</sup> Body temperature was monitored with a mercurial thermometer at the start of spinal anesthesia and treatment for shivering. The temperature of the operating room was between 21-23. Standard monitoring was used. After obtaining written consent, patients were divided into two groups of study and control with 45 patients in each group. The patients received 10ml/kg Ringer lactate IV and then their vital signs (heart rate, systolic and diastolic blood pressure) and arterial oxygen saturation percentage was recorded. Spinal Anesthesia (SA) was instituted in sitting position at the lumbar vertebrae 3-4 interspace by use of size 25 needle with lidocaine 5% 50-75 mg (depending on patients' height) before they were operated on.

During operation, heart rate and arterial oxygen saturation percentage were measured by pulse oxymetry equipment and their blood pressure by a non-invasive sphygmomanometer. Patients were supplemented with oxygen 6L/minutes. Face was covered with mask and sheets but not actively warmed during anesthesia and surgery. Near the end of operation, first the patients' vital signs and arterial oxygen saturation percentage were recorded, then 1mg/kg tramadol with 20ml (diluted by normal saline) was slowly injected intravenously in study group and 20ml of normal saline in the control group. Immediately at the end of injection (minute 0) and at minutes five, ten and fifteen after injection their vital signs and arterial oxygen saturation percentage were recorded. The post operative shivering and its severity, hemodynamic changes, nausea and vomiting and body temperature were also evaluated.

Temperature conditions of the operating room and recovery room were the same for all

Table-I: Demographic data of patients

Parameter	Tramadol	Placebo
Age (years)	26.8(4.5)	27.8 (5.1)
Heart rate	81.4(16.5)	88 (13.9)
Systolic blood pressure (mm Hg)	121.5(17.7)	125 (11.9)
Diastolic blood pressure (mm Hg)	74.1(9.7)	78.3 (11.8)
Arterial oxygen saturation %	99.68(3.54)	99.57 (4)

patients. Patients who experienced shivering during operation or had a history of convulsion or used antidepressant drugs and those who were transfused blood during the operation were excluded from the study. Collected data were analyzed by using the Chi-square test.

### RESULTS

This study enrolled 90 women with ASA 1 and/or 2 who were divided into control and study groups. There were no significant differences among the two groups as regards average age, systolic and diastolic blood pressure, body temperature and heart rate (Table-I). Four patients (8.8%) from study group and 39 patients (86.6%) from control group experienced shivering, thus there were significant difference between the two groups ( $P < 0.001$ ). 4.4% of parturients experienced mild shivering and 4.4% had moderate shivering in study group whereas 13.3% had mild shivering and 73.3% had moderate shivering in control group. Therefore from the point of shivering severity there was a significant difference ( $P < 0.001$ ). Severe shivering was not noticed in both the groups (Table-II).

Mean heart rate in the study group in the 5<sup>th</sup> minute showed a significant increase ( $P < 0.005$ ), but at 10<sup>th</sup> and 15<sup>th</sup> minutes did not

show any significant changes (Table-III). Similarly in both groups mean systolic and diastolic blood pressure did not show any significant difference (Table-III). As regards arterial oxygen saturation percentage, there was no significant statistical difference in both groups. Meaningful statistical differences as regards mean oral temperature did not exist between the two groups either (Table-IV). Since 30% of patients experienced nausea and vomiting in both groups, hence there was no significant difference.

### DISCUSSION

Post operation shivering is one of the unwanted and common complications. The exact mechanism of shivering under spinal anesthesia has not been fully established. The possible mechanisms of shivering during SA in parturients result from central thermoregulation. Pharmacologic drugs remain the most popular agents for treatment and prevention of shivering. In the present study effects of tramadol on reduction of shivering was investigated.

In this study, the incidence of shivering in the tramadol group (8.8%) was less frequent than in the control group (86.6%), which give a significant statistical difference ( $P < 0.001$ ). According to shivering severity, in tramadol

Table-II: Incidence of shivering and different degrees of shivering after injection of tramadol and/or placebo

Group Shivering severity	Zero		P.V	One		P.V	Two		P.V	Three	
	No.	%		No.	%		No.	%		No.	%
Tramadol	91.1	41	<0.001	4.4	2	<0.001	4.4	2	<0.001	–	–
Placebo	13.3	6	–	13.3	6	–	73.3	33	–	–	–

Table-III: Average of severity of homodynamic changes after injection of tramadol and/or placebo

Time of measurement	Group	Mean systolic blood pressure	Mean diastolic blood pressure	Mean heart rate	Arterial oxygen saturation %
Minute 0	Tramadol	119	69	87	99.68
	Placebo	121	72	96	99.57
Minute 5	Tramadol	120	69	95	99.53
	Placebo	118	70	96	99.56
Minute 10	Tramadol	120	70	93	99.53
	Placebo	118	70	95	99.62
Minute 15	Tramadol	120	68	91	99.62
	Placebo	118	68	94	99.62

group 50% experienced shivering grade<sup>2</sup> and 50% grade<sup>22</sup> whereas in control group only 13.3% experienced shivering grade<sup>2</sup> and 73.3% had shivering grade.<sup>22</sup> Therefore shivering severity was clearly lower in patients who used tramadol ( $P < 0.001$ ).

Tramadol is effective in preventing of post anesthetic shivering. Billota et al<sup>13</sup> compared tramadol and nefopam with placebo for shivering prevention and concluded that nefopam had a greater effect than tramadol and tramadol had a greater effect than placebo in prevention of shivering. Dewitt et al.,<sup>15</sup> compared tramadol of 0.5, 1 and 2 mg/kg with placebo and concluded that tramadol in treatment of post operation shivering is quite effective and has no unpleasant effects especially in patients with low cardio-pulmonary reserve. In the study by Chan et al.,<sup>9</sup> IV tramadol (0.25mg/kg) effectively controlled shivering during cesarean delivery under regional anesthesia with minimal side effects; however, increasing the tramadol dose to 0.5mg/kg did not increase its therapeutic effect.

Tramadol's distinct features in the treatment of shivering is its weak sedative and smaller respiratory depressive properties than morphin, particularly in parturients and

patients with low cardiopulmonary reserve. Tramadol inhibits the neuronal reuptake of norepinephrine and 5-hydroxytryptamine, facilitate 5-hydroxytryptamine release, and activates  $\mu$ -opioid receptors. Each of these actions is likely to influence thermoregulatory control. However tramadol had only slight thermoregulatory effects. Thus, it is unlikely to provoke hypothermia or to facilitate fever. The main opioid effect of tramadol is mediated via the  $\mu$  receptor, with minimal effect at kappa or sigma binding sites. The O-desmethyl metabolite ( $M_1$ ) of tramadol and its enantiomers are bound with higher affinity than the parent compounds at  $\mu$ -opioid receptors with less affinity for kappa and sigma opioid receptors, although still with a much lower affinity than morphine. Tramadol may induce its antishivering effect via the additive or synergistic action of both kappa opioid receptor and  $\alpha_2$  adrenergic mechanisms. The interaction of kappa opioid and  $\alpha_2$  adrenoceptor mechanisms working in a complementary or synergistic manner to produce anti shivering effects seems a possible explanation.<sup>17,18,21-23</sup>

Mildeh et al.,<sup>5</sup> compared tramadol and meperidin and concluded that tramadol has

Table-IV: Mean oral temperature of the patients (in degrees Celsius)

Time Group	Minute 0	Minute 15	Minute 30	Minute 45
Tramadol	36.5	36.3	36	35.9
Placebo	36.3	36.2	35.9	35.9

no effect on the respiratory pattern and hemodynamics of the patients, whereas meperidin caused reduction in tidal volume and dropped arterial oxygen saturation percentage, while meperidin was more effective in eliminating shivering.

Anchalee Techanivate et al study<sup>16</sup> investigated whether 20µg of intrathecally administered fentanyl would influence the incidence and severity of shivering. Seventy five percent of tramadol group and 100% of fentanyl group responded to antishivering effect of these drugs. Efficiency of anti shivering effect of tramadol was similar to our report (80-87%).

In Talakoub et al study<sup>20</sup> efficacy and harm of tramadol for treatment of post spinal anesthesia shivering in cesarean section were evaluated. They compared tramadol (0.5mg/kg) with pethedin (0.5mg/kg) to control of shivering and concluded that tramadol is more effective to control of shivering but results in more nausea, vomiting and somnolence.

S.Mathew et al.,<sup>1</sup> compared 1mg/kg of tramadol with placebo. Incidence of post operative shivering was 4% in the study group and 48% in the control group. These results compare with our results. Dewitte<sup>12</sup> compared 3 mg/kg of Tramadol with placebo for shivering prevention while closing the wound and no shivering was detected in the study group, and there were no undesirable changes (hemodynamic changes). This finding was also similar to our findings.

Mathew et al study<sup>1</sup> used tramadol 1mg/kg for treating post operation shivering and no, undesirable side effects (nausea and vomiting) were noted which is comparable with our study. In addition in other studies<sup>1,8-10,15,20</sup> tramadol had no effect on blood pressure, arterial oxygen saturation percentage and body temperature. Therefore these results are all in agreement with our findings.

In conclusion, tramadol was found to be safe and effective in prevention and treatment of post SA shivering. This drug had no hemodynamic side effect and did not effect arterial oxygen saturation percentage and body tem-

perature, As such we recommend the use of this drug for prevention of post spinal anesthesia shivering.

## ACKNOWLEDGMENT

The authors wish to thank and express their appreciations to Ms. Shabab, statistical advisor and all other associates who have assisted us in this study.

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