Received: 9.6.2005 **Accepted: 27.4.2006**

Original Article

Tramadol versus meperidine in the treatment of shivering during spinal anesthesia in cesarean section

R. Talakoub, Sh. Noori Meshkati***

Abstract

BACKGROUND: The aim of this study was to evaluate the efficacy and side effects of tramadol comparing with meperidine on post-spinal shivering in cesarean section.

METHODS: In a prospective, controlled, randomized, double-blind clinical trial 73 ASA-I pregnant patients candidates of cesarean section under spinal anesthesia who had shivering postoperatively were selected and classified into two groups receiving tramadol or meperidine to control postoperative shivering. Spinal anesthesia was done by injection of epinephrinized 5% lidocaine at L_3-L_4 or L_4-L_5 segment. Pruritis, somnolence, dizziness, nausea, vomiting and the duration of shivering control were evaluated and recorded. All data were analyzed by using Fisher and Chi-square tests.

RESULTS: There were no significant differences between two groups in age (P = 0.1) and weight (P = 0.8) of patients. There was no significant difference in response rate after injection of both drugs (P = 0.3). The time elapsed from treatment to ceased shivering was significantly less (P = 0.001) but frequency of somnolence (P = 0.001), nausea (P = 0.001) and vomiting (P = 0.005) were significantly more in tramadol group. Dizziness was significantly more common in meperidine group (P = 0.001) and pruritis was not seen in any group.

CONCLUSION: Tramadol is more effective in controlling post-spinal shivering but results in more frequent nausea, vomiting and somnolence in comparison with meperidine.

KEYWORDS: Shivering, meperidine, tramadol, spinal anesthesia, cesarean section.

JRMS 2006; 11(3): 151-155

Regional anesthesia (extraxdural/subarachnoid) is a safe and popular anesthetic technique for cesarean section, both in elective and emergency situations. One of the common complications of this technique is shivering.

The origin of postoperative shivering is unclear and various mechanisms have been proposed. Shivering may happen as a thermoregulatory response to hypothermia or muscle hyperactivity with clonic or tonic patterns, and different frequencies have been reported [1]. However, in the postoperative period, muscle activity may be increased even with normothermia suggesting that other mechanisms than heat loss and subsequent decrease in core temperature may contribute to the development of shivering [2]. These include inhibited spinal reflexes, postoperative pain, decreased sympathetic activity, pyrogen release, adrenal suppression and respiratory alkalosis [1].

Shivering causes distress to the patient. It may also increase metabolic rate by up to 400%, induce arterial hypoxemia and lactic acidosis, increase intracranial pressure and it may contribute to increased wound pain [3].

Numerous pharmacological interventions have been proposed for the treatment of postoperative shivering. Some researches suggest that apart from applying radiant heat to the body surface, shivering may be treated with meperidine, clonidine or ketanserin [1]. The

*Assistant professor of Anesthesiology, Isfahan University of Medical Sciences, Isfahan, Iran.
**Anesthesiologist
Correspondence to: Dr Reihanak Talakoub, Assistant Professor of Anesthesiology, Isfahan University of Medical Sciences, Al-Zahra Hospital, Isfahan, Iran. e-mail: reihanakt@yahoo.com

relative efficacy of these different medications however, remains unclear. Tramadol has been used as an analgesic for labour pain without adversely affecting the mother or newborn [4]. In addition, it has been shown to be effective in the treatment of postoperative shivering [5]. Tramadol and meperidine are approximately equipotent with respect to analgesia [6]. However, the antishivering and analgesic effects of these two agents may be mediated via different receptors.

This prospective, double-blind and randomized clinical study was performed to compare the antishivering effects and the accompanying side effects between tramadol and meperidine for the treatment of post-spinal shivering in parturients.

Methods

After approval of the ethics committee and obtaining patient's written informed consent, 73 ASA-I parturients who subsequently developed shivering intra or postoperatively during elective or emergency cesarean section under spinal anesthesia were studied. Patients with known hypersensitivity to tramadol, those with a known history of alcohol or substance abuse, or who received intramuscular meperidine for labour pain within one hour were excluded. Spinal anesthesia was instituted at either L_3-L4 or L_4-L_5 interspace by injection of 1.5 mg 5% epinephrinized lidocaine. The volume of preloading intravenous fluid, the use of ephedrine for hypotension, and the dose of local anesthetic were determined by the attending anesthesiologists and were not affected by enrollment in the study.

All preloading fluids and drugs were given at room temperature and the operating room temperature was kept at 21-23^{o}C. Standard monitoring of non-invasive blood pressure, ECG and pulse oximeter were used and body temperature was monitored via tympanic membrane. Patients eligible for study were randomized into two groups. Group T (tramadol) received 0.5 mg/kg tramadol and group M (meperidine) received 0.5 mg/kg meperidine. Both drugs were given as slowly as intravenous injection. Anesthesiologists and patients were blind to the treatment. Randomization and blindness of the study were assured by a strict protocol.

Shivering was graded with a scale similar to that validated by Crossley and Mahajan [7]; 0 = no shivering, 1 = piloerection or peripheral vasoconstriction but no visible shivering, 2 = muscular activity in only one muscle group, 3 = muscular activity in more than one muscle group but no generalized shivering, 4 = the whole body shivering. Only parturients who developed grade 3 or 4 shivering for at least 3 min were included. Before starting the operation, two syringes contained 10 mg/ml of either tramadol or meperidine in 5 ml solution were prepared. Should the parturients develop shivering and require treatment, an anesthetic assistant not involved in any other way in the study would pick randomly from the set of sealed envelops and pick out one of the two labeled syringes as instructed in the envelop. The label on the syringe was removed before passing to the anesthesiologist and kept by the assistant until the end of the operation. The administration of pre or intra-operative opioids was not permitted. Patients were supplemented with oxygen 6 L/min by face mask and covered with sheets but not actively warmed during anesthesia. The anti-shivering effect was assessed both by the parturients and by the observing anesthesiologist. The parturients were asked to evaluate five minutes after injection the effect of the treatment as either no improvement, slight improvement, or marked improvement. The attending anesthesiologist independently recorded the time that he or she subjectively assessed the shivering to have subsided and the response rate (shivering ceased after treatment in 15 min). If shivering did not subside after 15 min, the treatment was considered not effective. Recurrence of shivering, if any, was also recorded until the parturient left the operating theatre suite. Side effects such as pruritis, somnolence, dizziness, nausea and vomiting, also blood pressure, pulse and SpO_2 were recorded before and every five minutes till 15 min after spinal anesthesia as

well as 5 min after treatment. The parturient's tympanic temperature before starting operation, in the beginning of shivering and at the cessation of shivering was measured. If parturient developed nausea and vomiting after injection of the drugs, metoclopramide 10 mg IV was administered. Data were analyzed with SPSS program, using Chi-square and Fisher test. A P-value <0.05 was considered statistically significant.

Results

Seventy-three parturients experienced shivering at grade 3 or 4. There were no significant differences between two groups with respect to age, weight and tympanic temperature at the start of spinal anesthesia (table 1).

The response rate (shivering ceased after treatment in 15 min) was 97.2% and 91.9% for groups T and M respectively (table 2). The time that elapsed from treatment to the time of ceased shivering was significantly shorter in tramadol group (2.5 ± 1.07 min) (table 2). There was a significantly more frequent incidence of nausea, vomiting and somnolence in tramadol group. But, dizziness was more common in meperidine group (table 2).

No patient in any group developed pruritis or desaturation after injection of the drugs and none of the injections were before delivery of fetus. In addition, the results of arterial blood pressure, heart rate, respiratory rate, and oxygen saturation were not significantly different before and 15 min after spinal anesthesia and also 5 min after treatment of shivering between groups.

Table 1. Patient characteristics.

Variable	Tramadol	Meperidine	P value
n	36	37	
Age (yr)	29.3 ± 2.58	32.1 ± 3.23	0.1
Body weight (kg)	67.1 ± 8.87	72.1 ± 10.4	0.8
Tympanic temperature (^{oC}) before operation	36.6 ± 0.5	36.6 ± 0.3	0.14
Shivering grade (3/4)	27/9	19/18	>0.05

Values are number or mean ± SD.

Table 2. Post-spinal shivering responses and therapeutic complications.

Variable	Tramadol	Meperidine	P value
Response rate	35 (97.2%)	34 (91.9%)	0.3
Time elapsed from treatmen to ceased shivering (min)	2.54 ± 0.78	5.03 ± 1.07	0.001
Nausea	28 (77.8%)	0(0)	0.001
Vomiting	7 (19.4%)	0(0)	0.005
Somnolence	20 (55.6%)	0(0)	0.001
Dizziness	0 (0)	10 (27%)	0.001

Values are n (%) or mean (± SD)

Discussion

The results of this study indicate that both tramadol (0.5 mg/kg) and meperidine (0.5 mg/kg) effectively treated post-spinal shivering. The mechanism of shivering under general anesthesia is not fully understood. Possible contributing factors are a decrease in core temperature and misinformation from receptors. A decrease in core temperature may be due to 1) sympathetic block which results in peripheral vasodilatation, increased cutaneous blood flow, and subsequent increased heat lost via skin, 2) a cold operating room and/or the rapid infusion of crystalloid solutions at room

temperature or 3) the direct effects of cold anesthetic solutions upon thermo-sensitive receptors within the spinal cord.

Treatment modalities have included covering the patient with blankets, application of radiant heat and warming the operating room suits [8-12]. The use of warm local anesthetic solutions or warm intravenous fluid has met with varying degrees of success [11,13]. Our study was designed to standardize these possible confounding factors while reflecting the usual practice in our institution. Operating room temperature was held constant at 21 - 23^{o}C, intravenous fluids and drugs were administered at room temperature. Tympanic temperature was also recorded in the beginning of the operation.

Tramadol is an analgesic with agonist properties on opioid receptors. It also activates the monoaminergic receptors of the descending spinal inhibitory pathway of pain. The main opioid effect of tramadol is mediated via the μ-receptor, with minimal effect at kappa or sigma binding sites. Tramadol also inhibits in vitro synaptosomal noradrenaline and serotonin uptake, which contributes to its analgesic effects [6]. Our study demonstrated that tramadol, in a dose of 0.5 mg/kg controlled shivering in parturients undergoing cesarean section under regional anesthesia. It is also shown that the incidence of nausea, vomiting and somnolence at this dose were more in tramadol group which is different with the finding of Yu-chuan Tsai in this respect [14].

Based on our study it was not possible to draw conclusions about the mechanisms involved in the anti-shivering effect of tramadol. For meperidine, the effect is most likely mediated via receptors other than the μ-receptor, in particular the K-receptor. This is supported by observations that meperidine controlled shivering better than morphine and fentanyl, and that the anti-shivering effect of meperidine was not reversed by low dose, but by high dose naloxone [15,16].

Tramadol has minimal K-receptor activity [6]. The μ-receptor activity of tramadol was also unlikely to be important in the effect we observed.

Pure μ-agonists such as morphine and fentanyl do not have significant anti-shivering effects [15]. Thus, it is highly probable that the anti-shivering effect of tramadol was mediated via its serotonergic or noradrenergic activity or both.

Our study did not control tightly the various factors which might influence the incidence of shivering, such as the temperature of drugs and intravenous fluids. However, this should not have affected the validity of our comparisons. First, the current study focused on the response after treatment, rather than the incidence of shivering. Second, by randomization, both groups had been subjected to a similar degree of influence of these factors.

In this study, we have performed a comparison between tramadol and meperidine. However, tramadol does have advantages over meperidine in that it is not a controlled drug and it causes less respiratory depression and dizziness than other opioids at equivalent dosages [17,18].

In conclusion, both tramadol (0.5 mg/kg) and meperidine (0.5 mg/kg) effectively treated patients with post-spinal shivering, but the more frequent incidence of side effects of tramadol such as nausea, vomiting and somnolence may attenuated its use as an anti-shivering drug. Because of these side effects of tramadol, further study is required to find the minimum effective dose of tramadol to cease shivering.

References

1. Miller R. **Anesthesia.** 4 ed. Philadelphia: Lippincott Williams & Wilkins, 1994.
2. Horn EP, Sessler DI, Standl T, Schroeder F, Bartz HJ, Beyer JC et al. **Non-thermoregulatory shivering in patients recovering from isoflurane or desflurane anesthesia**. *Anesthesiology* 1998; 89(4):878-886.

3. Chan AM, Ng KF, Tong EW, Jan GS. **Control of shivering under regional anesthesia in obstetric patients with tramadol**. *Can J Anaesth* 1999; 46(3):253-258.
4. Viegas OA, Khaw B, Ratnam SS. **Tramadol in labour pain in primiparous patients. A prospective comparative clinical trial**. *Eur J Obstet Gynecol Reprod Biol* 1993; 49(3):131-135.
5. Pausawasdi S, Jirasirithum S, Phanarai C. **The use of tramadol hydrochloride in the treatment of post-anesthetic shivering**. *J Med Assoc Thai* 1990; 73(1):16-20.
6. Lee CR, McTavish D, Sorkin EM. **Tramadol. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute and chronic pain states**. *Drugs* 1993; 46(2):313-340.
7. Crossley AW, Mahajan RP. **The intensity of postoperative shivering is unrelated to axillary temperature**. *Anaesthesia* 1994; 49(3):205-207.
8. Chamberlain DP, Chamberlain BD. **Changes in the skin temperature of the trunk and their relationship to sympathetic blockade during spinal anesthesia**. *Anesthesiology* 1986; 65(2):139-143.
9. Pflug AE, Aasheim GM, Foster C, Martin RW. **Prevention of post-anaesthesia shivering**. *Can Anaesth Soc J* 1978; 25(1):43-49.
10. Waters HR, Rosen N, Perkins DH. **Extradural blockade with bupivacaine. A double blind trial of bupivacaine with adrenaline 1-200,000, and bupivacaine plain**. *Anaesthesia* 1970; 25(2):184-190.
11. Walmsley AJ, Giesecke AH, Lipton JM. **Contribution of extradural temperature to shivering during extradural anaesthesia**. *Br J Anaesth* 1986; 58(10):1130-1134.
12. Sharkey A, Lipton JM, Murphy MT, Giesecke AH. **Inhibition of postanesthetic shivering with radiant heat**. *Anesthesiology* 1987; 66(2):249-252.
13. Webb PJ, James FM, III, Wheeler AS. **Shivering during epidural analgesia in women in labor**. *Anesthesiology* 1981; 55(6):706-707.
14. Tsai YC, Chu KS. **A comparison of tramadol, amitriptyline, and meperidine for postepidural anesthetic shivering in parturients**. *Anesth Analg* 2001; 93(5):1288-1292.
15. Pauca AL, Savage RT, Simpson S, Roy RC. **Effect of pethidine, fentanyl and morphine on post-operative shivering in man**. *Acta Anaesthesiol Scand* 1984; 28(2):138-143.
16. Kurz M, Belani KG, Sessler DI, Kurz A, Larson MD, Schroeder M et al. **Naloxone, meperidine, and shivering**. *Anesthesiology* 1993; 79(6):1193-1201.
17. Houmes RJ, Voets MA, Verkaaik A, Erdmann W, Lachmann B. **Efficacy and safety of tramadol versus morphine for moderate and severe postoperative pain with special regard to respiratory depression**. *Anesth Analg* 1992; 74(4):510-514.
18. Vickers MD, Paravicini D. **Comparison of tramadol with morphine for post-operative pain following abdominal surgery**. *Eur J Anaesthesiol* 1995; 12(3):265-271.