ORIGINAL ARTICLE

The effects of warm and cold intrathecal bupivacaine on shivering during delivery under spinal anesthesia

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ABSTRACT

Background: Shivering associated with neuraxial anesthesia is a common problem that is uncomfortable for patients; it is of unknown ethnology and has no definite treatment. **Purpose:** The purpose of this study was to compare the effects of warm intrathecal bupivacaine stored at 23°C and cold intrathecal bupivacaine stored at 4°C on shivering during delivery under spinal anesthesia. **Methods:** Seventy-eight parturient women scheduled for nonemergency cesarean delivery were enrolled in the study and separated into 2 groups. The standard group received 10 mg of heavy bupivacaine 0.5% stored at room temperature (23°C) plus 10 μg of fentanyl intrathecally (warm group), and the case group received 10 mg of heavy bupivacaine 0.5% stored at 4°C plus 10μg of fentanyl intrathecally (cold group). Data collection, including sensory block level, blood pressure, core temperature, and shivering intensity, was first performed every minute for 10 min, then every 5 min for 35 min and, finally, every 10 min until the sensory level receded to L4. **Results:** There were no differences between the 2 groups in the amount of bleeding, pulse rate, oxygen saturation, neonatal Apgar, and incidence of vomiting. The incidence and intensity of shivering decreased in the warm group ($P=0.002$). **Conclusion:** Warming of solutions can reduce the incidence and intensity of shivering in parturient candidates for cesarean delivery under spinal anesthesia.

Key words: *Cesarean, cold bupivacaine 0.5%, intrathecal, shivering, warm bupivacaine 0.5%*

INTRODUCTION

Shivering associated with neuraxial anesthesia is a frequent complication that occurs in up to 55% of patients.[1] Shivering is uncomfortable for the patient and may interfere with the monitoring of electrocardiogram, blood pressure (BP), and oxygen saturation.[2] The metabolic and hemodynamic consequences of shivering include increased disbursement of cardiac and systemic energy, increased oxygen consumption and carbon dioxide production, and increased cardiac work.[3] Those effects are particularly bothersome in the obstetrical population.[4] The mechanisms chiefly responsible for shivering in patients undergoing surgery are intraoperative temperature loss; increased sympathetic tone, pain, and systemic release of pyrogens; and the direct effect of local anesthetic temperature on temperature-sensitive neurons in the spinal cord.[5-10] The central nervous system (CNS), including the spinal cord, receives thermal signals from the body and plays an essential role in the regulation and maintenance of body temperature. Although many studies have been undertaken to treat shivering after spinal anesthesia,[4-7] little is known about the exact etiology of shivering and the best way to prevent it.[2,7]

Spinal anesthesia for cesarean section continues to be a popular technique, as it provides many advantages, such as rapid onset, high success rate, minimal maternal and fetal drug exposure, and minimal maternal discomfort.[11] Mehta *et al.* confirmed that the combined use of warm parenteral fluids and warm local anesthetics significantly reduced the incidence of shivering Some researchers have studied the effects of local anesthetic temperature after injection into the epidural space on shivering.[10] The result of another study suggested the existence of thermosensory

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mechanisms in the human spinal canal and the effect of warming epidural anesthetic solutions prior to injection to reduce the incidence of shivering[12] but in another study Ponte *et al*. tested the hypothesis that cooling the extradural space may provoke shivering and concluded that shivering in extradural anesthesia does not result solely from cooling of the extradural space.[13] However, there is some controversy and no definite answer.[10-13] The purpose of this study was to evaluate our hypothesis "warm intrathecal bupivacaine is associated with less shivering and hemodynamic changes than cold intrathecal bupivacaine in parturient candidates for elective surgery under spinal anesthesia."

METHODS

This randomized, double-blinded clinical trial was conducted between November 2009 and November 2010 in the educational hospitals of Bushehr University of Medical Sciences, Bushehr, Iran. The study was approved by the ethics committee of Bushehr University of Medical Sciences and is registered at clinicaltrials.gov database (Reference No. IRCT201106271936N6). This study was performed according to the requirements of the Declaration of Helsinki.

After attaining informed consent the night before surgery by a physician not involved in study 78 parturient (ASA physical status I or II) scheduled for elective cesarean delivery under spinal anesthesia enrolled in this study. Subjects with contraindications to regional anesthesia, hypersensitivity to amide local anesthetics, history of headache, or severe pre-eclampsia were excluded.

The patients were randomly divided with a computerized random number generator into 2 equal groups for spinal anesthesia according to numbers inserted in sealed envelopes. Before the spinal anesthesia was performed, the patients were placed under standard monitoring and received IV lactated Ringer's solution 10 mL/kg. Oxygen was provided during anesthesia, and the patients were covered with drapes but not actively warmed. All fluids were warmed to 37°C. The patients were divided equally into 2 groups (n = 39). The standard group received 2 mL heavy bupivacaine 0.5% (10 mg) stored at room temperature (23°C) plus 10 μg of fentanyl (warm group) by using properly calibrated temperature. The case group received 2 mL heavy bupivacaine 0.5% (10 mg) stored at 4°C plus 10 μg of fentanyl (cold group). Spinal anesthesia was performed in a sitting position at the L4–L5 interspace with a midline approach, using a 25-gauge Quincke needle. Solutions were prepared by a second anesthesiologist so that the anesthesiologist performing the spinal block was blinded to the drug that was injected. The patient was placed in a supine position with left uterine displacement.

The time at the end of the injection was defined as T0. Sensory anesthesia was evaluated by pinprick at 1-min intervals for 10 min, 5-min intervals for 35 min, and then 10-min intervals until regression to L4. Once patients were in the postanesthesia care unit, motor blockade was assessed with the Bromage scale[14]: 1, unable to move feet; 2, able to move feet only; 3, just able to move the knees; and 4, full flexion of knees and feet. BP was measured simultaneously with sensory levels and shivering intensity. Hypotension was defined as a decrease in systolic BP to <90 mmHg or 30% less than baseline value and was treated with 5–10 mg of ephedrine IV. Bradycardia (heart rate <50) was treated with IV atropine 0.5 mg. Pruritus was treated with diphenhydramine 25 mg intravenously. Vomiting was scored yes or no; nausea was scored none, mild, moderate, or severe on a verbal patient/examiner/scale and metoclopramide 10 mg IV was administered for moderate to severe nausea and vomiting. Supplemental intraoperative analgesia was limited to IV fentanyl (1–2 μg/kg), which was standardized and used as a rescue dose if necessary. Tympanic temperature was monitored every 20 min on one side (right ear). Operating room temperature was maintained at 23°C. Shivering was graded on a scale described by Crossley and Mahajan[15]: 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 not generalized shivering; and 4, shivering involving the whole body. Pruritus, nausea, and vomiting were noted as they occurred. Apgar scores were recorded at 1, 5, and 10 minutes. All patients were enquired on the first and second postoperative days regarding occurrence of headache, backache, paresthesia, or pain in thighs, buttocks, leg, and so on.

The duration of surgery and weeks of pregnancy were all recorded precisely. The demographic data were collected by a blinded observer. The demographic data, except vomiting and maximal intensity of shivering, were compared using Kruskal–Wallis test. The maximal intensity of shivering and vomiting were compared using Chi-square test. To obtain at least 50% reduction in expected incidence, with α error of 0.05 and α error of 0.2, according to Altman's curve, a sample size of 39 patients per group was needed. In the analysis, $P<0.05$ was considered as statistically significant.

RESULTS

There were no significant differences between the groups in terms of demographic or surgical data [Table 1]. The

Table 1: Patient demographic and surgical data

	Mean (SD)		*P* value
	Warm bupivacaine	Cold bupivacaine	
Age	29 (5)	27 (5)	0.073
Weight	81 (10)	80 (8)	0.642
Shivering (incidence %)	8.3	39.1	0.001*
Amount of bleeding	307 (91)	310 (92)	0.064
Pulse rate (per min)	97 (11)	98 (10)	0.792
Operation duration (min)	34 (9)	32 (8)	0.356
Gestational age (weeks) median (range)	38 (37–39)	38 (36–40)	0.848
Apgar, median (range)	8 (6–9)	8 (6–9)	1.000
Min 1	9 (7–10)	9 (7–10)	1.000
Min 5	9 (7–10)	9 (7–10)	1.000
Min 10			
Vomiting (incidence %)	23.08	23.08	1.000
Highest segment blocked (median)	T2	T2	1.000
Time to reach highest block (min)	12±7	13±6	
Patient with residual block (Min=100) (percent of patient)	38	35	0.732
Patient with residual block (Min=150) (percent of patient)	4	3	1.000

*P<0.05 were considered significant

amount of bleeding, Pulse Rate, oxygen saturation, time of surgery, neonatal Apgar, and vomiting were equal in the groups after each time interval [Table 1].

Time to highest sensory level and maximum number of segments blocked also regression of sensory and motor blocks showed no difference between the groups [Table 1].

We lost 1 patient in the warm group due to failure of the spinal block. There was no need for rescue doses of fentanyl in either group. There were no signs of bradycardia or respiratory depression in either of the groups. None of the patients suffered from postspinal headache or other neurologic complications.

The incidences of shivering were 8.3% in the warm group and 39.1% in the cold group; P<0.05 [Figure 1].

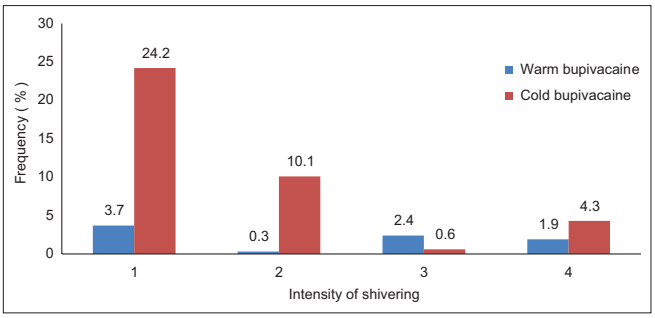

Figure 1: Frequency of intensity of shivering in warm and cold bupivacaine groups

DISCUSSION

This study is the first to investigate the effects of warm and cold local anesthetics injected into the subarachnoid space in humans. According to the obtained results, warming bupivacaine to 23°C reduces the incidence and intensity of shivering without affecting other hemodynamic variables.

Internal body temperature control in homeothermic animals depends on thermal input from thermosensitive neurons located throughout the body, both inside and outside the CNS.[16] Thermosensitive neurons in one site of the CNS are connected to thermosensitive neurons in other sites, thus forming a neural network of thermosensitive neurons that are hierarchically organized in the CNS.[17,18]

Temperature sensitivity of the spinal cord has clearly been established through *in vivo* experiments, by local changes in the temperature of the spinal cord evoking adequate heat gain and heat loss mechanisms, such as shivering, panting, and vasomotion, and by characterizing warm- and cold-sensitive ascending fibers of the anterolateral tract during thermal stimulation of the spinal cord.[19] *In vitro* experiments have confirmed the existence of intrinsically thermosensitive neurons within the spinal cord by recording extracellularly from neurons in slices of rat lumbar spinal cord.[19,20] Cooling of the thoracic part has been shown to produce tachycardia, while cooling of the lumbosacral part has resulted in bradycardia.[16]

In one study, Ponte *et al.* tested the hypothesis that cooling the extradural space may provoke shivering, by giving three 80-mL extradural injections of warm (39.8±1.2°C) or cold (17±2.2°C) saline to 4 healthy volunteers, while recording central temperature and electromyographic activity from 4 muscles.[13] The first injection (always cold) did not induce shivering in any of the subjects. The second and

third injections, randomly cold or warm, were given after induction of shivering with cold blankets, but they had no detectable effects on the intensity of shivering. This finding suggests that shivering in extradural anesthesia does not result solely from cooling of the extradural space. The difference between our results and those of this above-mentioned study might be related to the site and temperature of the injected saline.

Saito and colleagues tested the onset of hypothermia and the intensity of shivering during spinal and epidural anesthesia in patients undergoing cesarean delivery.[20] Spinal anesthesia was induced by injecting 2 mL 0.5% dibucaine into the L4–L5 interspace, and epidural anesthesia was induced with 20 mL 2% mepivacaine injected into the L2–L3 interspace. Tympanic membrane temperatures initially decreased more quickly during spinal anesthesia, but subsequently decreased at a rate of 0.5°C/h in both the groups. The researchers concluded that the onset and incidence of shivering did not differ significantly between the 2 groups; however, shivering intensity was significantly reduced during spinal anesthesia.

In another study, 30 patients undergoing postpartum tubal ligation under extradural anesthesia initially received bupivacaine at 4°C, and the incidence of shivering was 47%.[21] Further bupivacaine warmed to 41°C was injected into 8 patients in whom the resultant shivering was marked. In four of these patients, the shivering stopped. The authors concluded that thermosensitive tissue within the spinal canal contributes to the shivering observed in association with extradural anesthesia. This finding confirms our findings in this study.

The role of the temperature of the local anesthetic injected extradurally on shivering during epidural analgesia was investigated in another study.[12] Forty patients admitted for elective cesarean section under epidural anesthesia were divided into 2 equal groups. Bupivacaine warmed to 37°C was given to 20 patients, and 20 were given bupivacaine stored at 4°C. The overall incidence of shivering was 27.5%; 2 patients in the warm group and 9 in the cold group shivered. The authors concluded that there are thermosensory mechanisms in the human spinal canal and, therefore, epidural anesthetic solutions should be warmed to body temperature prior to injection to reduce the incidence of shivering. Unfortunately, there is no data about the effect of local anesthetic temperature on hemodynamics in this study; however, in the present study we found elevated systolic and diastolic blood pressure in the case group, as shivering can cause vasoconstriction and subsequent elevation of blood pressure. Although the site of the local anesthetic injection was different in this study, all of the findings confirm those of the present study.

There are some limitations in our study. First, it was impossible to keep the temperature of bupivacaine exactly at 40°C in case group because the small vial of bupivacaine would quickly change its temperature based on the ambient temperature. For overcoming this problem we kept a cooling system too near to the operating room and drug was transported to the operating room after receiving cerebrospinal fluid (CSF), thus the time for change of drug was too short. Second, in our hospital it was impossible to record temperature of CSF continuously. It can help us to explain and realize more of our results.

CONCLUSION

Shivering continues to be a common problem after spinal anesthesia for cesarean delivery. The etiology of this symptom is unknown, and there is no definite treatment. As shown in this study, warm bupivacaine injected into the subarachnoid space can decrease the incidence and intensity of shivering with no effect on modifying the efficacy of the sensory and motor block or its maximum spread, need for analgesic drugs, pruritus, or vomiting.

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