Original Article

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Anaesthesia Section

In Spinal Anaesthesia for Cesarean Section the Temperature of Bupivacaine Affects the Onset of Shivering but Not the Incidence: A Randomized Control Trial

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ABSTRACT

Introduction: Postoperative shivering is a frequent event after cesarean section under spinal anaesthesia. Shivering is uncomfortable for the patient and may interfere with monitoring. The exact aetiology of shivering is unknown and therefore has no definite treatment.

Aim: The temperature of injectate affects the spread of drug and so its effect. Therefore the aim of this study was to compare the effect of temperature of bupivacaine on post-spinal shivering in cesarean section.

Materials and Methods: In this prospective, randomized, controlled, double-blind clinical trial 105 ASA-I/II pregnant women scheduled for caesarean section under spinal anaesthesia were selected and randomized into three groups of 35 each. In all pregnant women spinal anaesthesia was achieved with 2.2 ml of 0.5% hyperbaric bupivacaine given either at L3-L4 or L4-L5 interspace. The temperature of bupivacaine was adjusted to 4°C (group T_4), 22°C (group T_{22}) and 37°C (group T_{37}). Shivering characteristic, onset and incidence was noted. All three groups were compared using analysis of variance (ANOVA), adverse effects was compared using chi-square test and Kruskal-Wallis H-test. The p-value < 0.05-considered as significant and p-value <0.01-considered highly significant

Results: There were no differences between the groups regarding age, weight, height, amount of fluid used and blood loss. The incidence of shivering was 51.42%, 51.42% and 45.71% in group T_4, group T_{22} and group T_{37} respectively, this difference in the incidence was statistically not significant (p=0.858). However, the onset of shivering was earliest (9.87±1.82 min) in group T_4 as compared to 14.27±3.02 min and 12.16±2.89 min in group T_{22} and group T_{37} respectively and this difference in the onset was highly significant (p= 0.0001)

Conclusion: In spinal anaesthesia for cesarean section, the temperature of bupivacaine does not influence the overall incidence of post spinal shivering; however cold bupivacaine can provoke early onset of shivering.

Keywords: Cold bupivacaine, Hypothermia, Post spinal shivering

INTRODUCTION

Spinal anaesthesia is considered a popular and well accepted technique for cesarean section, as it has certain advantages over general anaesthesia such as rapid onset, high success rate, less maternal and fetal side effects with minimal maternal discomfort [1]. However, as per a review of 21 studies, the shivering was found to be well recognized side effects of spinal anaesthesia and 55% incidence of shivering related to neuraxial anaesthesia was observed [2]. As a protective mechanism the shivering results in increase heat production of body through muscle contraction; however its side effects such as increased oxygen consumption, increase levels of pain usually interferes in monitoring of the patient [3]. Apart from pain, nausea and vomiting the shivering is also associated with patient discomfort, dissatisfaction and adverse postoperative outcomes such as increase surgical site bleeding, wound infection, and morbid cardiac events in patients undergoing cesarean section [4,5]. As the exact aetiology of shivering is unknown, the best way to prevent and treat shivering after spinal anaesthesia is unclear even after several studies conducted in the past [6-9]. Previous studies have suggested the existence of thermosensory mechanisms in the human spinal canal that are responsible for reduction of incidence of shivering after injection of warm epidural or spinal anaesthetic solutions. However, influence of temperature of the drug in spinal anaesthesia on shivering is still controversial [10-12]. Therefore, we conducted this study with an objective to analyse the impact of three different temperatures of the hyperbaric bupivacaine on the incidence of post-spinal shivering in cesarean section.

MATERIALS AND METHODS

After approval from ethics committee and obtaining the written informed consent from all patients, this randomized controlled double blind study was conducted in 105 parturients during the period from June 2013 to May 2014. The parturients with singleton pregnancy and American Society of Anaesthesiologist (ASA) physical status I or II, scheduled for elective caesarean section under spinal anaesthesia were included in the study. The parturients who refused to participate or were in labour were excluded from the study. Parturients having fever, pregnancy-induced hypertension, obesity (body mass index > 35 $kg.m^{-2}$) and failure of spinal anaesthesia requiring conversion to general anaesthesia or requiring blood transfusion were also excluded from the study. The patients were randomly allocated to one of the three groups of 35 in each with computer generated randomization to receive 2.2 ml of 0.5% hyperbaric bupivacaine stored at 4°C (group T_4), 22°C (group T_{22}) and 37°C (group T_{37}). All therapeutic interventions were standardized as per the hospital protocol. The temperature in the operating room was maintained at 21°C to 23°C.

Prior to spinal anaesthesia all the parturient were placed under standard monitoring and received warm lactated ringer's solution in a dose of 20ml/kg. Fluid warmer (Level 1® HOTLINE® L-70 by Smith Medical ASD, Inc. Rockland USA) was used for perioperative fluid therapy, total volume of the fluid was noted. Spinal anaesthesia was performed at the level of L3-L4 or L4-L5 with parturient in sitting position using a 25G Quincke's spinal needle. All parturients then received the study drug. The completion of injection was considered as time zero ("time 0"). Patient was covered but not actively

Variables	Group T_4 (n=35)	Group T_{22} (n=35)	Group T_{37} (n=35)	p-value
Age (years)	27.17±3.72	26.65±3.23	27.14±3.72	0.791*
Weight (kgs)	65.74±7.55	65.34±7.85	66.25±7.75	0.885*
Height (cm)	156.31±3.64	156.71±3.44	158.22±3.76	0.070*
Gestational Age (weeks)	37.65±1.78	37.71±1.65	36.97±2.40	0.223*
ASA I/II no.	22/13	26/9	24/11	0.585*
Maximum sensory block height median (number)	T4 (30)	T5 (29)	T4 (30)	0.929*
Time to achieve maximum sensory block height (min)	6.26±0.299	6.24±0.209	6.21±0.252	0.641*
Time to achieve bromage 3 (min)	7.34±0.707	7.22±0.190	7.19±0.359	0.340*
Apgar Score at 1 min at 5 min at10 min	9 (6-9) 10 (7-10) 10 (8-10)	9 (8-9) 10 (9-10) 10 (10)	9 (6-9) 10 (7-10) 10 (8-10)	1.00* 1.00 * 1.00*
Duration of surgery (min)	58.00±5.02	55.71±6.76	57.85±6.99	0.242*
Total iv fluid used (ml)	2535±82	2465±90	2505±48	0.320*
Blood loss (ml)	564±90	579±110	573±95	0.630*

[Table/Fig-1]: Demographic profile and surgical data of the parturients.
Values are expressed in mean±SD or in numbers
*Not significant (p-value > 0.05)

warmed. The anaesthesiologist who performed the spinal block was otherwise not involved in the study thereafter. The anaesthesiologist who performed the assessment of shivering was unaware of drug used in spinal anaesthesia. The sensory block was assessed with pin prick method [13] (score 0: sharp pain; score 1: touch sensation only; score 2: no sensation) at 1 minute interval for 15 minute and every 5 minute interval thereafter till 40 minute. Time to reach maximum sensory block height (duration in minutes) and the level of maximum sensory block height (noted as 'Tn' where 'T' represents the thoracic part and 'n' represents the level of the dermatome for example T4 and T5 are the 4th and 5th Thoracic dermatome level) was observed and noted. Motor block was assessed by using Bromage scale [14] (score 0: no block; score 1: ability to flex knees but not the hips; score 2: unable to flex knees, ankle movement present; score 3: no movement possible in any lower extremity) and time to achieve Bromage score 3 was recorded and noted. The core body temperature was measured using a rectal thermometer probe and noted at an interval of 1 minute for initial 30 minute and every 5 minute thereafter till the end of surgery. Outcome parameter like post spinal shivering was graded using a scale validated by Crossley and Mahajan [15] (score 0 = no shivering; score 1= No visible muscle activity, but one or more of piloerection, peripheral vasoconstriction or peripheral cyanosis (other cause exclude); score 2= muscular activity in only one muscle group; score 3= moderate muscular activity in more than one muscle group, but not generalized shaking; score 4= violent muscular activity that involves entire body). Onset time of shivering is defined as the duration of time between "time 0" and score 1. Parameters such as onset time and the grading of the shivering were noted. In post anaesthesia care unit active warming was done with warming unit (Bair Hugger™ model 750 by Arizant Healthcare Inc. USA) in that patient who require. Duration of surgery was defined as duration of time between skin incision to last skin suture. Perioperative blood loss was calculated by gravimetric method. Hypotension was defined as a fall in systolic blood pressure (SBP) >20 % or fall in SBP to <90 mmHg from the pre anaesthetic value. Any episode of hypotension was treated with a bolus infusion of crystalloid (250ml) and or ephedrine (3-6 mg i.v.). Bradycardia was defined as decrease in heart rate < 60 beats/min and was treated with atropine 20 mcg/kg intravenously. Apgar score of the newborn was determined by the paediatrician at 1,5and 10 minutes intervals. Postoperatively, any incidence of bradycardia, hypotension, nausea/vomiting was taken into account and managed accordingly.

STATISTICAL ANALYSIS

The analysis of the data was carried out using Microsoft Office Excel 2007 (Microsoft, Redmond, WA, USA) and IBM SPSS Statistics version 20 (IBM Corp, Armonk, NY, USA). The prior related studies [2,16] were taken into account to calculate the sample size. To obtain at least 50% reduction in expected incidence of shivering, a minimum of 35 numbers of patients in each group was calculated to achieve a power of 80% and a level of significance of 0.05. Therefore a total of 105 subjects were included in the study. Data is represented as Mean±SD (standard deviation) for continuous data and frequency (percentage %) or median (range) for non-parametric data. All three groups were compared using analysis of variance (ANOVA). The proportion of adverse effects was compared using chi-square test and shivering was compared using Kruskal-Wallis H-test. The p-value < 0.05-considered as significant and p-value <0.01-considered highly significant

RESULTS

A total of 105 parturients were enrolled in the present study and were randomized into three groups of 35 each (n=35). All three groups were comparable in respect to their demographical profile, Apgar score, duration of surgery; total intravenous fluid used and blood loss. (p-value > 0.05) [Table/Fig-1].

There was no difference in maximum sensory height, time to reach maximum sensory height, time to reach Bromage score 3 and duration of the surgery in all three groups. (p-value > 0.05) [Table/Fig-1].

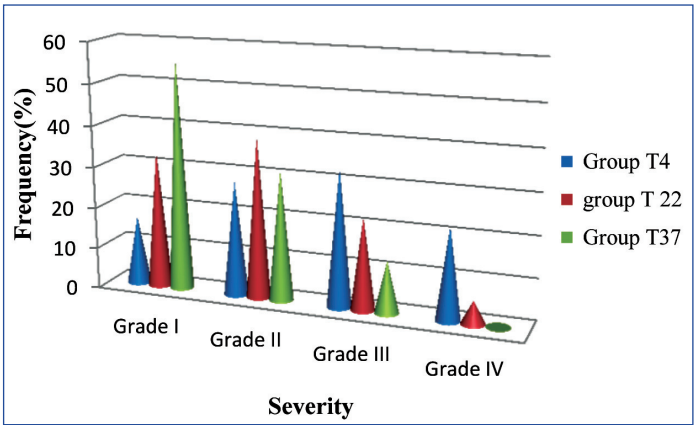
We did not found any significant difference in the incidence of shivering among all three groups. The incidence of shivering was 51.42% in group T_4, 51.42% in group T_{22} and 45.71% in group T_{37}. (p = 0.858) [Table/Fig-2].

However the onset of shivering was earliest (9.87±1.82 min) in group T_4 as compared to 14.27±3.02 min, 12.16±2.89 min in group T_{22} and group T_{37} respectively, this difference was statistically significant. (p= 0.0001) [Table/Fig-2].

The parturients of group T_4 also felt the shivering of higher intensity (grade III/IV) compared to group T_{22} and group T_{37} but statistically this difference in intensity was not found significant [Table/Fig-2,3].

Variables	Group T_4 (n=35)	Group T_{22} (n=35)	Group T_{37} (n=35)	p-value
Shivering, n (%)	18(51.42%)	18(51.42%)	16(45.71%)	0.858*
Shivering Onset (min)	9.87±1.82	14.27±3.02	12.16±2.89	0.000**
Severity				
Grade I	3 (16.66%)	6 (33.33%)	9 (56.25%)	0.163*
Grade II	5 (27.77%)	7(38.88%)	5 (31.25%)	0.755*
Grade III	6(33.33%)	4 (22.22%)	2 (12.5%)	0.323*
Grade IV	4 (22.22%)	1(5.55%)	0%	0.065*

[Table/Fig-2]: Shivering characteristics.
**Highly significant (p-value <0.01)
*Not significant (p-value > 0.05)



[Table/Fig-3]: Intensity of shivering

There was no significant difference in respect to heart rate, mean arterial pressure, and core body temperature and oxygen saturation between the three groups. Six parturient in group T_4, one in group T_{22} and five in group T_{37} developed hypotension however none of them required vasopressor. One parturient in group T_{37} had bradycardia and was treated with intravenous atropine. Three parturient in Group T_4 and two in Group T_{37} experienced nausea/vomiting.

DISCUSSION

Shivering is one of the common side effects of spinal anaesthesia; however the exact aetiology and the best way of prevention are still not known [9]. The incidence of shivering in neuraxial anaesthesia was reported around 55% [2]. In present study, temperature of bupivacaine was adjusted to 4°C, 22°C and 37°C for spinal anaesthesia and found that the overall incidence of shivering in all three groups was 49.52%. However cooling or warming the hyperbaric bupivacaine for spinal anaesthesia did not make any difference in the incidence of shivering when compared between the groups. In a review it has been shown that neuraxial block causes vasodilation below the level of blockage that is presumably responsible for body heat redistribution from central compartment to peripheral compartment [17]. Apart from this, previous study has also demonstrated that thresholds triggering vasoconstriction and shivering (above the level of the block) decrease about 0.6°C after epidural and spinal anaesthesia [18], although the mechanism by which peripheral administration of local anaesthesia impairs centrally mediated thermoregulation remains unknown, however this impairment in thermoregulation is proportional to the number of spinal segments blocked [19]. This can be possible that incidence of shivering in our groups did not show any significant difference probably due to the fact that the sensory block height in all the groups were similar. However in one study Najafianaraki et al., used hyperbaric bupivacaine at 4°C and 23°C for spinal anaesthesia in parturient for cesarean section and found that the incidence and intensity of shivering was less in warm group. Although the maximum sensory block height and time to achieve maximum sensory height in their study were clinically insignificant among the groups [10]. Najafianaraki et al., in their study used the 2 ml of drug at 4°C and 23°C while we used the drug at 4°C, 22°C and 37°C for spinal anaesthesia. The study showed that temperature can affect the viscosity and therefore the spread of drug in spinal anaesthesia [20], however the volume we used in our study was 2.2 ml, the volume that was very less in comparison to CSF volume present in spinal cord [21] and it has been demonstrated earlier that the temperature of local anaesthetic injected in subarachnoid space rapidly equilibrates with the core temperature of the CSF (37-38°C) [22]. This may be the possible mechanism for no difference in incidence of shivering. Although we did not found any significant difference in incidence of shivering, however the shivering was appeared significantly earlier in the group T_4 where the temperature of the bupivacaine was 4°C. As described in a previous study that all mammals and birds have spinal thermoreceptors, thus theoretically it is possible that injection of relatively cool (i.e., ambient temperature) local anaesthetic into the epidural space might provoke shivering by stimulating local temperature sensors cannot be ruled out [23]. Bromage et al., has also argued that onset of shivering does not match with the observed time course of event because shivering usually appears within minute after injection and long before sufficient time has elapsed for significant heat loss to have occurred [14], our finding are also in accordance with this fact. In another study Ponte et al., did not observe any detectable effects on the intensity of shivering after giving three 80-mL injections of warm (39.8±1.2°C) or cold (17±2.2°C) saline in extradural space of healthy volunteers. This finding suggests that only cooling of the extradural space does not result the shivering [11]. Previous studies have demonstrated that the incidence of shivering was comparable when warm or cold anaesthetic solution was given in to the epidural space of volunteers and non-pregnant patients [16,24]. The above data indicate that temperature of the local anaesthetic solution is not the only responsible factor for provoking shivering during spinal or epidural anaesthesia but there must be some other factor also.

LIMITATION

In the present study, we tried our best possible efforts to control those factors that influence the occurrence of shivering, like ambient temperature, temperature of IV fluids and the drugs, but variation in temperature cannot be eliminated completely. We therefore have some limitations in the present study. First, it was difficult to keep the temperature of bupivacaine exactly at 4°C and 37°C, as the small vial of bupivacaine would likely to gain or loss its temperature based on the ambient temperature. Therefore to overcome this problem we kept a cooling and warming system too near to the operating room and drug as well as syringe was transported to the operating room after receiving cerebrospinal fluid (CSF), thus making the time as short as possible for change in the temperature of drug. Second, we did not record the temperature of CSF.

CONCLUSION

Shivering is a cause of discomfort and dissatisfaction in patients undergoing cesarean section and the evidences suggested that perioperative hypothermia and shivering are associated with severe outcomes. Although many studies have been undertaken to prevent or treat the shivering after spinal anaesthesia. In our study we found that cooling or warming of bupivacaine does not influence the overall incidence of shivering however cooling of the drug can provoke early shivering.

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