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Intrathecal Clonidine Prevents Perioperative Shivering In Spinal Anaesthesia in Caesarian Section

Dr. P. Chalapathy[1], Dr.E.Jayasundaram[2]
[1,2][*Department of anesthesiology ,GOVT. Medical College, Ongole, A.P/Dr.NTR University of Health sciences, Vijayawada, India]*
Corresponding Author: Dr.E.Jayasundaram

***Abstract**: This is a double blind randomized controlled clinical study to evaluate effects of intrathecal clonidine in prevention of perioperative shivering during spinal anesthesia in caesarian sections. In this study 80 patients of ASA-1 aged between 18 to 35 years are enrolled and divided into A and B groups. Group A received 2 ml of 0.5% bupivacaine with clonidine 30µg[1.8ml of bupivacaine and 0.2ml of clonidine]and group B received 2ml of 0.5% bupivacaine [1.8ml of bupivacaine and 0.2ml of normal saline]. We observed incidence of perioperative shivering, hemodynamic stability, additional requirement of sedation or analgesia, vasopressor requirement, IV fluid requirement and any other side effects. We observed lower incidence of (5%)perioperative shivering, increased fluid requirement, increased vasopressar requirement in study group or group A when compared to control group. In control group 40% of shivering incidence is observed. Incidence of shivering, fluid requirement and vasopressor usage is statistically significant (P value<0.001). There is significant difference in mean arterial blood pressure between groups (<0.05).*

***Keywords:** Intrathecal clonidine, Perioperative shivering, Spinal anesthesia, Caesarian section.*

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I. Introduction

In homeothermic species, a thermoregulatory system coordinates defenses against cold and heat to maintain internal body temperature within a narrow range (36.5-37.5^{0}C), thus optimizing normal physiologic and metabolic function. The combination of anesthetic-induced thermoregulatory impairment and exposure to cool environment makes most unwarmed surgical patients hypothermic [1–7]. Although shivering is but one consequence of perioperative hypothermia, and rarely the most serious, it occurs frequently (*i.e.* 40–60% after volatile anesthetics, during spinal anesthesia incidence 56.7% was reported] [8-12] and it remains poorly understood. While cold-induced thermoregulatory shivering remains an obvious etiology, the phenomenon has also been attributed to numerous other causes.

Regional anesthesia (spinal anesthesia) is widely used as a safe anesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing surgery under regional anesthesia [13, 14] Shivering is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption (up to 100-600%) along with raised carbon dioxide (CO_2) production; ventilation and cardiac output; adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and morbid cardiac events. It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP) And electrocardiographic (ECG) monitoring.[15-17]

Shivering is very unpleasant, physiologically stressful for the patient undergoing surgery, and some patients find the accompanying cold sensation to be worse than the surgical pain. Though the mechanism of origin of shivering is not clear, various hypotheses have been proposed to explain its occurrence. Perioperative hypothermia is the primary cause, which occurs due to neuraxial anesthesia-induced inhibition of thermoregulatory mechanism. Shivering occurs as a thermoregulatory response to hypothermia or muscle activity with tonic or clonic patterns, and various frequencies have been noticed.[17] However, in the postoperative period, muscle activity may be increased even with normothermia, suggesting that mechanisms other than heat loss with subsequent decrease in the core temperature contribute to the origin of shivering. These may be uninhibited spinal reflexes, sympathetic over-activity, postoperative pain, adrenal suppression, pyrogen release and respiratory alkalosis [17] Due to shivering and thermal discomfort, the quality of patient recovery suffers. Moreover, shivering per se may aggravate postoperative pain, simply by stretching of surgical incision.

There are various methods available to control shivering during anesthesia, which include non-pharmacological methods and pharmacological methods using drugs which have anti-shivering properties. Non-

pharmacological methods using equipment to maintain normal temperature of the body are effective but expensive and lack practicality, while the pharmacological methods using drugs like pethidine, tramadol, clonidine, doxapram, ketanserin, nefopam, etc., are simple, cost-effective and easy to implement.

The aim of this prospective double-blind randomized clinically controlled study was to evaluate effects of intrathecal clonidine during spinal anesthesia in caesarian sections incidence of shivering, additional requirement of sedation or analgesia, fluid requirement, mean arterial pressures and vasopressor requirements.

II. Materials and methods

After obtaining approval of the ethics committee and written informed consent, 80 American Society of anesthesiologists grade-1 (ASA1) patients aged 18 to 35 years scheduled for elective caesarian section under spinal anesthesia with no prior pre-medication, were included in this prospective double –blind randomized clinically controlled study. Patients with Reynaud's syndrome, cardio pulmonary disease ,a history of sensitivity to clonidne ,thyroid disorders , renal disease, upper respiratory tract infections , urinary tract infections psychological disorder, severe diabetes, autonomic neuropathies and patients with hypothermia and fever were excluded from this study. Group A received 1.8ml of 0.5% hyperbaric bupivacaine and 0.2ml of clonidine(30µg) and group B received 1.8ml of 0.5% hyperbaric bupivacaine and 0.2ml of normal saline randomly. All the selected patients were examined pre-operatively, premedication and pre-operative fluid loading was not done to avoid interfere with incidence of shivering

Anesthesiology personnel who were not involved in the study made the trial preparations and recorded group randomization separately. The anesthesiologists conducting the case and recording the data were unaware of the preparation administered.

Subarachnoid block was given with the prepared drug in respective groups at L3-L4 or L4-L5 interspaces using 25-26 gauges Quincke's needle, and blockage up to T6 dermatome was achieved. All operation theatres in which the operations were performed maintained constant humidity (70%) and an ambient temperature around 21^0C to 23^0C. Oxygen was administered to all the patients of both groups at a rate of 6 L/min and patients were covered with drapes but not actively warmed. No means of active re-warming were used. Intravenous fluids and anesthetic drugs were administered at room temperature. Preloading was not done in both the groups as we did not want intravenous fluid to influence the onset of shivering mechanism. Before beginning of spinal anesthesia, standard monitoring procedures were established. Standard monitoring of pulse rate was done, and non-invasive blood pressure (NIBP), oxygen saturation (SPO_2), body temperature (axillary) were recorded before the commencement of the surgery and thereafter every five minutes of the base line i.e. subarachnoid block (SAB), for one hour and every fifteen minutes for the rest of the observation period. Grading of shivering was done as per Wrench, [18] which is as follows:

Grade 0: No shivering
Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis with, but without visible muscle activity.
Grade 2: Visible muscle activity confined to one muscle group.
Grade 3: Visible muscle activity in more than one muscle group.
Grade 4: Gross muscle activity involving the whole body.

Patients who developed grade 3 or grade 4 of shivering were included in the study. Patients with the shivering were treated with injection tramadol and extra draping for the upper body. The side effects like nausea and vomiting, bradycardia (<60/min), hypotension (>20% of base line), dizziness and sedation score were recorded. Sedation score was assessed with a four-point scale as per Filos: [19]

1: Awake and alert
2: Drowsy, responsive to verbal stimuli
3: Drowsy, arousable to physical stimuli
4: Unarousable

Bradycardia, hypotension and vomiting were treated with atropine, mephenteramine and metoclopramide respectively in titrated doses when required. Pentazocin and promethazine were used for additional sedation or analgesia whenever required and recorded. For requirement of vasopressor, mephenteramine is used in titrated doses and recorded. Statistical analysis was done using suitable statistical software, and student t test and Chi-square test were applied for the interpretation of results. A P value <0.05 was considered statistically significant.

III. Results

A total of 80 patients were enrolled in the present study and were randomized into two groups of forty each (n=40). All are female patients underwent lower segment caesarian section. Both the groups were comparable with respect to age, height, weight, volume of intravenous fluids administered and results were tabulated.

	Group A (n=40)	Group B (n=40)	P value
Age	20±4.45	22±5.68	0.85
Weight (in kg)	50±10.85	52±12.80	0.72
Height (in cm)	160±4.08	161±5.60	0.92
IV fluids (in liters)	2340.75±248.14	2120.24±206.12	0.03
MAP	67±5.3	73±7.3	0.04
Heart rate	76±9.177	75±9.110	0.06

Perioperative shivering scores of the patient:

Shivering score	Group A (n=40)	Group B (n=40)
0	38	24
1	0	0
2	0	0
3	1	6
4	1	10

p value<0.001, Chi-square test.

Shivering incidence:

Group	Shivering	No shivering	Total
A	2(5%)	38(95%)	40
B	16(40%)	24(60%)	40
Total	18(22.5%)	62(77.5%)	80

P Value : <0.001, Chi-square test.

Sedation score of the patients:

Sedation score	Group A (n=40)	Group B (n=40)
1	8(20%)	35(87.5%)
2	32(80%)	5(12.5%)
3	0	0
4	0	0

P Value : <0.001, Chi-square test

Additional sedation or analgesia:

Group	Required	Not required	Total
A	8(20%)	32(80%)	40
B	25(62.5%)	15(37.5%)	40
Total	33(41.25%)	47(58.75%)	80

P Value : <0.001, Chi-square test

Vasopressor requirement:

Group	Required	Not required	Total
A	20(50%)	20(50%)	40
B	10(25%)	30(75%)	40
Total	30(37.5%)	50(62.5%)	80

P Value : <0.001, Chi-square test

Perioperative adverse events of patients:

Adverse events	Group A	Group B
Hypotension	20	5
Nausea-vomiting	2	15
Brady cardia	1	0
Total spinal block	0	0

Significant difference in hypotension and nausea- vomiting is observed between the groups

IV. Discussion

Regional anesthesia, either central neuraxial block or peripheral nerve block is a safe and very popular technique used for various surgeries. However, 40% to 70% of patients undergoing regional anesthesia develop shivering, though it is also found to occur after general anesthesia.[13,14]

The mechanism which leads to shivering after regional anesthesia is not very clear, but the probable mechanisms could be decrease in core body temperature secondary to sympathetic block; peripheral vasodilatation; increased cutaneous blood flow, which leads to increased heat loss through skin; cold

temperature of operation theatre; rapid infusion of cold IV fluids; and effect of cold anesthetic drugs upon the thermo sensitive receptors in the spinal cord.[20,21]

There are many non-pharmacological and pharmacological methods used to prevent heat loss and decrease shivering. Non-pharmacological methods include radiant heat warmers, warming the operation theatre, blankets, warm IV fluids and using anesthetic drugs at body temperature.[22,23] The present study was designed to standardize these possible compounding factors, while reflecting the common practice in our institution. The temperature in the operating room was maintained constant at 21°C to 23°C. IV fluids and drugs were given at room temperature. Axillary temperature was recorded at regular intervals intraoperatively.

Pharmacological methods to prevent and treat shivering include pethidine, tramadol, ketanserin, nefopam, alfentanyl, doxapram, magnesium sulphate, dexmeditomidin, clonidine, ketamine, fentanyl etc.

A limitation of this study is that we could not measure the core body temperature. For measurement of core body temperature, the probe needs to be put in the oesophagus or near the tympanic membrane. Both these are uncomfortable and unacceptable who has been given spinal anesthesia. Rectal temperature monitoring was a possibility but was not tried.

In the present study, we evaluated the efficacy of clonidine in prevention of shivering after spinal anesthesia in patients undergoing elective lower segment caesarian section . Clonidine is a centrally acting selective α2 agonist. Clonidine exerts its anti-shivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of α2 adrenoceptors and hence is effective in treating the established post-anesthetic shivering.[24,25] It also reduces spontaneous firing in locus coeruleus — a pro-shivering centre in pons.[26] At the spinal cord level, it activates the α2 adrenoreceptors and release of dynorphine, norepinephrine and acetylcholine.[26] The depressor effects of these neurotransmitters at the dorsal horn modulate cutaneous thermal inputs.[27] Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier.[28] Due to these merits, interaction at the α2 adrenoreceptors at spinal and supraspinal sites occurs within the central nervous system.[29]

In present study we found that clonidine is effective in prevention of perioperative shivering in spinal anesthesia. The median incidence of shivering related to neuraxial anesthesia in the control groups of 21 studies is 55% (inter cortile range of 40 to 60%) [30], which is nearly similar to that of the control group in our study (40%). In our study incidence of shivering is 5%. Shivering incidence in our study is statistically significant between two groups (p value<0.001, chi-square test). Incidence of shivering in control group is also similar to common incidence reported by Joris.J, etal[25] and Powel RM, etal [26]. Shivering incidence in our study is contrary to Jeon YT, etal [31]. Jeon YT, etal in their study reported intrathecal clonidine 150µg doesn't prevent post spinal shivering but 1µg/kg IV clonidine prevented the shivering. Lesser number of studies were available in literature regarding intrathecal clonidine and prevention of post spinal shivering. So further research is needed in this subject with varying doses of intrathecal clonidine in prevention of post spinal shivering.

In our study we observed clonidine group is associated with lower mean arterial pressures increased requirement of IV fluids and vasopressor. This is similar to Thakur A, etal who observed in their study increased incidence of hypotension with intrathecal clonidine 30 µg. This is statistically significant between 2 groups (p value<0.05, student- t test). So in clonidine group 50% of patients needed mephenteramine to maintain hemodynamic stability.

In clonidine group 80% of patients were with a sedation score 2 and 20% with 1. In control group 87.5% of patients were with sedation score with 1 and 62.5% of them were needed additional sedation or analgesia with pentazocin and promethazine in titrated doses. This is statistically significant between 2 groups (p value <0.001, chi-square test).

In our study 20 patients were associated with hypotension with clonidine group and were treated with titrated doses of IV fluids and mephentaramine. 15 patients in control group were associated with nausea-vomiting and were treated with titrated doses of metochlopramide. 1 patient in clonidine group associated with bradycardia and treated with atropine.

V. Conclusion

Intrathecal clonidine 30 µg is effective in prevention of perioperative shivering and associated with hypotension and increased requirement of IV fluids, vasopressor and decreased requirement of additional sedation or analgesia.

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