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Original Research Article

A Retrospective, Randomized, Double-Blind Study Was Done to Compare between Intrathecal Dexmedetomidine (5mcg) and Intrathecal Meperidine (0.2mg/Kg) for Decreasing the Incidence and Intensity of Shivering after Spinal Anesthesia for Lower Abdominal Operations.

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Abstract

Aim: to compare between intrathecal dexmedetomidine (5mcg) and intrathecal meperidine (0.2mg/kg) for decreasing the incidence and intensity of shivering after spinal anesthesia for lower abdominal operations.

Methods: The present study was conducted in the Department of Anesthesia, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India from jan 2017 to December 2017, and ninety patients scheduled for lower abdominal operations under spinal anesthesia were randomly allocated to three groups. Spinal anesthesia consisted of 12.5 mg hyperbaric bupivacaine 0.5% in addition to dexmedetomidine (5mcg) (group D) or meperidine (0.2 mg/kg) (group M) or, normal saline (group S). Different parameters, including sublingual temperature, sensory block, motor block, incidence and intensity of shivering, blood pressure, heart rate, pruritus, nausea, and vomiting was performed at 10-minute intervals.

Results: Hypothermia was recorded in 17 patients in group D, 16 patients in group M and 18 patients in group S, while shivering developed in 6 patients in group D, 7 patients in group M and 8 patients in group S, however, pruritus, nausea and vomiting was more common in the meperidine group compared to the other two groups.

Conclusion: To conclude, intrathecal dexmedetomidine and meperidine lowered the incidence of shivering and increased duration of sensory and motor block during lower abdominal operations. Intrathecal meperidine caused more pruritus, nausea and vomiting than intrathecal dexmedetomidine.

Keywords: Anesthesia, Dexmedetomidine, Meperidine, Shivering, Spinal

Introduction

Shivering is a protective mechanism by which heat production occurs, by vigorous involuntary muscle activity, to compensate for the decreased core temperature in a normal healthy living body. The main mechanisms of shivering in patients undergoing surgery are mainly intraoperative heat loss, increased sympathetic tone, pain, and systemic release of pyrogens. [1] Spinal anesthesia impairs the thermoregulation system, it inhibits the tonic vasoconstriction, which plays a significant role in temperature regulation. [2] Spinal anesthesia also causes redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These two effects predispose patients to hypothermia and shivering. [3] Shivering increases oxygen consumption, carbon dioxide production, lactic acidosis and metabolic rate by up to 400%. [4,5] Dexmedetomidine is a highly selective alpha-2-adrenoceptor agonist with potent effects on the central nervous system and it was used for prevention and treatment of shivering associated with general or spinal anesthesia. [6-8]

Many other drugs have been used to treat peri anesthetic shivering, including meperidine, clonidine, ketanserin, and doxa pram; and most studies have concluded that meperidine is considerably more effective in treating shivering

than others. [9-11] Adding a small dose of meperidine to the intrathecal mixture during spinal anesthesia reduces the incidence and severity of shivering. and is known to retain characteristics of the sensory block. [12-14]

Dexmedetomidine has highly specific α2-adrenergic receptor-agonist properties, with strong impacts on the central nervous system without respiratory depression. [3,7] It is postulated that intravenous dexmedetomidine could reduce shivering thresholds via its centrally mediated actions without any major adverse effects. [8,9]

The aim of this study was to compare between intrathecal dexmedetomidine and meperidine on the incidence and severity of shivering following spinal anesthesia.

Material and Methods

The present study was conducted in the Department of Anesthesia, Vardhman Institute of Medical Science, Pawapuri, Nalanda, Bihar, India from jan 2017 to December 2017 and ninety patients scheduled for lower abdominal operations under spinal anesthesia were randomly allocated to three groups. Spinal anesthesia consisted of 12.5 mg hyperbaric bupivacaine 0.5% in addition to dexmedetomidine (5mcg) (group D) or meperidine (0.2 mg/kg) (group M) or, normal saline (group S). Different parameters, including sublingual temperature, sensory block, motor block, incidence and intensity of shivering, blood pressure, heart rate, pruritus, nausea, and vomiting was performed at 10-minute intervals.

seventy-five patients (American Society of Anesthesiologists physical status I or II, aged 20-50 years) scheduled for elective minor lower abdominal operations under spinal anesthesia, were enrolled in the study.

Exclusion criteria include patients with thyroid disease, Parkinson's disease, dysautonomia, Raynaud's syndrome, cardiopulmonary disease, a history of allergy to the agents to be used, a need for blood transfusion during surgery, an initial core temperature above 37.5˚C or below 36.5˚C, use of vasodilators, or having contraindications to spinal anesthesia. All patients gave written informed consent to participate in this study. The temperature of the operating room was maintained at 21˚C to 22 ˚C (measured by a wall thermometer).

Intravenous fluids were administered at room temperature and given without warming. One layer of surgical drapes over the chest, thighs, and calves were placed during the operation and then one cotton blanket over the entire body postoperatively. No other warming device was used. A core temperature below 36˚C was considered hypothermia. Preloading with 10 ml/kg of Ringer acetate solution was given to each patient. Spinal anesthesia was induced in the semi-sitting position at either the L3-4 or L4-5 interspaces. Patients were allocated into three equal groups, a dexmedetomidine (Group D, n=30), meperidine group (Group M, n = 3-) or a saline control group (Group S, n = 30) by a computer-generated randomization method. To detect a 50% reduction of shivering incidence, a sample size of 18 patients per group was required (with an $\alpha = 0.05$, $\beta = 0.2$, and a power of 80%). It was determined that 25 patients would be included in each group with a power of 90%. The drug mixture was prepared by an investigator who was not otherwise involved in the study, he prepared syringes containing hyperbaric bupivacaine plus

dexmedetomidine, meperidine or saline.; thus, the study was double blinded.

The drug mixture was 12.5 mg hyperbaric bupivacaine 0.5% plus 5 mcg dexmedetomidine in 0.5 ml normal saline (Group D), 12.5 mg hyperbaric bupivacaine 0.5% plus 0.2 mg/Kg meperidine hydrochloride 5% in 0.5 normal saline (Group M), and 12.5 mg hyperbaric bupivacaine plus 0.5 ml of normal saline (Group S). A total volume of 3 ml of drug mixture (2.5 ml of hyperbaric bupivacaine 0.5% plus 0.5 ml of the study drugs (dexmedetomidine, meperidine or normal saline) was injected using a 27 G Quincke spinal needle.

Supplemental oxygen (4 L/min) was delivered via a facemask during the operation.

The incidence and intensity of shivering, blood pressure (BP), heart rate, SpO2 and sublingual temperature were evaluated each 10 minutes for 180 minutes. Side effects like pruritus, nausea or vomiting were recorded. Shivering was graded using the 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; 4 = shivering involving the whole body). Sublingual temperature was monitored using an oral temperature probe with a monitor (Infinity Delta Monitor En, Draeger Medical S Sensory block was assessed by pinprick test with a 22 G hypodermic needle every minute during the first 10 minutes, and then every 10 minutes, the motor block was assessed by modified boomage scale (0, no motor block; 1, hip blocked; 2, hip and knee blocked; 3, hip, knee, and, ankle blocked).

The presence of shivering was assessed by a blinded observer after the completion of subarachnoid drug injection. Sublingual temperature, sensory block, motor block, incidence and severity of shivering were recorded at 10-min intervals during the operation and in the recovery room. Side effects,

such as hypotension, bradycardia, pruritus, nausea and vomiting were recorded. If the patient's heart rate fell below 50 bpm, 0.5 mg intravenous atropine was administered. Hypotension was defined as a decrease in the mean arterial pressure (MAP) of more than 20 % from baseline (baseline MAP was calculated from three measurements taken in the ward before surgery). Hypotension was treated with 6 mg ephedrine boluses. If patients developed nausea and vomiting, 10 mg metoclopramide was administered intravenously. Postoperatively, all patients were monitored, given oxygen via a facemask and were covered with one layer of drapes and one cotton blanket. The post-anesthesia care unit temperature was maintained at 25˚C to 26 ˚C and constant humidity.

Statistical analyses were performed using statistical package for social sciences (SPSS) version 15.0 for windows. Quantitative variables were compared between groups using Student's t-test or a Mann-Whitney U-test where appropriate. Within-group data for core temperature were analyzed by using repeated-measures analysis of variance followed by Bonferroni's post-hoc testing. Within-group data for heart rate and mean arterial pressure were analyzed using a Friedman test. Chi-square analysis was used for comparison of categorical variables. The results are shown as median (range), mean (¡SD), exact numbers or proportions are expressed as a percentage. p,0.05 was considered statistically significant.

Results

Table 1: Demographic data in the three studied groups

	Group D	Group M	Group S	P1	P2	P3
Age(years)	34.88 ± 10.16	34.88 ± 9.83	33.80 ± 9.81	.500	0.368	0.350
Height(cm)	168.48 ± 6.22	168.40 ± 6.91	168.88 ± 6.00	0.483	0.410	0.397
Weight(Kg)	82.48 ± 11.69	87.48 ± 10.77	83.56 ± 11.52	0.128	0.355	.110
Male	20	18	15	.712	-	.712
Female	10	12	15			

Regarding demographic data (age, height, weight, gender) and surgery duration, there were insignificant differences between the three studied groups. P1 is a comparison between group D and group M, p2 is a comparison between group D and group S and P3 is a comparison between group M and group S, - means that no applicable statistics because the same results in the two groups.

Table 2: Hypothrtmia, sensory-motor block duration, incidence and degree of shivering and surgery time among the three studied groups.

	Group D	Group M	Group S	P1	P2	P3
Hypothermia	17	16	18	0.765	0.757	0.403
Motor block duration	199.52 ± 58.61	210.96 ± 46.74	159.16 ± 40.79	0.247	0.009	0.000
Sensory block duration	277.56 ± 109.27	260.56 ± 73.92	206.60 ± 49.65	0.259	0.005	0.002
Incidence of shivering	6	7	8	0.732	0.001	0.001
Degree of shivering	1.40 ± 0.55	1.50 ± 0.84	2.09 ± 0.79	-	0.108	0.061
Surgery time(minutes)	66.48 ± 19.57	65.92 ± 19.17	66.92 ± 14.43	0.450	0.464	0.418

Regarding hypothermia, it was recorded in 17 patients in dexmedetomidine group, in 16 patients in meperidine group and in 18 patients in the control group with no significant differences between the three studied groups. Regarding motor and sensory block duration, patients of group D and M had longer duration than patients of group S, with significant statistical difference. Regarding shivering, patients of group D and M had less shivering than patients of group S, with significant statistical difference. Regarding the degree of shivering, patients of group D & M had lower degree of shivering than control group, but this difference did not reach statistical significance. P1 is a comparison between group D and group M, p2 is a comparison between group D and group S and P3 is a comparison between group M and group S, - means that no applicable statistics because the same results in the two groups.

Table 3: Bradycardia, hypotension, pruritus, nausea and vomiting among the three studied groups.

	Group D	Group M	Group S	P1	P2	P3
Bradycardia	7	8	4	0.683	0.633	-
Hypotension	6	5	5	0.479	-	0.450
Pruritus	6	4	2	0.081	0.300	0.020
Nausea vomiting	5	3	1	0.044	-	0.50

Regarding bradycardia and hypotension, there were insignificant differences between the three studied groups. Regarding pruritus, pruritus developed in 5 patients in group M, 1 patient in group D, and none in group S, with significant difference between group M and the other 2 groups. Regarding nausea and vomiting, 3 patients in group D and S, while 5 patients in group M developed nausea and vomiting with significant difference between group M and the other 2 groups. Hypothermia was recorded in 17 patients in group D, 16 patients in group M and 18 patients in group S, while shivering developed in 6 patients in group D, 7 patients in group M and 8 patients in group S. Intrathecal dexmedetomidine and intrathecal meperidine decreased the incidence of shivering and increased the sensory and motor block duration. Intrathecal meperidine caused more pruritus, nausea and vomiting than intrathecal dexmedetomidine.

Discussion

Shivering profoundly increases oxygen consumption (by 200- 500%) and carbon dioxide production and decreases mixed venous oxygen saturation.[5] Three major factors contribute to core hypothermia during regional anesthesia: heat loss to the environment, inhibition of central thermoregulatory control, and redistribution of body heat. [3,13] When the body is exposed to a cold environment, the body temperature drops, and it worsens when cold IV fluid or blood is administered without warming. [14,15] Although one limitation of this study was measuring sublingual temperature instead of core temperature of tympanic membrane, sublingual and axillary temperatures are thought to reflect core temperature with reasonable accuracy. [16,17] It has been reported, though, that axillary temperature does not correlate well with perioperative shivering and that the sublingual temperature reflects changes in body temperature better than the axillary temperature. [18]

Regarding demographic data (age, height, weight, gender) and surgery duration, there were insignificant differences between the three studied groups. P1 is a comparison between group D and group M, p2 is a comparison between group D and group S and P3 is a comparison between group M and group S, - means that no applicable statistics because the same results in the two groups. The autonomic thermoregulatory responses to cold are shivering and vasoconstriction. Normally, upon exposure to cold stress, the cutaneous vasculature constricts to reduce heat loss, metabolic heat production increases, and shivering begins in an effort to maintain core body temperature. Spinal anesthesia alters autonomic thermoregulatory responses by significantly decreasing the thresholds for vasoconstriction and shivering. [19]

Regarding hypothermia, it was recorded in 17 patients in dexmedetomidine group, in 16 patients in meperidine group and in 18 patients in the control group with no significant differences between the three studied groups. Regarding motor and sensory block duration, patients of group D and M had longer duration than patients of group S, with significant statistical difference. Regarding shivering, patients of group D and M had less shivering than patients of group S, with significant statistical difference. Regarding the degree of shivering, patients of group D & M had lower degree of shivering than control group, but this difference did not reach statistical significance. P1 is a comparison between group D and group M, p2 is a comparison between group D and group S and P3 is a comparison between group M and group S, - means that no applicable statistics because the same results in the two groups. Shivering during spinal anesthesia is thought to occur due to a loss of thermoregulatory vasoconstriction and a loss of heat-by-heat redistribution from core to peripheral parts of the body. However, the decrease in core body temperature is not remarkable when compared with general anesthesia because spinal anesthesia causes only redistribution of heat in the lower half of the body. [3,19] Regardless of its cause, shivering has the undesirable effects of markedly increasing oxygen consumption and carbon dioxide production and decreasing mixed venous oxygen saturation. Cardiac output and minute ventilation, as well as mean BP, increases.[20] If these compensatory mechanisms fail, then hypoxemia may occur. These effects are often poorly tolerated by patients with limited cardiac or pulmonary reserve. Therefore, shivering prevention is more important than its treatment in these patients.

Regarding bradycardia and hypotension, there were insignificant differences between the three studied groups. Regarding pruritus, pruritus developed in 5 patients in group M, 1 patient in group D, and none in group S, with significant difference between group M and the other 2 groups. Regarding nausea and vomiting, 3 patients in group D and S, while 5 patients in group M developed nausea and vomiting with significant difference between group M and the other 2 groups. Hypothermia was recorded in 17 patients in group D, 16 patients in group M and 18 patients in group S, while shivering developed in 6 patients in group D, 7 patients in group M and 8 patients in group S. Intrathecal dexmedetomidine and intathecal meperidine decreased the incidence of shivering and increased the sensory and motor block duration. Intrathecal meperidine caused more pruritus, nausea and vomiting than intrathecal dexmedetomidine. Adding a small amount of meperidine during spinal anesthesia may aid high risk patients from developing shivering. In treating shivering, meperidine is much more effective than equipotent doses of other μ-opioid agonists, such as

fentanyl, alfentanil, sufentanil, or morphine. [21] The ant shivering property of meperidine is not fully understood. Several studies have suggested that the anti-shivering effect of meperidine is mediated by κ-opioid receptor agonist activity. [10,22] Also meperidine suppresses the shivering threshold almost twice as much as the vasoconstriction threshold and this suppression in the shivering threshold appears to underlie the anti shivering effect of meperidine. [23] Potential side effects of meperidine such as nausea, vomiting, pruritus and hypotension must also be considered when administering meperidine. [24]

Alpha-2 adrenergic agonists are widely used nowadays in clinical practice of anesthesiology and intensive care. The α-2 receptor agonists are known to prevent shivering to a moderate extent without any associated respiratory depression as with other anti shivering drugs like meperidine.[23] Dexmedetomidine reduces shivering by suppressing vasoconstriction and shivering thresholds [25]

Alpha-2 adrenergic agonists decrease the central thermo-sensitivity by suppressing the neuronal conductance. [26] This is mediated by the increased potassium conductance through G-coupled proteins which causes hyperpolarization of neurons. [27,28] Augmentation of neural suppression response is further mediated by restriction of calcium entry into nerve cells which causes inhibition of neurotransmitter release. [29] The increased accumulation of calcium ions on the neuron's surface in the posterior hypothalamus lowers the firing rate of heat gain units by stabilizing the cell membrane. [30] α-2 adrenergic agonists suppress the spontaneous firing rate of neurons in the locus coeruleus and neurotransmitter mediated firing of neurons in the dorsal raphe nucleus when administered intravenously. [31]

All these central actions of α-2 agonists are possible due to a high density of α-2 adrenoceptors in the hypothalamus and activation of these receptors produces hypothermia by reduction of heat generated by metabolic activity. [32] Intrathecal DXM when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fibers transmitters and by hyperpolarization of postsynaptic dorsal horn neurons. [33] Motor block prolongation by 2- adrenoreceptor agonists may result from binding these agonists to motor neurons in the dorsal horn of the spinal cord. [34]

Conclusion

To conclude, intrathecal dexmedetomidine and meperidine lowered the incidence of shivering and increased duration of sensory and motor block during lower abdominal operations. Intrathecal meperidine caused more pruritus, nausea and vomiting than intrathecal dexmedetomidine.

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