

COMPARISON OF DEXMEDETOMIDINE AND ONDANSETRON FOR PREVENTION OF SHIVERING IN LOWER LIMB SURGERIES AFTER SPINAL ANAESTHESIA

Afia Arshed Dodhy

Department of Anesthesia, PGMI/LGH/Ameer ud Din Medical College, Lahore - Pakistan

ABSTRACT

Objective: The purpose of the study was to compare the effectiveness of dexmedetomidine and ondansetron to prevent shivering in patients undergoing lower limb surgeries after spinal anaesthesia .

Material & Methods: This randomised double-blind and placebo-control study trial was held in orthopaedic operation theatre of Lahore General Hospital, Lahore from February 2020 to July 2020. Total of 120 adult patients who underwent elective orthopaedic surgery of lower limbs after spinal anaesthesia were divided into 3 batches. In Batch S, saline was given as placebo, in Batch O ondansetron and in Batch D dexmedetomidine was administered and shivering score were assessed for 45 min. A shivering score of ≥ 3 was considered as primary outcome.

Results: There is statistically considerable difference, in the incidence of significant shivering (grade 3 & 4), among batches, as established by one way ANOVA. The significance value is 0.004 (i.e. $p=0.004$). There was no significant difference statistically between batch D and batch O ($p=0.878$)

Conclusion: The incidence of shivering in batch S was considerably higher than that of both Batch O and batch D while no significant relationship could be proved in between batch D and batch O

Keywords: Dexmedetomidine, Ondansetron, Shivering, Spinal Anaesthesia

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INTRODUCTION

Shivering is the main factor of distress for patients undergoing spinal anaesthesia. It not only causes emotional trauma for the patient but also causes 200–500% increase in O₂ consumption leading to increase in production of carbon dioxide.¹ This phenomenon is more pronounced in patients with inadequate respiratory reserve, cardiac patients with fixed cardiac output and with those with intrapulmonary shunts.¹ Shivering also causes raised intraocular pressure, raised intracranial pressure, hypoxemia as well as it also hinders with basic monitoring like electrocardiogram (ECG), oxygen saturation and non-invasive blood pressure monitoring.² The precise pathogenesis for the origin of shivering is still not completely understood. Numerous mechanisms are suggested for its pathogenesis like various non-thermoregulatory and hindrance with thermoregulation.³ One of the main reason is

inhibition of thermoregulatory mechanism by anaesthetics. Vasodilation of skin, uninhibited spinal reflexes and pain are the further proposed mechanisms. Various receptors like serotonin, opioid and α_2 receptors are also involved.³ In the recent years, because of increased understanding of adverse effects of shivering, its prevention has become an essential part of anaesthesia care.

Different methods like administering warm intravenous fluids and warming the skin surfaces are described to prevent shivering but none of them proved to be beneficial. However, many drugs like α_2 -agonists, corticosteroids, anticholinergics and CNS stimulants have shown to be useful but their use is limited due to various side effects.⁴ Ondansetron, which is commonly used as an antiemetic in the perioperative period, is an antagonist of 5HT₃ receptor. It is also used safely for the prevention of shivering and is quite effective too. The mechanism of its anti-shivering property might be due to inhibition of reuptake of serotonin in pre-optic anterior hypothalamic area. 5-HT₃ receptors also effect heat loss and production pathways.⁵ Dexmedetomidine decreases the threshold of shivering and vasoconstriction; therefore it acts on the central mechanism of thermoregulatory system and do not inhibit shivering peripherally. It also blocks α_2 receptors at the level of spinal cord and brain stem and so

Correspondence

Dr. Afia Arshed Dodhy

Assistant Professor

Department of Anaesthesia & ICU PGMI/LGH/Ameer Ud Din Medical College, Lahore - Pakistan.

Email: afiashujaat@yahoo.com

Cell: +92-306-4191949

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it also causes analgesia and sedation.⁶ The goal of the trial was to compare the efficacy of dexmedetomidine and ondansetron to prevent shivering in patients undergoing lower limb surgeries after spinal anaesthesia.

MATERIAL AND METHODS

This randomised double-blind and placebo-control study was performed in Lahore General Hospital for the period of 6 months from February 2020 to July 2020. After taking permission from ethical committee, 120 patients of both genders undergoing elective orthopaedic surgery of lower limbs were included. All patients underwent spinal anaesthesia. Other inclusion criteria includes age 20 to 60 years and American Society of Anaesthesiologist (ASA) I and II patients. Patients with any co morbid disease, reduced cardiopulmonary reserve, requirement of blood transfusion during surgery, pregnancy and history of allergies were excluded from the study. The sample size of 120 (40 in each batch) was calculated at 80% power of test and 95% confidence interval and taking expected percentage of shivering as 57.5% in batch S, 17.5% in batch O and 27.5% in batch D. After taking informed consent, patients were randomized using computer generated method with closed envelopes into 3 batches i.e. Saline batch (Batch S), Dexmedetomidine batch (Batch D) and Ondansetron batch (Batch O) each with 40 patients .

After taking informed consent, standard monitoring was used i.e. non-invasive blood pressure (NIBP), oxygen saturation, heart rate, ECG, and body temperature through axillary probe. Temperature of the operation theatre was maintained at 24°C–26°C. Ringer lactate @ 10ml/kg was infused. Spinal anaesthesia with injection bupivacaine 15mg at level of L 4-5 with Quincke's needle 25 gauge was given with standard protocols. Blockade up to the level of dermatome T10 was attained . All patients were administered 3L/min of oxygen via face mask. No active rewarming used and all fluids were given at room temperature. After spinal anaesthesia, one of the study drug was given intravenously.

Batch S patients were given saline as placebo, Batch O were administered ondansetron 8 mg, and Batch D patients were administered dexmedetomidine in dose of 1 µg/kg intravenously. The anaesthesiologists was kept blinded about the preparation of the drug. After every 5 minutes, shivering score were assessed for 45 min and classified using a scale validated by Tsai and Chu.⁸ (Grade 0: when no shivering is observed, Grade 1: when piloerection is observed but no visible shivering is present, Grade 2: muscular activity is observed in only one group of muscle, Grade 3: muscular activity is observed in more than one group of muscle but it is not generalised and Grade 4: generalised shivering is present in entire body). A shivering score of ≥ 3 in 45 minutes after spinal anaesthesia was considered as primary outcome. Bradycardia, hypotension, sedation, nausea and vomiting were also noted

which were considered as secondary outcomes. Rescue drug injection tramadol 0.5mg/kg intravenously was given for control of shivering. Demographic details as gender, age, height and weight were also recorded.

RESULTS

All batches were comparable in terms of age, sex, height, weight, and duration of surgery ($P > 0.05$) as shown in Table 1. Secondary outcomes i.e. sedation, hypotension, nausea & vomiting and bradycardia were also comparable with no significant differences (Table 2). The frequency of shivering in batch S (55%) was considerably more than that of both Batch O (22.5%) batch D (27.5%). There was a significant difference in the prevalence of significant shivering (grade 3 & 4) between batches as determined by one way ANOVA test. The significance value is 0.004 (i.e. $p=0.004$) which is below 0.05.

To know which of the specific batch differed, Turkey post hoc test was applied. It revealed that incidence of shivering was statistically higher in batch S (which is a control batch) as compared to batch O ($p=0.006$) and batch D ($p=0.023$). There was no statistically significant difference between batch O and batch D ($p=0.878$). See Table 4 for details.

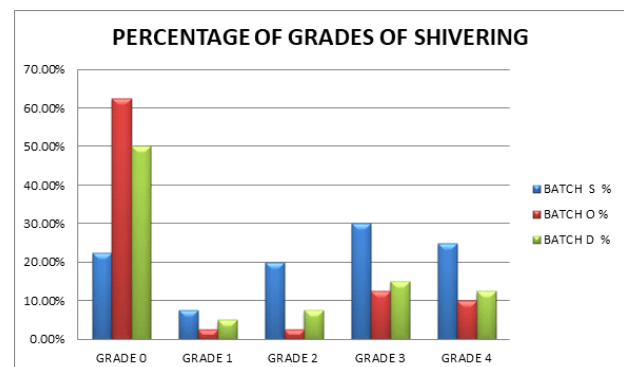


Fig 1: Percentage of Grades of Shivering

DISCUSSION

The outcome of the present study proves the efficacy and safe use of prophylactic administration of drugs, dexmedetomidine and ondansetron, in decreasing the occurrence as well as severity of shivering that may occur after spinal anaesthesia when it was compared with saline as placebo. The adverse effects associated with these drugs were temporary and easily tolerable by majority of the patients. Our results are comparable with the study carried out by Botros et al. who established prophylactic use ondansetron or dexmedetomidine effectively reduces the severity and incidence of shivering after intrathecal block when it was compared with placebo with bearable side effects.⁷ The exact mechanism by which shivering occurs in spinal anaesthesia is still not fully understood. Pharmacologic preparations remain the most common

Table 1: Demographic data of Batches

Parameter	Batch S Mean ±SD	Batch O Mean ±SD	Batch D Mean ±SD	P Value
Age	41.8 ±9.8	39.35±11.47	43.7±9.91	0.179
Weight (kg)	60.33±11.07	58.6±9.9	57.8±10.1	0.535
Height(cm)	155.55±5.787	154.97±5.855	155.13±5.750	0.854
Duration of Surgry (min)	85.95±18.47	80.08±20.46	87.05±17.917	0.214
Gender (N) %				
Male	23 (57.5%)	25 (62.5%)	21 (52.5%)	0.670
female	17 (42.5%)	15 (37.5%)	19 (47.5%)	

Table 2: Secondary Outcomes of Study Batches

Parameter	Batch S N (%)	Batch O N (%)	Batch D N (%)	P Value
Sedation	0 (0%)	0 (0%)	1 (2.5%)	0.371
Hypotension	12 (25%)	13 (32.5%)	12 (30%)	0.759
Bradycardia	9 (22.5%)	8 (20 %)	8 (20%)	0.952
Nausea & Vomiting	9 (22.5%)	3 (7.5%)	6 (15%)	0.174

Table 3: Percentage of Grades of Shivering

Grades	Batch S % (N)	Batch O % (N)	Batch D % (N)
Grade 0	22.5% (9)	62.5% (25)	50% (20)
Grade 1	7.5% (3)	2.5% (1)	5% (2)
Grade 2	20% (8)	2.5% (1)	7.5% (3)
Grade 3	30% (12)	12.5% (5)	15% (6)
Grade 4	25% (10)	10 % (4)	12.5% (5)

Table 4: Percentage of Grades of Shivering

SHIVERING	Batch S N (%)	Batch O N (%)	Batch D N (%)	P Value	P Value		
					S/O	S/D	O/D
GRADE III/IV	22 (55%)	9 (22.5%)	11 (27.5%)	0.004*	0.006*	0.023*	0.878

ANOVA followed by post Hoc test to compare the three batches.

S/O: Batch S versus Batch O.

S/D: Batch S versus Batch D.

O/D: Batch O versus Batch D.

approach for treatment and prevention of shivering⁸. The action of dexmedetomidine on prevention of shivering seems to be because of inhibition of central thermoregulation. It lowers the shivering threshold temperature by increasing the range of temperature thereby not stimulating the thermoregulatory defence mechanism of the body.⁹ Ondansetron, which is 5-HT3 antagonist, is a common anti-emetic, and can be used to prevent post spinal shivering. Reduced incidence of shivering is attributed to inhibition of 5-hydroxytryptamine- 3 (5- HT3) system¹⁰. Noaman et al. concluded in their study that in comparison to pethidine, ondansetron was as effective in prevention of post-operative shivering yet it was quite more safer than pethidine as there is less incidence of sedation and nausea and vomiting.¹⁰ Shakya et al. proved the safety and efficacy of ondansetron and ketamine in low dose for prevention of shivering after anaesthesia when it was compared with placebo.¹¹ Badawy AA and Mokhtar AM. also observed in their study, that by using Ondansetron, there is significant

reduction in terms of the positive shivering (score ≥ 3) in comparison to placebo in obstetric patients having caesarean section delivery after spinal anaesthesia.¹²

Bajwa, et al , in their clinical trial , verified that that dexmedetomidine act as an anti shivering drug in a dose of 1 µg/kg. Although some of the adverse effects like dry mouth and sedation are upsetting for the patient but they were easily tolerable and did not affect overall clinical outcome.¹³

In our trial, although dexmedetomidine caused a statistically non-significant hypotension and bradycardia, it did not produce any major adverse event in patients.

Insignificant hypotension and bradycardia was also observed with ondansetron which was transitory and self-limited in most of the patients. Sharma, et al. when compared ondansetron with saline, they found complications were higher in saline batch as compared to the ondansetron batch.¹⁴ The incidence of nausea in saline

batch was found to be 40% and was greater to ondansetron batch. The frequency of hypotension was also higher in saline batch as compared to ondansetron batch.¹⁴

Kundra, et al when compared dexmedetomidine with tramadol observed more adverse effects in tramadol group as compared to dexmedetomidine group¹⁵ while Chowdhury, et al. proves Ondansetron as more haemodynamically stable and lessens the occurrence of postoperative nausea and vomiting when compared with tramadol.¹⁶

Callaway CW et al. ,in their study, proves that dexmedetomidine in dose of 1.0 µg/kg ,in normal patients, decreases the average threshold of temperature for shivering by at least 0.8°C.¹⁷ Shivering during a regional anaesthesia could have possibly unfavourable effects and it may lead to exaggerated pain in wounds.¹⁸

In the present study, efficacy of both drugs is established for control of shivering when given prophylactically while no significant adverse effects were seen in both the study batches.

One of the limitations of the current trial was that standard anti-shivering medicine like meperidine was not used as a control . Also validity of results might not be appropriate in general anaesthesia and complicated surgeries requiring large volume intravenous fluids. The study was limited to (ASA) I and II patient.

CONCLUSION

The current study highlighted that use of ondansetron or dexmedetomidine prophylactically reduces the incidence as well as severity of shivering after intrathecal block when compared to saline as a placebo with non significant side effects.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Dodhy AA: Concept, Data collection, writing manuscript, analysis, bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.