

Original Research Article

Randomised Double-Blind Comparative Study of Dexmedetomidine and Tramadol for Post-Spinal Anaesthesia Shivering.

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Abstract

Background And Aims:

Dexmedetomidine has been used for prevention of post anaesthesia shivering. Its use for the treatment of post-spinal anaesthesia shivering has not been evaluated. The aim of this study was to evaluate and compare the efficacy, haemodynamic and adverse effects of dexmedetomidine with those of tramadol, when used for control of post-spinal anaesthesia shivering.

Methods:

A prospective, randomised, study was conducted in 60 American Society of Anaesthesiologists Grade I and II patients of either gender, aged between 18 and 65 years, scheduled for various surgical procedures under spinal anaesthesia. The patients were randomised in two groups of 30 patients each to receive either dexmedetomidine 0.5 µg/kg or tramadol 0.5 mg/kg as a slow intravenous bolus. Grade of shivering, onset of shivering, time for cessation of shivering, recurrence, response rate, and adverse effects were observed at scheduled intervals. Unpaired t-test was used for analysing the data.

Results:

Time taken for cessation of shivering was significantly less with dexmedetomidine when compared to tramadol. Nausea and vomiting was observed only in tramadol group (26% and; 22% respectively). There was not much difference in the sedation profile of both the drugs.

Conclusion:

We conclude that although both drugs are effective, the time taken for cessation of shivering is less with dexmedetomidine when compared to tramadol. Moreover, dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.

Keywords: Dexmedetomidine; post-spinal anaesthesia shivering; tramadol

1. INTRODUCTION

Shivering may contribute to increased wound pain, delaye ,it is an oscillatory, involuntary mechanical muscular activity and a natural protective mechanism to the reduction of body temperatured wound healing, and delayed discharge from post- anaesthetic care. Apart from

being an uncomfortable experience, its deleterious effects deserve primary prevention and rapid control on occurrence.

The main causes of intra/post-operative shivering are temperature loss, increased sympathetic tone, pain, and systemic release of pyrogens. Spinal anaesthesia significantly impairs the thermoregulation system by inhibiting tonic vasoconstriction, which plays a significant role in temperature regulation. It also causes a redistribution of core heat from the trunk (below the block level) to the peripheral tissues. These factors predispose patients to hypothermia and shivering.

The treatment of shivering includes both pharmacological and non-pharmacological methods. The non-pharmacological management is by external heating like the use of forced air warming, warming blankets, warmed fluids etc., According to the results of a meta-analysis, the most frequently reported pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine. Unfortunately, no gold standard treatment is known for shivering as the administration of all the available drugs is associated with various adverse effects.

Tramadol has become a favoured and commonly used drug for post-spinal anaesthesia shivering. However, it has many adverse effects like nausea, vomiting, dizziness etc., which cause further discomfort to the patient. Clonidine is another agent which has gained popularity during the last few years. Various studies, which have been conducted to compare them have concluded that clonidine has better efficacy and less adverse effects as compared to tramadol. But there was 5-10% incidence of hypotension and bradycardia with clonidine. Dexmedetomidine, a congener of clonidine, is a highly selective α_2 -adrenoceptor agonist. It has been used as a sedative agent and is known to reduce the shivering threshold. Few studies which have explored its anti-shivering potential have inferred that dexmedetomidine is an effective drug without any major adverse effect and provides good haemodynamic stability. Hence, we planned to do a comparative study of the efficacy, haemodynamic, and adverse effects of tramadol and dexmedetomidine when used for the control of post-spinal anaesthesia shivering.

2. METHODS

This was a double blind comparative, observational study was conducted in Shyam Shah Medical college Rewa. All subjects gave written informed consent to participate in the study. 60 American Society of Anaesthesiologists (ASA) Grade I and II consenting patients of either gender aged 18-65 years scheduled for elective, lower limb, orthopaedic under spinal anaesthesia were included in the study. Patients with known hypersensitivity to dexmedetomidine or tramadol, cardio-pulmonary, renal or hepatic disease, severe diabetes or autonomic neuropathies were not included in the study.

All patients who fulfilled the inclusion criteria and developed post-spinal anaesthesia shivering were enrolled and randomised using chit in box method with allocation ratio of 1:1 into either of the two groups.

Group D ($n = 30$) were administered dexmedetomidine 0.5 $\mu\text{g}/\text{kg}$ intravenous (IV)

Group T ($n = 30$) received tramadol 0.5 mg/kg IV. After arrival in the operation theatre, an 18G venous cannula was inserted and preloading done with Ringer's Lactate solution 10 ml/kg before giving spinal anaesthesia and maintained at 6 ml/kg/h after spinal anaesthesia. Before starting the procedure, standard monitors were attached and all the baseline parameters such as heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SPO_2), electrocardiography (ECG), and body temperature (axillary) were recorded. Subarachnoid anaesthesia was administered with 0.5% heavy bupivacaine (15 mg) at L₃₋₄ interspace using 25G Quincke's spinal needle under aseptic conditions. All operation theatres were maintained at an ambient temperature of around 24°C-25°C. Supplemental oxygen was administered to all the patients at the rate of 5 l/min with face mask and patients were covered with drapes. IV fluids and anaesthetics were administered at room temperature. Vital parameters such as HR, NIBP, and SPO_2 were recorded at intervals of every 5 min for first 30 min and every 15 min for the rest of the observation period. Continuous ECG monitoring was done.

Shivering was graded using a four point scale as per Wrench.: Grade 0: No shivering, Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis, but without visible muscle activity, Grade 2: Visible muscle activity confined to one muscle group, Grade 3: Visible muscle activity in more than 1 muscle group and Grade 4: Gross muscle activity involving the whole body. Patients who developed either Grades 3 or 4 shivering were included in the study. Either of the two drugs was given as slow IV bolus injection. The drugs were diluted to a volume of 5 ml in a 5 ml syringe. The attending anaesthesiologist recorded the time in minutes at which shivering started after spinal anaesthesia (onset of shivering), severity of the shivering, time to the disappearance of shivering and response rate (shivering ceasing within 15 min after treatment). Duration of surgery was recorded and duration of spinal anaesthesia was noted by assessing spontaneous recovery of sensory block using the pin-prick method and observing spontaneous movements of limbs in the post-operative period. Recurrence of shivering was also noted. In case there was recurrence of shivering, patients were treated with an additional dose of dexmedetomidine (0.5 μ g/kg IV) or tramadol (0.5 mg/kg IV) in the respective groups. Adverse effects such as nausea, vomiting, bradycardia (<50/min), hypotension (>20% of baseline), dizziness; and sedation score were noted.

Nausea and vomiting were treated with injection metoclopramide 10 mg IV as and when require. Power analysis was based on the detectable difference between the means of time taken for cessation of post-spinal shivering after treatment with dexmedetomidine or tramadol = 190 s. With a standard deviation (SD) of 190 s considering $\alpha = 0.05$ and power of 90% (two-tailed test), sample size calculated to be 22.03 patients per group. P value was calculated, and $P < 0.05$ was considered to be statistically significant. Numerical data were presented as mean \pm SD and categorical data as proportions (%). The comparison of the mean levels of all variables between two groups was made by the unpaired t -test.

3. RESULTS

Both groups were comparable with respect to age, gender, ASA grade, duration of surgery and

the duration of spinal anaesthesia. Duration of surgery varied from 40 min to 90 min. Duration of spinal anaesthesia ranged from 90 min to 148 min

Table 1 : Demographic profile of patients of both groups

Parameters	Group-D(Dexmedetomidine)	Group-T(Tramadol)	P-Value
Age(years)	36.1±6.6	35.33±4.5	0.6
Gender(M/F)	15/14	16/15	
Duration of surgery(Min)	45.17±10.38	46.00±11.48	0.76
Duration of anaesthesia (Min)	135.58±12.31	127.68±16.20	0.32

All the patients had Grade 3 shivering. There was no statistically significant difference in time for the onset of shivering between the two groups. However, the difference in the time interval between administration of drug after the onset of shivering and cessation of shivering was significantly shorter in the dexmedetomidine group when compared to tramadol group. There was recurrence of shivering in 1 patient in dexmedetomidine group and 2 patients in tramadol group. The patients were given rescue doses of dexmedetomidine or tramadol, respectively

Table 2: Parameters for post-spinal anaesthesia shivering

Parameters	Group-D(Dexmedetomidine)	Group-T(Tramadol)	P-Value
Onset of shivering(min)	21.49±12.68	18.58±11.99	0.69
Cessation of shivering after medication(min)	2.32±0.32	4.67±0.67	0.002
Response rate(%)	100	100	
Recurrence	1/30	2/30	

Nausea and vomiting was observed only in tramadol group, and there was no incidence in the dexmedetomidine group. Almost similar number of patients were sedated in both groups and the sedation score in all the patients was 2. There was no evidence of respiratory depression, hypotension or bradycardia in any of the patients. HR, mean blood pressure, body temperature, and SPO₂ remained within normal limits throughout the procedure in both groups .

4. DISCUSSION

The shivering is a protective response occurring as part of a centrally mediated thermoregulatory defense mechanism to hypothermia. The shivering is a frequent complication under regional anesthesia occurring either as a result of a decrease in core body temperature or misinformation from receptors. Potential risk factors for hypothermia in spinal anaesthesia include ageing, level of sensory block, temperature of the operation theatre and IV solutions. In this study, all operation theatres (OTs) maintained an ambient temperature of 23-25°C, and all fluids and drugs were at room temperature during the surgery. Demographic factors such as age, gender, duration of anaesthesia and surgery have also been matched to reduce any confounding bias.

The neurotransmitter pathways involved in shivering are multiple and involve opioids, α_2 adrenergic, serotonergic, and anticholinergic receptors. Drugs acting on these systems which include opioids (pethidine, nalbuphine, or tramadol), propofol, clonidine, ketamine are utilized in the treatment of shivering. However, adverse effects such as hypotension, hypertension, sedation, respiratory depression, nausea and vomiting limit their use. Hence, the hunt for an ideal anti-shivering agent is continuing.

Tramadol is an opioid analgesic with opioid effect mainly mediated via mu receptor with minimal effect on kappa and delta receptors. It also activates the monoaminergic receptors of the descending spinal inhibitory pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both.

Alpha-2 adrenergic agonists are widely used nowadays in anaesthesia and intensive care settings. Dexmedetomidine is an α_2 adrenoceptor agonist, with antihypertensive, sedative, analgesic, and anti-shivering properties. The anti-shivering effects of alpha adrenoceptor agonists are mediated by binding to α_2 receptors that mediate vasoconstriction and the anti-shivering effect. In addition, it has hypothalamic thermoregulatory effects. Dexmedetomidine comparably reduces the vasoconstriction and shivering thresholds, thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally. It has been successfully used as an adjunct to local anaesthetics in spinal anaesthesia and peripheral nerve blockade, for the sedation of mechanically ventilated patients in the Intensive Care Unit. The role of dexmedetomidine in the treatment of shivering has been evaluated in a few studies. It may be a good choice because of its dual effects related 'anti-shivering' and sedation.

With same dose, that is, 0.5 mg/kg of tramadol, the response rate reported by Shukla *et al.* was 92.5%, by Reddy . We found 100% response rate in our study. Maheshwari *et al.* reported similar recurrence rate with tramadol as in our study (8.5%) but the dose used in their study was 1 mg/kg. The incidence of nausea and vomiting with tramadol in our study was 26% and 22%, respectively. These variations could be explained by the peculiar patient characteristics in different studies. Maheshwari *et al.* have reported a very high incidence of sedation to the extent of 84%, which as mentioned earlier could be due to the higher dose as opposed to 29% sedation in our study.

There was no recurrence of shivering and no adverse effects occurred. We found a response rate of 100% and apart from sedation, there was no other adverse effect observed. But there was recurrence in 1 patient who had to be given a rescue dose. All other studies have used higher dose of dexmedetomidine (1 µg/kg), so comparison of results would not be appropriate. In our study, the incidence of sedation was 21.4%, which is similar to other studies. One contradictory report was by Karaman *et al.* according to whom intra-operative dexmedetomidine infusion caused negligible sedation inspite of using a loading dose of 1 µg/kg followed by a maintenance infusion of 0.5 µg/kg/h.

The results of this study indicate that dexmedetomidine takes lesser time to control shivering. The incidence of adverse effects like nausea and vomiting was found to be higher in case of tramadol compared to dexmedetomidine. More studies need to be undertaken with varying dose ranges to extrapolate the results of this study.

There was not much difference in the number of patients who were sedated in either group. The sedation seen with dexmedetomidine, in the absence of nausea and vomiting, is beneficial for the surgeon, anaesthetist as well as the patient. It provided more comfort to the patient, maintained more cardio-respiratory stability, improved surgical conditions and also provided amnesia during surgery.

The limitations of our study include a relatively smaller size sample. Though dexmedetomidine was effective in the treatment of shivering, side effects were reported with it which was treatable. A larger study is needed to report an ideal drug for shivering. Secondly, we did not measure the core temperature but used the axillary temperature in all patients. Thirdly, the incidence of shivering would have been less if we have used external warming devices for all patients.

The search continues for drugs that sufficiently improve the tolerance of thermoregulation without simultaneously producing respiratory depression, or haemodynamic instability. Dexmedetomidine might prove to be a valuable addition in the current armamentarium of the available drugs.

5.CONCLUSION

We conclude that dexmedetomidine is more effective than tramadol in the treatment of shivering

because of its faster onset, lesser recurrence rate, and better sedation. The complications reported with dexmedetomidine were easily treatable and did not have much clinical impact.

More studies of different dose ranges of dexmedetomidine need to be conducted in order to cement its position as an efficient anti-shivering agent.

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