

COMPARISON OF INTRAVENOUS DEXMEDETOMIDINE AND TRAMADOL FOR TREATMENT OF POST SPINAL ANAESTHESIA SHIVERING: A RANDOMIZED CONTROL TRIAL.

Anaesthesiology

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ABSTRACT

Background: Shivering occurs in 40 – 64% of the patients undergoing surgery under spinal anaesthesia. Tramadol is widely used drug for controlling shivering, causes nausea, vomiting and recurrence of shivering in few patients. Dexmedetomidine, a highly selective α_2 -adrenoceptor agonist, has been used as a sedative agent and is known to reduce the shivering threshold. Aim of this study was to compare the efficacy of dexmedetomidine and tramadol in controlling the shivering post spinal anaesthesia.

Methodology: A prospective randomized controlled double blinded study was conducted among 120 patients undergoing surgery under spinal anaesthesia. Both sex of age 20 – 60 years with ASA grade I-II and who developed post spinal anaesthesia shivering intraoperatively were included. The study population was randomly allocated into two. Group D (n=60) consisted of patients treated shivering with injection Dexmedetomidine 1 mcg/kg diluted to 10 ml saline and Group T (n=60) consisted of patients treated shivering with injection Tramadol 0.5 mg/kg diluted to 10 ml saline. Duration of onset of shivering, time for control of shivering, recurrence of shivering, side effects and sedation score were recorded. **Results:** The time for control of shivering was 2.84 ($\pm$ 0.39) min among dexmedetomidine group which is lesser compared to Tramadol group which had 5.61 ($\pm$ 0.53) min (p = 0.001). Among the dexmedetomidine group, none had nausea or vomiting whereas 18.3% patients among Tramadol group had nausea and 15% patients had vomiting. Again the recurrence of shivering was seen among 10% of the patients in Tramadol group whereas none had recurrence in dexmedetomidine group.

Conclusion: Dexmedetomidine can be used a better alternative for tramadol in treatment of shivering in patients undergoing surgery under spinal anaesthesia in terms of time for control of shivering, recurrence and side effects like nausea and vomiting.

KEYWORDS

Dexmedetomidine, Tramadol, shivering, spinal anaesthesia

INTRODUCTION

Shivering is physiological thermoregulatory response to cold or hypothermia and defined as an involuntary, repetitive activity in skeletal muscles.^[1] Shivering occurs in about 50% in patients with a core temperature of 35.5°C and in 90% with a core temperature of 34.5°C.^[2] 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.^[3] Various methods are available for the control of shivering. These may be non-pharmacological or pharmacological. Intra-operative hypothermia can be minimized by any technique that limits cutaneous heat loss to the environment such as those due to cold operating room, evaporation from surgical incisions and conductive cooling produced by administration of cold intravenous fluids. Tramadol is an opioid receptor agonist and acts as inhibitor of the re-uptake of serotonin (5-hydroxytryptamine) and norepinephrine in the spinal cord. This facilitates 5-hydroxytryptamine release, which influences thermoregulatory control.^[4] At present, it is widely used as drug for the control of shivering. But it causes nausea and vomiting and few recurrence of shivering even after first dose which is very distressing for the patient.^[5] Hence the need to find a better drug which has comparable efficacy to tramadol and at the same time has less of side effects. Dexmedetomidine is a highly selective α_2 -adrenoceptor agonist with potent effects on the central nervous system. It has been used as a sedative agent and is known to reduce the shivering threshold.^[6] Both the drugs tramadol and dexmedetomidine are easily available and cost effective. Our study was designed to compare a small dose of dexmedetomidine, a α_2 -adrenoceptor agonist, with that of tramadol, an opioid analgesic in the treatment of post-spinal anaesthesia shivering as well as their side-effect profile.

MATERIALS AND METHODS

A prospective randomized controlled double blinded study was conducted among the patients undergoing surgery at a tertiary care hospital in India during February to August 2020. The study included 120 patients undergoing surgery under spinal anaesthesia. Both sex of

age 20 – 60 years with height $\geq$ 150 cms, weight of 50-80 kgs with ASA grade I-II and who developed post spinal anaesthesia shivering intraoperatively were included. Patients who had history of acute infection, fever or sepsis, pregnancy, chronic history of headache and backache, spinal deformity or infection at the local site or allergic to experimental drugs were excluded from the study. The patients were subjected for detailed pre anesthetic checkup. These patients who qualify as per the selection criteria were given explanation in their vernacular language regarding surgical procedure, anaesthesia procedure & drugs to be used. The study was conducted after the approval from ethical committee of the institution. Written informed consent was obtained from all the patients.

Sample Size

According to Tanveer Singh et al study^[7], considering the mean difference of time to disappearance of shivering in Dexmedetomidine and Tramadol as 1 min, and average standard deviation of 2 min, at 95% confidence interval with 80% power, the sample size is calculated using the formula, $N = (Z_{1-\alpha/2} + Z_{1-\beta})^2 * 2 * \sigma^2 / (\mu_1 - \mu_2)^2$ where $Z_{1-\alpha/2}$ is two tailed probability for 95% confidence interval = 1.96, $Z_{1-\beta}$ - two tailed probability for 80% power = 0.84, $\mu_1 - \mu_2$ - difference in mean time to disappearance of shivering between Dexmedetomidine and Tramadol groups = 1 min and σ is average standard deviation of time to disappearance of shivering in Dexmedetomidine and Tramadol groups = 2 min. $N = 62.79$. Approximating, the sample size required for each group is taken as 60 and the total sample size is 120.

Randomization Procedure

The study population was randomly allocated into two groups. The randomization was done by sealed envelope method. A total of 120 envelop (60 per group) were made, each envelop mentioning a computer generated random number based on which allocated to a particular study group. On start of shivering in the patient, an anaesthetist different from anaesthetist (principal investigator) who conducted the study were asked to open the envelope and prepared the study drug to be given to the patient according to the group allocated. Double blinding technique was followed for the reliability of the results.

Study Procedure

Initiation of subarachnoid block was done by injection bupivacaine (0.5%) at L2-3 or L3-4 interspace. There was no active warming of patients and the fluids were used at room temperature. All vital parameters including systolic blood pressure, diastolic blood pressure, pulse rate, SpO₂ and axillary temperature were recorded in the beginning of the surgery and at the onset of shivering, after cessation of shivering and then every 5 min till the end point of study. Those patients who developed shivering after administration of spinal anaesthesia were included in the study.

Grading of shivering was done as follows: Grade 0: No shivering; Grade 1: One or more of the following: Piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause, 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 either Grade 3 or Grade 4 of shivering were included in the study. The time at which shivering started after subarachnoid block (onset of shivering) and time to disappearance of shivering (in minutes) were noted.

If the shivering did not subside by 15 min, the treatment was considered to be not effective. Recurrence of shivering was also noticed. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of dexmedetomidine (0.25 µg/kg IV) or tramadol (0.25 mg/kg IV) in the respective groups. Side effects like nausea, vomiting, itching, bradycardia (<60/min), hypotension (decrease >20% of baseline of systolic blood pressure/diastolic blood pressure [SBP/DBP]) and sedation score were recorded. Bradycardia, hypotension, and vomiting were treated with Inj atropine 0.6 mg i/v, Inj ephedrine in 6 mg boluses i/v titrated until blood pressure (BP) reached within 20% of baseline BP and Inj ondansetron 4mg i/v, respectively, when required.

Sedation score was assessed as per modified Ramsay score: 1: Anxious and agitated or restless or both; 2: Cooperative, oriented and tranquil; 3: Responding to commands only; 4: Brisk response to light glabellar tap or loud auditory stimulus; 5: Sluggish response to light glabellar tap or loud auditory stimulus; 6: No response to stimulus.

Study Algorithm

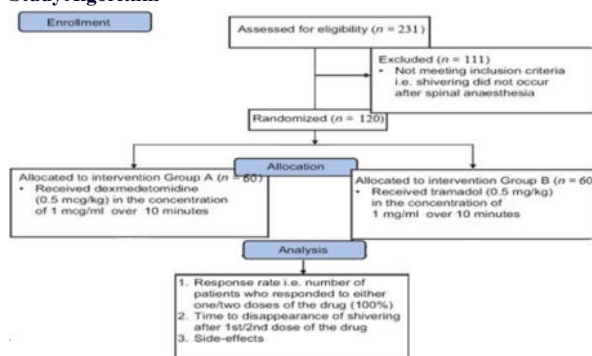


Fig 1: Flow chart of the study procedure

Statistical Methods

Data collected was entered in MS Excel (MS Office 16) and analyzed using SPSS software version 21. Continuous variables were represented in mean $\pm$ standard deviation. Categorical variables were represented in frequencies and percentages. Line diagrams were shown to depict the vital parameters recorded at different timings. Chi square test was used to determine the significance of the association between two categorical variables. Fisher's exact test was used when more than 20% of the cell values have expected cell value less than 5. Student 't' test was used to determine the significance of difference between two means. p values less than 0.05 were considered statistically significant.

RESULTS

The incidence of shivering among patients subjected to spinal anaesthesia was 51.94%.

In the study population, both the groups did not had any significant difference with respect to Age, Sex, weight of the patients, ASA grade,

duration of surgery and spinal anaesthesia.

Table 1: Demographic Characteristics Of The Study Population

		Group		p value
		Group D	Group T	
Age (years)		41.7 (± 7.5)	40.1 (± 10.4)	0.352
Sex	Male	52 (54.2%)	44 (45.8%)	0.068
	Female	8 (33.3%)	16 (66.7%)	
Weight (kg)		62.9 (± 7.3)	61 (± 7.8)	0.177
ASA	I	39 (48.1%)	42 (51.9%)	0.559
	II	21 (53.8%)	18 (46.2%)	
Duration of surgery		60.4 (± 13.3)	61.4 (± 14.8)	0.679
Duration of Spinal Anaesthesia		162.1 (± 14.8)	161.8 (± 12.6)	0.905

Table 2: Shivering Timing of the subjects in the study population

		Group		p value by 't' test
		Group D	Group T	
Time for onset of Shivering (min)		22.02 (± 2.5)	22.52 (± 2.29)	0.256
Time for control of shivering (min)		2.84 (± 0.39)	5.61 (± 0.53)	0.001

Shivering disappeared in all patients in both groups who received dexmedetomidine and tramadol and both the drugs were found to be effective in reducing shivering. The time of onset of shivering was around 22 minutes and there was no significant difference between two groups. The time for control of shivering was found to be lesser among dexmedetomidine group (2.84 (± 0.39) min) compared to Tramadol group which had 5.61 (± 0.53) min ($p < 0.05$).

Table 3: Side effects and recurrence of shivering among the subjects in the study population

		Group		p value
		Group D	Group T	
Side effects	Nil	60 (100%)	40 (66.7%)	0.001
	Nausea	0 (0%)	11 (18.3%)	
	Vomiting	0 (0%)	9 (15%)	
Sedation Score	2	5 (8.3%)	6 (10%)	0.752
	3	55 (91.7%)	54 (90%)	
Recurrence		0 (0%)	6 (10%)	0.014

Among the dexmedetomidine group, none had nausea or vomiting whereas 18.3% patients among Tramadol group had nausea and 15% patients had vomiting. This difference was statistically significant ($p < 0.05$). Again the recurrence of shivering was seen among 10% of the patients in Tramadol group whereas none had recurrence in dexmedetomidine group and this difference was also statistically significant ($p < 0.05$).

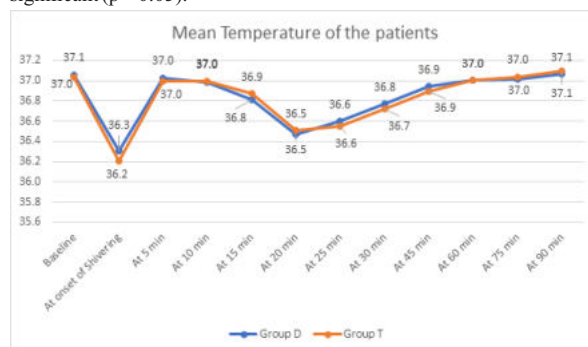


Fig 2: Mean Temperature Of The Subjects In The Study Population

The Vital parameters namely heart rate, temperature, systolic and diastolic blood pressure were comparable in patients among both the groups and there was no statistically significant difference between the two groups for the above parameters.

DISCUSSION

Patients undergoing surgery under neuraxial anaesthesia experience shivering as a more common complication. Crowley et al^[1] depicted that shivering is seen in 40 – 64% of the patients undergoing surgery under neuraxial anaesthesia. The present study showed an incidence of 51.94% of shivering in the study population which is well within the

range mentioned by Crowley et al^[1].

The present study aimed to compare the efficacy of dexmedetomidine with tramadol in the treatment of shivering in the patients after sub arachnoid block. The time for control of shivering using dexmedetomidine in this study was 2.84 ($\pm$ 0.39) min. Tanveer et al^[7] showed the shivering was controlled using dexmedetomidine in 2.9 $\pm$ 0.23 min which is almost equal to the findings of the present study. The time for control of shivering using tramadol was 5.61 ($\pm$ 0.53) min in the present study which is also comparable to Tanveer et al^[7] showing 4.61 ($\pm$ 0.38) min and Shukla et al^[8] showing 5.01 ($\pm$ 1.02) min. The difference in the time for control of shivering between dexmedetomidine and tramadol was statistically significant ($p < 0.001$) which is also resembled in Tanveer et al^[7].

Ten percentages of the patients in Tramadol group had recurrence of shivering whereas none of the patients in the Dexmedetomidine group had recurrence of shivering. The difference was statistically significant ($p < 0.05$). Tanveer et al^[7] also showed higher incidence of recurrence of shivering in Tramadol group (16%) compared to Dexmedetomidine group (6%).

The side effects of nausea and vomiting had a different distribution in the two study groups. None of the patients in the Dexmedetomidine group had nausea and vomiting while 18.3% patients had nausea and 15% had vomiting in the Tramadol group and the difference was statistically significant ($p < 0.001$). Tanveer et al^[7] also showed higher incidence of nausea and vomiting in Tramadol group of patients compared to Dexmedetomidine group of patients. There was no incidence of side effects like hypotension and itching in either of the study groups.

The study population had a Ramsay sedation score of 2 to 3 with almost equal distribution between two groups. However, no patient in the study population had a level of sedation above Grade 4 and these patients were able to maintain their airway and SpO₂ on room air.

Comparing the overall results, Dexmedetomidine has a good efficacy in treatment of shivering in patients post sub arachnoid block compared to tramadol in shorter timing of control of shivering, lower recurrence of shivering and fewer side effects.

The core temperature of the patients could not be measured which may be considered as a limitation. We had to resort to continuous measurement of axillary temperature by thermometer as we felt that a nasal, oesophageal or rectal probe would be uncomfortable for the patients.

CONCLUSION

Dexmedetomidine can be used a better alternative for tramadol in treatment of shivering in patients undergoing surgery under neuraxial anaesthesia in terms of time for control of shivering, recurrence and side effects like nausea and vomiting.

REFERENCES

1. Crowley LJ, Buggy DJ. Shivering and Neuraxial Anesthesia. *Reg Anesth Pain Med* 2008;33(3):241–52.
2. Bhattacharya PK, Bhattacharya L, Jain RK, Agarwal RC. Post anaesthesia shivering (PAS): A Review Article. *Indian J Anaesth* 2003;47(2):88.
3. Sessler DL. Temperature monitoring and perioperative thermoregulation. *Anesthesiology* 2008;109(2):318–38.
4. Lee CR, McTavish D, Sorkin EM. Tramadol. A preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute and chronic pain states. *Drugs* 1993;46(2):313–40.
5. Tobi K, Edomwonyi N, Imarengiaye C. TRAMADOL EFFECTS ON PERIOPERATIVE SHIVERING IN LOWER LIMB ORTHOPAEDIC SURGERIES UNDER SPINAL ANAESTHESIA. *J West Afr Coll Surg* 2012;2(2):46–62.
6. Kim Y, Kim Y, Seo K, Kang H. Optimal Dose of Prophylactic Dexmedetomidine for Preventing Postoperative Shivering. *Int J Med Sci* 2013;10(10):1327–32.
7. Kundra TS, Kuthiala G, Shrivastava A, Kaur P. A comparative study on the efficacy of dexmedetomidine and tramadol on post-spinal anesthesia shivering. *Saudi J Anaesth* 2017;11(1):2–8.
8. Shukla U, Malhotra K, Prabhakar T. A comparative study of the effect of clonidine and tramadol on post-spinal anaesthesia shivering. *Indian J Anaesth* 2011;55(3):242–6.