



Efficacy and Safety of Tramadol and Dexmedetomidine in Treatment of Shivering Following Spinal Anaesthesia: A Randomized Controlled Study

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ABSTRACT

Context: Shivering occurs in approximately 50% of cases after administration of spinal anaesthesia. Post spinal shivering is distressing to the patient. Pharmacological agents are method of choice for control of post-spinal shivering.

Aim and Objectives: To determine effectiveness of tramadol and dexmedetomidine in control of post spinal shivering and comparison of their side effects.

Materials and Methods: Hundred patients, ASA I and II, aged between 16-65 years were grouped in two groups, group T (tramadol) and group D (dexmedetomidine) according to computer generated randomised control table. Shivering scores were calculated at 0, 5, 10, 15, 30, 90 & 120 mins after spinal anaesthesia. Patients in group T received Inj Tramadol 0.5mg/kg and group D Inj Dexmedetomidine 0.5µg/kg in 100 ml of normal saline (NS) over 10 mins intravenously (IV) after development of grade 2 shivering. Postoperative nausea vomiting (PONV) and sedation scores were calculated. Incidence of side effects i.e. bradycardia, hypotension and respiratory depression were also studied.

Statistical Analysis Used: Continuous data was analysed using independent 't' test and categorical data was analysed using Chi-square test.

Results: There were 50 patients in each group. Additional measures for control of shivering was required in 2 patients in group T and none in group D. Mean time for control of shivering in group T was 14.08±11.83 mins vs. group D 8.74±5.54mins ($p=0.002$). Sedation was higher in group D ($p < 0.001$) but PONV was seen in group T only ($p < 0.001$).

Conclusion: Dexmedetomidine is a better agent for control of post spinal shivering.

Key words: Post spinal shivering, tramadol, dexmedetomidine.

Introduction

Shivering is defined as an involuntary repetitive activity of skeletal muscles.

The incidence of shivering following spinal anaesthesia has been noted to be around 50-60% in various studies.^{1,2} It is distressing and uncomfortable to patient. Shivering interferes with monitoring and increases oxygen consumption. It can lead to various metabolic derangements such

as hypoxemia, lactic acidosis and hypercarbia.^{3,4,5}

It is thus beneficial to avoid shivering, to prevent increased hemodynamic and metabolic demands. Spinal anaesthesia impairs thermoregulation by causing vasodilatation which leads to distribution of core heat to the peripheries.⁶ Various pharmacological and non pharmacological agents are available for control of shivering. But hunt for an ideal antishivering agent is ongoing.⁷ Tramadol

has been used as an anti-shivering agent but has side effects such as nausea and vomiting.¹ Dexmedetomidine, has been shown to reduce shivering threshold.⁸ However studies showing its efficacy are lacking.

Thus the present study was undertaken to compare the effectiveness of tramadol and dexmedetomidine in treatment of post spinal shivering.

Materials and Methods

This prospective randomised control study was conducted after approval of institutional ethical research committee, in a tertiary care hospital on 100 ASA1 and 2 patients aged between 16-65 years undergoing both elective and emergency surgeries under spinal anaesthesia. Pregnant females, patients with hemodynamic instability, known allergies, coagulation disorders, heart diseases, arrhythmias and use of sedative drugs were excluded from the study.

After taking written and informed consent, patients were divided into two groups, group T and group D, of 50 each with help of computer generated randomisation table, done by WINPEPI Software. CONSORT guidelines were followed.

A large bore IV cannula was secured and patients were adequately preloaded with crystalloid. Standard monitors were attached for continuous monitoring of ECG, heart rate, blood pressure, oxygen saturation and respiratory rate. Patients were given spinal anaesthesia under all aseptic precautions in L3-4 space with 3-3.6ml of Inj 0.5% hyperbaric bupivacaine stored at room temperature depending on the height of the patient. After spinal anaesthesia all patients received oxygen supplementation at 4L/min and appropriate fluid. All patients were continuously monitored for heart rate, blood pressure, respiratory rate, shivering, sedation, nausea and vomiting.(0, 5, 10,15, 30,45,60,90 and 120mins after administration of spinal anaesthesia).

Shivering was evaluated by Crossly and Mahajan⁹ on 5 point scale with score 0- no shivering, 1- piloerrection or peripheral vasoconstriction but no visible shivering, 2- muscular activity in 1 muscle

group, 3- muscular activity in more than 1 muscle group, 4- whole body shivering.

If patients had grade 2 or more shivering they were included in the study and given the study drug. The patients in group D received Inj Dexmedetomidine 0.5µg/kg in 100 ml Normal saline over 10 mins and in group T received Inj Tramadol 0.5mg/kg in 100ml Normal saline over 10 minutes intravenously.

Time taken for cessation of shivering after administration of study drug (in mins) was recorded.

If patients still had persistent grade 3 or 4 shivering they were additionally given Inj Ketamine 25mg IV bolus.

The sedation score was scored on a scale of 0-4 with 0- alert and awake, 1- resting with eyes closed, 2- drowsy responding to verbal stimuli, 3- drowsy responding to physical stimuli, 4- unarousable.⁹ PONV was graded on a score of 0-3 with 0- no nausea/ vomiting, 1- nausea, 2- retching, 3- vomiting.⁹

Patients with nausea and vomiting were given Inj ondansetron 0.08mg/kg.

Patients were observed for adverse effects like bradycardia, hypotension and respiratory depression.

Bradycardia was defined as heart rate <50/min and treated by Inj atropine 0.6mg IV bolus. Hypotension was defined as systolic blood pressure less than 90mmHg or a fall of >20% of the baseline blood pressure and was treated by Inj mephentermine 6-12mg and infusion of fluids. Respiratory depression was defined as respiratory rate <8/min and patients were given oxygen supplementation and assisted ventilation if required.

Data was entered in excel sheet. Statistical analysis was performed using Statistical Programme for Social Sciences (SPSS) 11 for Windows system. Data was summarized using proportions and mean. Continuous data was analysed using independent 't' test and categorical data was analysed using Chi-square test. A 'p' value of <0.05 was regarded as statistically significant.

Results

A total of 100 patients (50 in each group) were randomised over a period of 6 months from October 2015 to February 2016. Both the groups were comparable in the demographic characteri-

stics i.e. age, weight and duration of surgery. (Table 1). In group D, 25 patients were females and 25 were males; where as in group T there were 19 females and 31 males.

Table 1: Demographic Characteristics between two Groups

Parameter	Group D	Group T	p value
Age(yrs)	42.38±15.86	41.78±15.83	0.850
Weight(kg)	57.3±12.46	61.9±12.61	0.070
Duration of surgery(mins)	53.90±27.99	60.20±29.42	0.275

After analysis using independent t test and chi square test, it was noted that there was no significant difference between the mean shivering

scores throughout the surgery in both the groups. (Table 2)

Table 2: Mean Shivering Score at Various Intervals in Two Groups

	Group D		Group T		p value
	Mean shivering score	Standard deviation	Mean shivering score	Standard deviation	
0 mins	0.28	0.454	0.20	0.404	0.354
5 mins	1.08	1.158	0.98	1.134	0.664
10 mins	1.70	1.055	1.42	1.012	0.179
15 mins	1.30	0.931	1.46	1.034	0.418
30 mins	0.84	0.976	1.02	1.078	0.384
45 mins	0.40	0.639	0.42	0.642	0.876
60 mins	0.14	0.351	0.33	0.718	0.103
90 mins	0.04	0.198	0.14	0.351	0.082
120 mins	0.02	0.141	0.08	0.274	0.172

All the patients in group D, responded to dexmedetomidine and no additional measures were required for control of shivering. In group T, however, 1 patient did not respond to treatment with tramadol. 1 patient developed recurrent shivering after initial control of shivering with Inj Tramadol. Both these patients were given Inj Ketamine as rescue drug for control of shivering. Even though there was no significant difference between the mean shivering scores throughout the

surgery in both the groups, yet the time taken by dexmedetomidine in control of shivering was significantly lower as compared to tramadol.(8.74±5.54 mins vs 14.08±11.83mins) (p = 0.005) (Table 5)

Patients in group D were more sedated as compared to group T. (p<0.001) (Table 3, 5)

Table 3: Mean Sedation Score

Sedation Score	Number of Patients	
	Group D	Group T
0	11	36
1	25	12
2	14	1
3	0	1
4	0	0
Mean Score	1.06±0.712	0.34±0.626

In group D none of the patients had PONV whereas 50% of patients in group T had PONV.

Table 4: Mean PONV Score

PONV Score	Number of Patients	
	Group D	Group T
0	50	25
1	0	10
2	0	9
3	0	6
Mean Score	0	0.92±1.085

Thus PONV scores were significantly higher in group T. ($p < 0.001$) (Table 4, 5)

Table 5: Comparison of Study Variables in Two Groups

	Group D	Group T	p value
Mean Time taken for control of shivering	8.74±5.54 mins	14.08±11.83 mins	0.005
Mean Sedation score	1.06±0.712	0.34±0.626	<0.001
Mean PONV score	0.00±0.000	0.92±1.085	<0.001

There was no significant difference between the complications observed in both the groups. (Table 6)

Table 6: Incidence of Complications in Two Groups

	Group D		Group T	
	Yes	No	Yes	No
Adverse Events In Percentage (%)				
Hypotension	2	98	4	96
Bradycardia	6	94	2	98
Respiratory Depression	0	100	0	100

Discussion

Shivering after administration of anaesthesia is distressing both to the patient and anaesthetist.

The exact mechanism of shivering during spinal anaesthesia is not known. Various hypothesis states that impairment of central thermoregulation, internal redistribution of body heat, and heat loss to the environment are the most probable causes for shivering under spinal anaesthesia. Potential risk factors for hypothermia in spinal anaesthesia include ageing, level of autonomic block, temperature of the operation theatre and IV solutions.¹

The neurotransmitter pathways involved in shivering are multiple and involve opioids, α_2 adrenergic, serotonergic, and anticholinergic receptors.¹⁰ Thus drugs acting on these receptors are used in control of shivering. But adverse effects such as bradycardia, hypotension, hypertension, sedation, respiratory depression, nausea and vomiting limit the use of these drugs.

In our study intravenous tramadol (opioid) and dexmedetomidine (α_2 adrenergic agonist) were

compared for their effects on control of post spinal shivering and also the adverse effects related to administration of these drugs such as PONV, sedation, bradycardia, hypotension and respiratory depression were studied.

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.^{11,12} This is the most commonly used drug to control post spinal shivering.¹³

Dexmedetomidine is α_2 adrenoceptor agonist, with antihypertensive, sedative, analgesic, and anti-shivering properties.¹⁴The anti-shivering effects of α -adrenoceptor agonists are mediated by binding to α_2 receptors that mediate vasoconstriction and the anti-shivering effect.¹⁵ In addition, it has hypothalamic thermoregulatory effects.⁸

Dexmedetomidine comparably reduces the vasoconstriction and shivering thresholds, thus suggesting that it acts on the central thermoregulatory system rather than preventing shivering peripherally.¹⁶

Our study was a prospective randomised controlled trial, conducted on 100 patients between 16 to 65 years age, having physical status ASA I or II, and undergoing either elective or emergency surgery under spinal anaesthesia. Patients were randomly divided into two groups of 50 each based on computer generated software. The patients in our study were observed after administration of spinal anaesthesia and were given the study drug as per randomisation.

In Group D (dexmedetomidine), Inj. Dexmedetomidine 0.5µg/kg in 100 ml NS was given IV whereas patients in Group T received Inj tramadol 0.5mg/kg IV in 100 ml NS. The study drug was administered slowly IV over a period of 10 mins after development of grade 2 or more shivering. Time taken for cessation of shivering was noted. Patients were also monitored continuously for heart rate, blood pressure, oxygen saturation, nausea/ vomiting and sedation.

Demographic data and the duration of surgery in both our study groups were comparable.

Our study showed that even though there was no significant difference between mean shivering scores at 0,5,10,15,30,45,60,90 and 120 min interval in both the groups, the time taken by dexmedetomidine in control of shivering was significantly lesser as compared to tramadol group. (8.74±5.54 mins vs 14.08±11.83 mins) (p=0.005).

In a similar study conducted by Mittal G. et al¹ (2014) a same amount of dose of both the drugs was given as a 5ml IV bolus. Only elective cases were included in their study. Also the patients were given study drug after development of grade 3 shivering but in our study the drugs were administered after development of grade 2 shivering. In their study comparatively lesser time was taken for control of shivering as compared to our study (group D 2.52±0.44mins vs group T

5.92±0.81mins) (p=0.0024) and there were no failure cases in any of the group. This might probably be due to the fact that drugs were administered at a later interval in their study and were given as bolus rather than slow IV administration in our study.

In study conducted by Shukla U. et al¹⁷(2011) time taken for control of shivering with Inj tramadol IV was 5.01±1.02 mins which was comparable to the study conducted by Mittal G. et al. However in this study also the drug was given as a fast IV bolus as compared to slow IV infusion over 10mins in our study.

In our study all the patients in group D responded to treatment with intravenous dexmedetomidine and there were no failure cases. But in group T, 1 patient (2%) had persistent shivering even after administration of intravenous tramadol and 1 patient developed recurrent shivering almost 25 mins after the initial control of shivering. Thus 2 patients (4%) out of 50 patients in group T did not have desired response to treatment with intravenous tramadol.

In a study conducted by Al Maruf A.¹⁸(2015) on pregnant patients posted for lower segment caesarean section under spinal anaesthesia a similar rate of recurrence of shivering was seen with IV Inj Tramadol (3.33% vs 2% in our study). Also a study conducted by Kulshrestha S.¹⁹(2014) showed a failure rate of 8.9% with IV tramadol. A higher dose of IV tramadol(50mg) was used in this study.

In our study patients in group D had higher sedation scores as compared to group T (1.06±0.712 vs 0.34±0.626) (p<0.001). Even though more patients were sedated in group D as compared to group T, 1 patient in group T had a sedation score of 3 whereas none of the patient had a score of 3 in group D. The patient in group T with higher sedation score was the patient which did not respond to treatment with Inj Tramadol IV and had to be given Inj Ketamine IV. Thus higher sedation score might be due to additional effect of administration of IV ketamine.

In a study conducted by Sathyamoorthy V. et al²⁰ (2016) sedation scores in dexmedetomidine group were significantly higher than the baseline values and values in tramadol group ($p < 0.0001$). In the study by Bozgeyik et al¹² (2015) showed average sedation score of 3 in dexmedetomidine group which was statistically significant when compared to average score 2 in tramadol group intraoperatively. In study conducted by Mittal G. et al¹ (2014) no difference was seen in the sedation profile in both the groups.

In our study none of the patients in group D experienced any nausea and vomiting whereas 50% of the patients in group T had nausea and vomiting. Out of these 38% (19 patients) had complaints of nausea and retching and 12% (6 patients) experienced vomiting. Thus PONV score in group T was 0.92 ± 1.085 which was significantly higher in comparison to group D. ($p < 0.001$).

In study conducted by Shukla U. et al¹⁷ (2011) the incidence of nausea/vomiting was 77.5% as compared to 50% in our study. In the study conducted by Mittal G. et al¹ (2014) a similar incidence of nausea and vomiting was seen (48%). However as described previously, in both these studies the drug was given as IV bolus rather than slow IV infusion as in our study.

In our study there was no significant difference in incidence of bradycardia, hypotension and respiratory depression in both the study groups.

Thus the results of our study show that dexmedetomidine when administered IV leads to earlier cessation of shivering as compared to IV tramadol. The incidence of side effects such as nausea and vomiting is also lesser with dexmedetomidine as compared to tramadol. Also the sedation caused by dexmedetomidine has an anxiolytic effect and no major adverse effects are seen with this dose.

Thus it can be concluded that the sedation seen with dexmedetomidine, in the absence of nausea and vomiting, is beneficial for the surgeon, anaesthetist as well as the patient. Dexmedeto-

midine has the potential to replace tramadol as a potent anti-shivering agent.

The major limitation of our study was that the core body temperature and operating room temperature was not measured. Also we had a smaller sample size. The sedation scores and PONV scores were subjective. Also the IV fluids administered at room temperature could have led to hypothermia. All these factors can effect intraoperative shivering and may have acted as confounding factors in our study.

Further studies can be conducted to determine the role of these drugs on cessation of shivering using a larger sample size. Also it can be seen whether a still lower dose of dexmedetomidine can lead to cessation of shivering. Efficacy of various other routes of administration such as oral for tramadol and intrathecal for both tramadol and dexmedetomidine can also be studied for control of shivering.

Conclusion

It can be safely concluded that Inj Dexmedetomidine has the potential to replace Inj Tramadol as a preferred anti-shivering agent. The sedation provided by Inj Dexmedetomidine in absence of nausea and vomiting is beneficial to the patient and also acts as an anxiolytic.

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