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Comparing the efficacy of tramadol, ketamine and dexmedetomidine in the prevention of intraoperative shivering in patients undergoing surgery under subarachnoid blockade

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ABSTRACT

Background: The most common nagging and inconveniencing complication of spinal anesthesia is intra operative shivering. Central neuraxial blockade blunts the thermoregulatory mechanism by restricting vasoconstriction, resulting in shifting of central heat to the periphery from the trunk. Various pharmacological and non pharmacological methods are used for the control of intraoperative shivering.

Aim: The aim of our study was to compare the efficacy of Tramadol, Ketamine and Dexmedetomidine in the prevention of intra operative shivering in patients undergoing surgeries under subarachnoid blockade.

Materials and Methods: 90 patients of age group between 20 to 65 years belonging to ASA 1 and 2 posted for elective surgery under spinal anaesthesia will participate in this study. The patients were randomly allocated into 3 groups of 30 each and were named as by computer generated random table number. Group T received Tramadol 0.5 mg/kg in 100 ml NS over 10 – 15 mins; Group K Ketamine 0.25 mg/kg in 100 ml NS over 10 – 15 mins and Group D Dexmedetomidine 0.5 µg/kg in 100 ml NS over 10 – 15 mins.

Observation and Results: Data were statistically analysed with the SPSS version 22.0 software using two-sided unpaired t-test and Chi-square test. A repeated measure of ANOVA was applied for the three groups to know the with-in subject variability in prevention of shivering following subarachnoid blockade and p value < 0.05 was considered to be significant.

Conclusion: The conclusion of our study is that Dexmedetomidine at the dose of 0.5 µg/kg decreases effectively in the prevention of intra operative shivering in patients undergoing surgery under subarachnoid blockade when compared with Tramadol and Ketamine.

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1. Introduction

Subarachnoid blockade or spinal anesthesia is the commonest regional anesthesia technique performed for surgeries involving lower abdomen, pelvis and lower limb extremities. The most common nagging and inconveniencing complication of spinal anesthesia is intra operative shivering which is very distressing experience causing physiological stress both to the patients as well as the perioperative physicians and operating surgeon.

Shivering is the involuntary recurrent muscle action of skeletal muscles, is a normal thermo regulatory mechanism and the reported occurrence is wide varied ranging from 40 – 70 % from the literature.^{1,2} Central neuraxial blockade blunts the thermoregulatory mechanism by restricting vasoconstriction, resulting in shifting of central heat to the periphery from the trunk (below the level of subarachnoid block).^{3,4}

Hypothermia worsens in perioperative period insulating in major adverse cardiac events and it doubles to triples the requirement of oxygen consumption, rising the metabolic

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rate by 100 to 600%, thereby increasing the catecholamine production resulting in lactic acidosis, which is very detrimental in poor cardio respiratory reserve patients.⁵ Shivering can produce motion artifacts in anaesthesia monitors showing erroneous values.²

Various pharmacological and non-pharmacological methods are dealt for the management of intraoperative shivering.⁵ Pethidine have been used for many years as the treatment modality for shivering.⁶ In our study, we have used Tramadol, Ketamine and Dexmedetomidine to study the effect of preventing the intra operative shivering in patients undergoing surgery under spinal anaesthesia.

2. Aim and Objectives of the Study

The main aim is to compare the efficacy of Tramadol, Ketamine and Dexmedetomidine in the prevention of intra operative shivering in patients undergoing surgeries under subarachnoid blockade. This study also focuses on effects of drugs on intra operative haemodynamics, monitoring the temperature, comparing the level of sedation and other undesirable effects.

3. Materials and Methods

A study titled “Comparing the efficacy of Tramadol, Ketamine and Dexmedetomidine in the prevention of intraoperative shivering in patients undergoing surgery under subarachnoid blockade” was done in PSG Institute of Medical Sciences & Research, Coimbatore. This study was done after obtaining Institutional Human ethics committee clearance from the institution and informed written consent from all the patients who participated in the study. It is a prospective randomised control study and the sample size was calculated using 95% confidence interval and power of the study being 80%. The sample size was 30 in each group with allocation ratio being 1:1:1.

90 patients of age group between 20 to 65 years corresponding to ASA 1 and 2 posted for elective surgery under subarachnoid blockade will participate in this study. The patients were assigned at random with 30 participants in each group and were called as Group T receiving (Tramadol 0.5 mg/kg), Group K (Ketamine 0.25 mg/kg) and Group D (Dexmedetomidine 0.5 µg/kg). Patients were randomly allocated to one of the three groups by computer generated random table number (numbered from 1 to 90) and the corresponding number was represented with the concerned group of the study drug. It is a double blinded study and the performer is also unaware of the group of the drug till the end of the trial.

Patients aged between 20 – 65 years belonging to ASA 1 and ASA 2 undergoing elective surgery under spinal anaesthesia < 150 minutes duration with surgeries involving lower abdomen, urological, gynaecological, orthopaedic and lower limb extremity was considered the

inclusion criteria for our study. Patient denial, absolute contraindications for subarachnoid blockade, inability to communicate with the patient, combined spinal and general anaesthesia, known drug intolerance or proven allergic reactions to study drugs, baseline core temperature >37.5°C or < 35.5°C, blood transfusion during surgery, pregnancy and lactating mothers were excluded from the study.

Routine pre-operative assessment was done and the patients were kept nil per oral from 10 pm the day prior to surgery. Informed written consent was obtained. All the patients were pre-medicated with tablet Pantoprazole 40 mg and Alprazolam 0.25 mg orally the day prior to surgery at night and Pantoprazole 40 mg at 6 am on the morning of day of surgery. Patients were assigned individually to one among the three groups by computer generated random table number.

Group T: Tramadol (n=30) 0.5 mg/kg in 100 ml NS over 10 – 15 mins

Group K: Ketamine (n= 30) 0.25 mg/kg in 100 ml NS over 10 – 15 mins

Group D: Dexmedetomidine (n=30) 0.5 µg/kg in 100 ml NS over 10 – 15 mins

In the pre operative room, an 18G intravenous cannula was inserted and an infusion of Plasmalyte solution started at 2ml/ kg/ hr. On arrival in the operation theatre, pre induction monitors like ECG, NIBP and SpO₂ were connected and monitoring of these parameters started after noting the baseline values. The operating room ambient was continued at 25°C. The patient was placed in right lateral posture and under standard universal precautions, sterile painting draping done. After skin infiltration with 2 ml of 2% Lignocaine, spinal puncture was attempted in L₃L₄ or L₄ L₅ interspace with 26G Quincke spinal needle. After establishment of free flow of CSF, intrathecal administration of 15mg 0.5% Bupivacaine Heavy was given over a period of 30 seconds as per the random allocation and patient was turned supine post spinal injection. No tilt was given to any patients. The study drug was infused by the blind observer. Oxygen delivered at a rate of 5L/min using Hudsons mask and injection Ondansetron 4 mg was supplemented to all patients. Surgery was commenced when the spinal blockade level reached T7/T8 and Patients were observed for 120 minutes or until the end of the surgery; considering the longer duration among them.

The haemodynamic parameters were monitored. Hypotension (Systolic BP <90mmHg and Diastolic BP < 50 mm Hg was treated with intravenous fluids ± vasopressors – Injection Ephedrine or Mephentremine 6 mg IV bolus SOS. Bradycardia (Heart rate <50/min) was treated with injection Glycopyrrolate 0.004 mg/kg IV bolus SOS. Intra operative temperature monitoring and level of sedation was also assessed. The patients who developed shivering intra operatively were supplemented with injection Pethidine 0.25 mg/kg as rescue drug.

Shivering was observed by a grading system as described by 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.

Grade 4 : Gross muscle activity involving the whole body
Sedation was assessed by a four point scale as per Filos et al.

Grade 1 : Awake and alert.

Grade 2 : Drowsy, responsive to verbal stimuli.

Grade 3 : Drowsy, arousable to physical stimuli.

Grade 4 : Unarousable.

Data were statistically analysed with the SPSS version 22.0 software using Chisquare and ANOVA. Baseline characteristics were presented as mean $\pm$ S.D. Two-sided unpaired t-test and Chi-square test was applied to analyze the data and p value less than 0.05 were considered as significant. A repeated measure of ANOVA was applied for the three groups to know the with-in subject variability in prevention of shivering following subarachnoid blockade and $p < 0.05$ was considered to be significant.

4. Result and Discussion

Homeothermic mammals maintain a uniform isothermal characteristics internally and the central temperature varies between 36.5°C and 37.5°C in humans. Anterior hypothalamus incorporates the thermal inputs from various tissues of the body and differentiates peripheral information with a set point to reach or approach the temperature lower than this set point; resulting in responses to warm the body, while higher temperatures will initiate reflexes to cool the body.²

Autonomic thermoregulation is attenuated during central neuraxial blockade resulting in decrease in central or core temperature. Central neuraxial blockade decrease the shivering and vasoconstriction thresholds cephalad to the level of the neuraxial block by 0.6°C. The concept of postanaesthesia shivering resembling like seizures or tremors remains still unproven. The postulates suggest that the decrease in reflex response in the descending spinal reflexes due to central neuraxial blockade could be the cause for tremors.³ The two variants of tremor patterns noted could be either a tonic pattern resembling normal shivering with 4 – 8 cycle/min waxing and waning model or a phasic pattern with 5 to 7 Hz shattering pattern similar to pathologic clonus response. The net effect of this tonic and phasic patterns are due to thermoregulatory responses superseding with drop in temperature and arteriovenous shunt vasoconstriction.⁷

The consequences of hypothermia and shivering includes reversible coagulopathy, increased blood loss necessitating blood transfusion, impaired wound healing, delayed drug metabolism, altered mental status, cardiac arrhythmias and ischaemia, increased risk of infection, myocardial oxygen consumption and basal metabolic rate.⁴

Treatment of shivering includes both non pharmacological methods like use of forced air warmers, warmed blankets, warmed intravenous fluids, use of plastic sheets and surgical drapes and maintaining warmed humidified operating room; and pharmacological methods that includes usage of drugs like pethidine, tramadol, meperidine, clonidine, ketamine, magnesium sulphate, dexmedetomidine, alfentanil and nefopam.

In our study, extremities of population like paediatric, pregnancy and geriatric patients were not chosen due to variable confounding factors in relation to their age. Demographic profile in all the groups are comparable but statistically insignificant.

The primary objective in our study was about the drugs in causing decreased incidence of shivering in the desired study group population.⁸ Dexmedetomidine had better prevalence in decreased incidence of intra operative shivering compared to Tramadol and Ketamine as only one patient had shivering at 30 minutes following subarachnoid blockade in close equivalent with Lim fern et al⁹ studies with similar outcome. 6 patients at 15 minutes and 11 patients at 30 minutes in Tramadol group had the highest incidence of shivering with shivering grade more than two and showed statistical significance with p value 0.045 and 0.003 respectively. Only one patient in Ketamine group had shivering at 30 mins. Mittal et al¹⁰ in his study compared dexmedetomidine with tramadol supplementing the drug after the onset of shivering and concluded that both drugs were equally efficacious and dexmedetomidine had a faster onset of action. Bozgeyik et al¹¹ used dexmedetomidine and tramadol compared with a placebo and commented both drugs were equally similar in the prevention of shivering. Dhimar et al.¹² in his study used Tramadol 100 mg in all patients which showed variation in their results while comparing with our study. Though the shivering was seen in all the groups at 45 and 60 minutes, with varying grades statistically it was insignificant. Statistical insignificance was noted at 90 and 105 mins since none of the patient had shivering. Prophylactic low dose Ketamine was found to be effective in preventing postoperative shivering in Gecaj-Gashi et al¹³ and similar results were seen in our study also. Yong shin et al¹⁴ in their study used 0.75 with 1 μ g/kg and found to be effective against 0.5 μ g/kg in our study. Genopadhyay et al.¹⁵ concluded that pethidine, tramadol and ketamine effectively prevent shivering following spinal anaesthesia, prove ketamine was smart and effective alternative over two drugs due to the better haemodynamic stability and less adverse effect.

Table 1: Demographic data of all three groups

Parameters	Group T	Group K	Group D	p value	Significance
Age					
Mean age in yrs $\pm$ S.D	39.97 $\pm$ 9.84	40.80 $\pm$ 9.81	38.70 $\pm$ 9.64	0.715	Statistically insignificant
Sex distribution					
Male	21 (23.3%)	27 (30%)	25 (27.8%)	0.131	Statistically insignificant
Female	9 (10%)	3 (3.3%)	5 (5.5%)		
Weight (kg)	65.24 $\pm$ 9.86	66.13 $\pm$ 9.06	64.33 $\pm$ 10.26	0.720	Statistically insignificant
Height (cm)	162.8 $\pm$ 7.04	167.57 $\pm$ 6.59	163.33 $\pm$ 6.99	0.533	Statistically insignificant
ASA Grading					
I	23(76.7%)	23(76.7%)	24(80%)	0.938	Statistically insignificant
II	7 (23.3%)	7 (23.3%)	6 (20%)		

Table 2: Incidence of shivering between three groups

Time (mins)	Group T	Group K	Group D	p value	Significance
Baseline	0	0	0	0	N.S*
5	0	0	0	0	N.S
10	0	0	0	0	N.S
15	6	0	0	0.045	H.S [£]
30	11	2	1	0.003	H.S
45	3	0	1	0.384	N.S
60	1	0	0	0.364	N.S
75	1	1	0	0.403	N.S
90	0	0	0	0	N.S
105	0	0	0	0	N.S
120	0	1	0	0.364	N.S

* - N.S - Nil significant

£- H.S - Highly significant

Table 3: Incidence of sedation between three groups

Time (mins)	Group T	Group K	Group D	p value	Significance
Baseline	0	0	0	0	N.S
5	0	0	25	0.000	H.S
10	0	0	27	0.000	H.S
15	5	17	28	0.000	H.S
30	13	22	29	0.004	H.S
45	14	21	29	0.008	H.S
60	15	15	26	0.000	H.S
75	11	11	24	0.000	H.S
90	7	6	22	0.000	H.S
105	0	1	13	0.000	H.S
120	0	0	0	0	N.S

Dal et al,¹⁶ in their study found that the number of patients shivering on arrival in the recovery room, and at 10 and 20 min after operation were significantly less in Groups P (pethidine 20 mg) and K (ketamine 0.5 mg/kg) than in Group S (normal saline) and concluded that use of Prophylactic low-dose ketamine was very useful in preventing postoperative shivering.

The secondary objective of the study was sedation¹⁷ and all our used study group drugs can produce drowsiness

to a certain extent; hence none of the study population were supplemented with sedatives, hypnotics or anxiolytics. Dexmedetomidine showed good sedation score of 3 within 5 minutes in majority of the population comfortably lasting for about 90 minutes without producing haemodynamic disturbances comparing with other two drugs. Initiation of sedation was slow in onset, peaking around 15 minutes for a sedation score of 2 in 40% in Tramadol group. Ketamine had a sedation score superior to tramadol, almost similar

Table 4: Mean axillary temperature (°C) between groups

Time (mins)	Group T	Group K	Group D	p value	Significance
Baseline	36.21	36.29	36.29	0.130	N.S
5	36.18	36.15	36.15	0.671	N.S
10	36.21	36.22	36.19	0.759	N.S
15	36.03	36.10	35.98	0.560	N.S
30	36.09	36.03	36.03	0.637	N.S
45	36.13	36.15	36.18	0.727	N.S
60	36.21	36.13	36.19	0.367	N.S
75	36.12	36.22	36.28	0.098	N.S
90	36.20	36.34	36.34	0.092	N.S
105	36.31	36.28	36.28	0.856	N.S
120	36.40	36.39	36.34	0.516	N.S

Table 5: Rescue drug usage between groups

Rescue	Group T	Group K	Group D	p value	Significance
Yes	12	3	1	0.001	Highly significant
No	18	27	29		

to dexmedetomidine with peak effect within 15 minutes producing good sedation score but lacked in awakening state. Mittal et al¹⁰ in his studies concluded sedation due to dexmedetomidine provides additional comfort to the patient. Bozgeyik et al¹¹ also reported similar results of sedation within 5 minutes about dexmedetomidine in his study. Usta B et al¹⁸ showed higher sedation scores in dexmedetomidine group providing conveniencing sedation for the patient. Dexmedetomidine sedated population followed oral commands and maintained in a tranquil state as seen in Elvan et al¹⁹ studies. Bradycardia was reported in 3 patients and hypotension in 2 patients only in dexmedetomidine group necessitating conservative treatment but proved statistically insignificant similar to Usta B et al.¹⁷ There was no incidence of respiratory depression, nausea, vomiting and headache in all the three groups. No statistical significance was noted in the axillary temperatures measurement in all the 3 groups.

The limitations noted in our study are ideal Dexmedetomidine dose needs to be evaluated to produce negligible haemodynamic instability.²⁰ Tramadol used at 0.5mg/kg seemed to be inconclusive necessitating the work up of optimal dose to prevent shivering.²¹ Dosage of 0.25mg/kg Ketamine as studied by Kose et al.²² was used in our study and needs reconsideration.

To summarise Dexmedetomidine was more effective in the prevention of shivering when compared with Ketamine and Tramadol with an added advantage of adequate reliable sedation and stable haemodynamics without any detrimental adverse effects.

5. Conclusion

The conclusion of our study is that Dexmedetomidine at the dose of 0.5 µg/kg decreases effectively in

the prevention of intra operative shivering in patients undergoing surgery under subarachnoid blockade when compared with Tramadol and Ketamine.

6. Source of Funding

None.

7. Conflict of Interest

The author declares no conflict of interest.

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