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Research Article

A Comparative Study of the Effect of Clonidine and Tramadol for Control of Shivering Under Spinal Anesthesia

Dr. Subodh S Kamtikar*, Dr. Deepak V Dhummansure
Department of Anesthesia, BRIMS, Bidar, 585401, India

***Corresponding author**
Dr. Subodh S Kamtikar
Email: cdkad@rediffmail.com

Abstract: Spinal anesthesia is known to significantly impair thermoregulation through inhibiting vasomotor and shivering responses and through redistributing heat from core body to peripheral tissues with subsequent rapid hypothermia during anesthesia. Among pharmacological therapies a recent meta-analysis, reported use of Clonidine, Tramadol, pethidine, nefopam and ketamine as the most common agents. There are few studies from this region comparing Cloniidne and Tramadol, hence the present study. This was a open label randomized study conducted in a tertiary care hospital in South India, from June 2014 to November 2014. The participants were allocated to receive Clonidine (Group C; n = 40) or Tramadol (Group T; n=40). Group C (n=40) received Clonidine 0.5 µg/kg (intravenously) IV, and group T (n=40) received Tramadol 0.5 mg/kg IV. Patients who developed grade 3 or 4 shivering for at least 3 minutes after spinal anesthesia were included in the study. Student's T test has been used to find the significance of study parameters between two groups of patients, Chisquare/ 2x3 Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. In the present study, it was observed that both Clonidine and Tramadol are effective in treating post spinal shivering, but the time interval from the commencement of treatment to cessation of shivering is quite less with Clonidine ($P<0.01$). The response rate was 100% in Clonidine group and recurrence was nil. Complications like hypotension, bradycardia, and dry mouth were observed in Clonidine group and nausea and vomiting in Tramadol group. The sedation score was higher in Clonidine group. Both Clonidine and Tramadol are effective in treating patients with post-spinal anesthesia shivering. The higher incidence of side effects of tramadol, like nausea, vomiting and dizziness, may limit its use as an anti-shivering drug.
Keywords: Clonidine, Tramadol, Shivering, Spinal anesthesia

INTRODUCTION

Spinal anesthesia is known to significantly impair thermoregulation through inhibiting vasomotor and shivering responses and through redistributing heat from core body to peripheral tissues with subsequent rapid hypothermia during anesthesia [1]. Shivering can be a potentially serious complication, resulting in various sihns and symptoms like increased metabolic rate, increased oxygen consumption along with raised carbon dioxide (CO2) production, increased surgical bleeding, arterial hypoxemia, lactic acidosis, increased intracranial pressure and interferes with pulse rate, blood pressure [2, 3].

Regional anesthesia prevents peripheral vasoconstriction and impairs autonomic thermoregulation leading to intra-operative core hypothermia. The thresholds for vasoconstriction and shivering are decreased by 0.6^0C, above the level of block and the reduction is proportional to the number of spinal segments blocked [4,5]. Non-pharmacological management is by measures of external heating like warming blankets, forced air warming, warmed fluids etc., Among pharmacological therapies a recent meta-analysis, reported use of Clonidine, Tramadol , pethidine, ,nefopam and ketamine as the most common agents [6].

The drugs available for the management of shivering have its own adverse effect and the ideal anti-shivering still not found [2, 7]. Comparative studies between Clonidine and Tramadol for control of shivering but have reported contrasting findings, while some studies have reported [7] that Clonidine offers a better relief , others workers[8] are in favor of Tramadol. There are few studies from this region comparing Cloniidne and Tramadol, hence the present study.

MATERIAL AND METHODS

This was a open label randomized study conducted in a tertiary care hospital in South India,

from June 2014 to November 2014. The study was approve by institutional ethics committee and informed consent was taken from the subjects.

Inclusion criteria

- Patients of either sex aged between 25 to 50 years undergoing elective surgery under spinal anesthesia
- American Society of anaesthesiologists grade-I & II patients who developed intra-operative shivering post spinal anesthesia of grade 3 or 4 lasting for minimum period of 2 minutes.

Exclusion criteria

- Patient with history of sensitivity to drugs used.
- Patients who developed shivering even before administering spinal anesthesia
- Patients requiring supplementation with general anesthesia
- Patients with medical disorders like ischemic heart disease, kidney and liver disease, autonomic neuropathy and uncontrolled hypertension.

On the day of surgery the patients were brought to the operation theatre (OT), i.v. was line secured, standard monitors attached and baseline parameters were recorded. Upon arrival in the operation theatre, an 18G venous canula was inserted and preloading done with Ringer's Lactate solution 10 ml/kg before giving spinal anesthesia and maintained at 6 ml/kg/h after spinal anesthesia. Subarachnoid anesthesia was administered with 0.5% heavy bupivacaine (15 mg) at L3-4 or L4-5interspace using 26G Quincke's spinal needle under aseptic conditions.

The participants were allocated to receive Clonidine (Group C; n = 40) or Tramadol (Group T; n=40). Group C (n=40) received Clonidine 0.5 µg/kg (intravenously) IV, and group T (n=40) received Tramadol 0.5 mg/kg IV. Patients who developed grade 3 or 4 shivering for at least 3 minutes after spinal anesthesia were included in the study. Both the drugs were given as slow IV bolus injection. Response to drug was assessed as: Success-(absence of shivering), Null-(shivering intensity not changed). Response time i.e. The time to cessation of shivering after treatment was noted. Patients were monitored for side effects or any complications following drug administration, such as nausea, vomiting, pruritus, sedation, respiratory depression and bradycardia.

Grading of shivering was done as per Wrench [9] which is as follows:

- Grade 0: No shivering
- Grade 1: One or more of the following: Piloerection, Peripheral vasoconstriction, peripheral cyanosis with, 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

The attending anesthetist recorded the time in minutes at which shivering started after spinal anesthesia (onset of shivering), severity of the shivering, time to disappearance of shivering (in minutes) and response rate (shivering ceased after treatment in 15 minutes). Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of Clonidine (0.5 µg/kg IV) or Tramadol (0.5 mg/kg IV) in the respective groups.

Sedation score was assessed with a four-point scale as per Filos [10]

1: Awake and alert
2: Drowsy, responsive to verbal stimuli
3: Drowsy, arousable to physical stimuli
4: Unarousable

Statistical analysis

Previous studies have found an incidence of shivering of the range of 40-65%. We anticipated an incidence of 50%. Hence, we assumed that <35 parturients were required in each group for a type I error of 0.05 and the power of the study was > 90%, a sample size of 40 was calculated. The data was recorded and analyzed using SPSS software (version 16). Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Student's T test has been used to find the significance of study parameters between two groups of patients, Chisquare/ 2x3 Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. P<0.01 was considered statistically significant

RESULTS

A total of 40 patients in each group were included in the study. The demographic characteristics of the participants are shown in table 1.

There was no statistically significant difference in the demographic characteristics between the groups. The parameters for post-spinal anesthesia shivering and responses are shown in table 2.

The sedation score and side effects of both the groups is shown in table 3.

Complications like hypotension, bradycardia, and dry mouth were observed in Clonidine group and nausea and vomiting in Tramadol group. The sedation score was higher in Clonidine group.

Table 1: Demographic characteristics of the participants

Parameter	Group C	Group T
Age	32.14±2.79	30.46±3.21
Gender		
Male	22	25
Female	18	15
Weight(kg)	67.78±7.88	69.21±8.22
Height (cms)	171.23±7.53	169.67±8.02
ASA grade I/II	16/24	19/21
Duration of surgery (Minutes)	93.24±6.22	91.76±5.69
Duration of spinal anesthesia (Minutes)	126.92±14.27	129.14±15.18

ASA = American Society of anaesthesiologists

Table 2: Parameters for post-spinal anesthesia shivering and responses

Parameter	Group C	Group T
Onset of shivering (Minutes)	13.56±7.14	14.21±7.09
Severity of shivering (Grade)	3	
Time for cessation of shivering after medication (Minutes)	3.09 ± 0.47	5.67 ± 0.85*****
Response rate (%)	100	39 (97.5)
Recurrence of shivering (%)	Nil	2 (5)

***** P<0.01 = highly significant

Table 3: Side effects and sedation score in the study groups

Parameter	Group C	Group T
Sedation score 2 or more	22 (55%)	14 (35%)
Nausea	2 (5%)	6 (15%)
Vomiting	0	2 (5%)
Hypotension	3 (7.5%)	0
Dizziness	1 (2.5%)	9 (22.5%)
Bradycardia	4 (10%)	1(2.5%)
Dry mouth	2 (5%)	0

DISCUSSION

Shivering is an involuntary, oscillatory muscular activity, occurs as a thermoregulatory response to hypothermia in an attempt to augment the metabolic heat production. It presents as a common peri-operative problem causing hypertension, tachycardia and increase metabolic demands. Various risk factors associated with shivering include type and duration of anesthesia, level of sensory blockade, age of patient, and temperature of operating room and infusion fluids [11].

The neurotransmitter pathways involved in shivering are multiple and involve opioids, α 2adrenergic, serotenergic, and anticholinergic receptors. Hence, drugs acting on these systems which include opioids (pethidine, nalbuphine, or Tramadol), ketanserin, propofol, doxapram, Clonidine, ketamine and nefopam are utilized in the treatment of shivering. Clonidine is a centrally acting selective a2 agonist. Clonidine exerts its anti-shivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord [12-13].

Tramadol is an opioid analgesic with opioid action preferably mediated via μ (mu) receptor with minimal effect on kappa and delta binding sites. The anti-shivering action of Tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both [14-15]. In the present study, it was observed that both Clonidine and Tramadol are effective in treating post spinal shivering, but the time interval from the commencement of treatment to cessation of shivering is quite less with Clonidine (P<0.01). The response rate was 100% in Clonidine group and recurrence was nil (table 2). These findings were similar to other studies comparing Clonidine with other drugs having anti-shivering properties [7, 16-18].

Response rate with Clonidine was 100% and recurrence of shivering was noted in 2 cases of

Tramadol. In the present study, incidence of nausea, vomiting and dizziness was higher in Tramadol group while sedation was higher in Clonidine group. These findings are similar to other studies [7, 17]. Our result showed the superiority of Clonidine over Tramadol for control of intra-operative shivering post spinal anesthesia, as the time taken for control of shivering was less in Clonidine group and showed statistically significant difference from Tramadol group. But other studies have found contrasting finings, where Tramadol was more effective than Clonidine [8, 19-20].

Limitations of the study

This was a open liable study and the sample size was small. Future studies should double blind, mulitcentric and should contain a large sample size. Another limitation was that the present study included short duration surgeries. The anti-shivering effect of Clonidine and Tramadol needs to be evaluated in surgeries of longer duration where chances of developing hypothermia are more.

CONCLUSION

Both Clonidine (0.5 µg/kg) and Tramadol (0.5 mg/kg) are effective in treating patients with post-spinal anesthesia shivering, but time taken for complete cessation of shivering was shorter with Clonidine as compared to tramadol, the difference being statistically significant. The higher incidence of side effects of tramadol, like nausea, vomiting and dizziness, may limit its use as an anti-shivering drug.

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