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COMPARATIVE STUDY OF INTRAVENOUS CLONIDINE VERSUS TRAMADOL FOR CONTROLLING SHIVERING IN REGIONAL ANAESTHESIA FOR CAESAREAN SECTION IN TERMS OF EFFICIENCY, SIDE EFFECTS & COMPLICATIONS

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ABSTRACT

Background: Spinal anaesthesia is popular and safe anaesthesia technique for various surgeries. Shivering that develops following spinal anaesthesia is common problem due to impairment of thermoregulatory control. Present study was aimed to compare the efficacy and safety of intravenous Tramadol with intravenous Clonidine in controlling shivering in obstetric patients under regional anaesthesia for caesarean section. **Material and Methods:** Present study was single-center, prospective, comparative study, conducted in pregnant women, 18-40 years age, ASA grade I & II, developing shivering intra operative or postoperative in emergency or elective section. Drug therapy started as per patient group after delivery of baby

as Group C received Clonidine 0.5mcg per kg i.v while group T- received tramadol 0.5mg per kg i.v. **Results:** There was no significant difference in pre operative temperature, HR, SBP, DBP and SpO2 in both groups and even after the control of shivering. Mean time required to control the shivering in Tramadol group is 2.77 minutes is significantly less as compared to the Clonidine group which is 5.47 minutes ($p< 0.001$). Response rate that is the percentage of patients in which shivering controlled in 15 minutes after the treatment is 95% in Tramadol group and 82.5% in Clonidine group. The difference was not significant statistically (P-value 0.155). No side effects were noted in tramadol group, while 3 patients had side effects in clonidine group (3 cases had sedation), difference was not significant statistically. **Conclusion:** Tramadol as compared to Clonidine is safe and effective in controlling the shivering in obstetric patients receiving spinal anaesthesia. Side effects were

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nil with tramadol, while patients received Clonidine were more sedated. Tramadol should be used for management of intra-operative shivering in regional anaesthesia for caesarean section.

Keywords: Tramadol, Clonidine, shivering, spinal anaesthesia

INTRODUCTION

Spinal anaesthesia is popular and safe anaesthesia technique for various surgeries. Redistribution of body heat during spinal or epidural anaesthesia typically decreases core temperature 0.5-1.0 degree Celsius.[1] Shivering that develops following spinal anaesthesia is common problem due to impairment of thermoregulatory control. It occurs in 19%-33% of patients receiving spinal anaesthesia.[2]

Shivering is response of the body to hypothermia. It is an involuntary, oscillatory muscular activity that can double or triple the oxygen consumption and carbon dioxide production. It is specifically disturbing to the mothers during labour and delivery. Vigorous shivering increases the metabolic heat up to 600% above the base level.[3]

Various non-pharmacological measures have been studied to control Shivering under Spinal anaesthesia, e.g. radiant warmer, pre warming of patients, space blankets, warm fluids, electric warming blankets etc.[4] Various pharmacological treatments like i.v. opioids, alfentanil, pethidine; nalbuphine and meperidine, 5-HT3 antagonists; ondansetron, dolasetron and cholinomimetic agent physostigmine have been used; however, side effects like hypotension, hypertension, sedation, respiratory depression, nausea and vomiting, limit their use.[4,5]

Pharmacological intervention does not raise body temperature, but resets the shivering threshold to a lower level, thereby decreasing rigors and its episodes. Present study was aimed to compare the efficacy and safety of intravenous Tramadol with intravenous Clonidine in controlling shivering in obstetric patients under regional anaesthesia for caesarean section.

MATERIAL AND METHODS

Present study was single-center, prospective, comparative study, conducted in Department of Anesthesiology, Dr. Vasantrao Pawar Medical College Hospital and Research centre, Nashik. Study duration was of 2 years (September 2019 to August 2021). Study was approved by institutional ethical committee.

Inclusion criteria

- Pregnant women, 18-40 years age, ASA grade I & II, developing shivering intra operative or postoperative in emergency or elective section.

Exclusion criteria

- Pregnant women with medical disorders, known case of alcohol or drug abuse,
- Pregnant women with hypersensitivity to study drugs
- Pregnant women with receiving drug for labour analgesia or other medication likely affect thermoregulation.
- Pregnant women not willing to participate

Pregnant women selected for study, underwent counselling for study procedure, & drugs to be used in their vernacular language. Patients willing to participate were considered

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for study. Detailed demographic, obstetric, medical details, examination findings, laboratory/radiological investigations were noted. Patients fit for anaesthesia, were kept NBM (nil by mouth) for at least 6 hours prior to procedure.

In surgical theater, an i.v cannula of 18G was secured and monitors were attached. Preloading with ringer lactate was done. Subarachnoid block given with inj bupivacaine 0.5H (1.5 to 2.5cc as per height of patient) at L3-L4 or L4-L5 space using 25G Quincke's needle adequate action set. Operating room temperature kept between 21 to 23^{o}C

Intraoperatively shivering was recorded at 5-minute interval up to 60 minutes of surgery, using a scale validated by Wrench.[6]

Grade 0: No shivering,

Grade 1: Piloerection but no visible muscular activity,

Grade 2: Visible muscular activity confined to one muscle group,

Grade 3: Visible muscular activity in more than one muscle group but not generalized,

Grade 4: Gross muscular activity (Shivering) involving the whole body.

Among 80 cases undergoing elective caesarean section, patients were divided into two groups of 40 each using computerized randomization charts. Drug therapy started as per patient group after delivery of baby

1. Group C - Received Clonidine 0.5mcg per kg i.v
2. Group T- Received Tramadol 0.5mg per kg i.v

Pulse rate, blood pressure, oxygen saturation and body temperature (in axilla) recorded before commencement of surgery and there after every 5min for one hour, every 15min for rest of procedure. Post operative side effects/adverse events noted were Nausea, Vomiting, Hypotension, Bradycardia, Dry mouth, Skin rash, Sedation, Extent of shivering & Sedation.

Sedation score was assessed as per Filo's:

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

Fifteen minutes after the administration of study drug if shivering grade remain same, the treatment regarded as less effective and rescue treatment in the form of intravenous dexamethasone 5mg was administered to control the shivering.

Statistical analysis was done using descriptive statistics.

Variables studied were time of appearance of shivering, response rate (Percentage of patients in which shivering controlled within 15 minutes), failure to control the shivering, recurrence of shivering & side effect and complications are noted.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

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RESULTS

In present study, age, weight, ASA grade, type of surgery (elective/ emergency) was comparable among both groups & difference was not significant statistically.

Table 1: General parameters

Parameters	Group T (Mean ± SD)	Group C (Mean ± SD)	P-value
Age (years)	25.10 ± 5.66	25.28 ± 5.52	0.889
Weight (kg)	62.90 ± 2.19	63.20 ± 2.70	0.587
ASA grade			0.820
I	23	24	
II	17	16	
Surgery			0.823
Emergency	20	21	
Elective	20	19	

There was no significant difference in pre operative temperature, HR, SBP, DBP and SpO2 in both groups and even after the control of shivering. Mean time required to control the shivering in Tramadol group is 2.77 minutes is significantly less as compared to the Clonidine group which is 5.47 minutes ($p< 0.001$).

Table 2: Intra-operative parameters

	Group T (n= 40) (Mean ± SD)	Group C (n= 40) (Mean ± SD)	P-value
● Temperature			
Pre operative	37.00 ± 0.14	37.01 ± 0.16	0.717
During shivering	36.35 ± 0.09	36.34 ± 0.13	0.55
● Heart rate			
During shivering	84.10 ± 7.99	84.15 ± 7.91	0.978
After control of shivering	79.05 ± 7.59	79.00 ± 7.58	0.977
● Systolic blood pressure (SBP)			
During shivering	121.05 ± 2.60	121.10 ± 2.64	0.932
After control of shivering	116.45 ± 3.52	116.35 ± 3.42	0.898
● Diastolic blood pressure (DBP)			
During shivering	80.50 ± 2.11	80.45 ± 2.10	0.916
After control of shivering	75.85 ± 4.01	76.10 ± 3.95	0.779
● SpO2			
During shivering	98.88 ± 0.40	98.78 ± 0.53	0.346
After control of shivering	98.90 ± 0.38	98.88 ± 0.40	0.776
● Mean time required to control shivering (min.) after treatment	2.77 ± 3.19	5.47 ± 5.11	< 0.001

Response rate that is the percentage of patients in which shivering controlled in 15 minutes after the treatment is 95% in Tramadol group and 82.5% in Clonidine group. The difference was not significant statistically (P-value 0.155).

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Table 3: Response rate

Time required to control shivering	Group T	Group C	Total
≤ 15	38 (95.0%)	33 (82.50%)	71
> 15	2 (5.0%)	7 (17.50%)	9

In present study, no side effects were noted in tramadol group, while 3 patients had side effects in clonidine group (3 cases had sedation), difference was not significant statistically.

Table 4: Comparison of occurrence of side effect in group 1 and group 2.

Side effect	Group T	Group C	Total	P-value
Present	0	3	3	0.255
Absent	40	37	77	

DISCUSSION

The mechanism which leads to shivering after regional anesthesia is not very clear, but the probable mechanisms could be decrease in core body temperature secondary to sympathetic block;[7] peripheral vasodilatation; increased cutaneous blood flow, which leads to increased heat loss through skin; cold temperature of operation theatre; rapid infusion of cold IV fluids; and effect of cold anaesthetic drugs upon the thermosensitive receptors in the spinal cord.

Several factors including age, duration of surgery, temperature of the operating room, and infusion solution, are risk factors for hypothermia and shivering.[2] The temperature of operating room was maintained at 21° to 23° C and infusions of crystalloid solution were warmed.

Pharmacological intervention does not raise body temperature, but resets the shivering threshold to a lower level, thereby decreasing rigors and its episodes. Various pharmacological therapies have been tried to prevent or treat shivering, but debate for an 'ideal anti-shivering drug' continues.

Tramadol may induce its antishivering effect via the additive or synergistic action of both kappa opioid receptor and 2 adrenergic mechanisms. The interaction of kappa opioid and 2 adrenoceptor mechanisms working in a complementary or synergistic manner to produce anti-shivering effects seems a possible explanation.[8]

Clonidine is an α_2 adrenoceptor agonist, with antihypertensive, sedative, analgesic and anti-shivering properties. The anti-shivering effects of alpha (α) adrenoceptor agonists are mediated by binding to α_2 receptors mainly the α_{2b} receptors that mediate vasoconstriction and the anti-shivering effect.[9]

Pausaudi s.et al.,[10] studied tramadol in dosages of 1mg/kg intravenously. In all patients shivering controlled in 45 seconds to 6 minutes. In our study also mean time required for tramadol to control the shivering is 2.77 minutes which is in accordance to the Paussaudi's study. Tramadol is effective in preventing of post anesthetic shivering.

De Witte J et al.,[11] assessed the effects of tramadol (0.5 mg. kg-1, 1 mg.kg-1 and 2 mg.kg-1 i.v.) or normal saline on shivering. They concluded Tramadol's distinct features in the treatment of shivering reside in its high safety profile and weak sedative properties,

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particularly in patients with poor cardiorespiratory reserve, in outpatients and on recurrence of shivering. In our study Tramadol used in 0.5mg/kg is effective in controlling the shivering and observed minimal side effects. These results are in accordance with our study results.

In the study by Chan et al.,[12] used IV tramadol (0.25mg/kg) effectively controlled shivering during cesarean delivery under regional anesthesia with minimal side effects. Hence the concluded that i.v Tramadol was effective in controlling shivering under regional anaesthesia as well in obstetric patients and there was no demonstrable difference in response rate or incidence of side effects between the two doses of 0.5mg/kg and 0.25mg/kg. There was no increased incidence of side effects in the treatment groups. Even in our study we used Tramadol in dosages of 0.5mg/ kg and we observed that there are no side effects with these doses.

Gangopadhyay *et al*.,[13] observed a significant number of cases of nausea and vomiting with tramadol; this high number of cases in the tramadol group could be explained by the fact that they used tramadol at 1 mg/kg i.v. as compared with 0.5 mg/kg i.v. in this study. This is even observation of our study that use of 0.5mg/kg tramadol there is no side effects such as nausea and vomiting.

Usha Shukla et al.,[14] used tramadol and clonidine in dosages of 0.5mg/kg and 0.5mcg/kg intravenously. They concluded both clonidine (0.5 μg/kg) and tramadol (0.5 mg/kg) effectively treated patients with post–spinal anaesthesia shivering. Complication rates were significantly higher in group T than in group C. Nausea, vomiting and dizziness were higher in group T than in group C. More patients of group C were sedated than of group T. Even in our study both drugs are effective in controlling the shivering. We observed that there are nil side effects in Tramadol group while patients in Clonidine group are more sedated.

Mean time required to control shivering in T group is 2.77 minutes which is in accordance with the studies of Pausaudi S.et al.,[9] Bhatnagar S Saxena .et al.,[15] Talakoub.et al.,[16] Velayudha S. Reddy .et al.,[17] Mean time required to control shivering in C group is 5.47 minutes which is in accordance with the studies of Capogna G .et al[18] P-value was <0.001. By using Mann-Whitney U test p-value < 0.05 therefore there is significant difference between median time required to control shivering in group T and Group C.

In group T side effects are nil which is in accordance with the study of Chan et al,[12] Gangopadhyay *et al,*[13] While in group C 3 patients experienced side effect in the form of sedation. The finding that side effect of clonidine is sedation which is in accordance with Usha Shukla et al., [17] & Velayudha s. Reddy et al.[14] p-value is 0.225. By using Fisher's exact test p-value > 0.05 therefore there is no association between occurrence of side effect with group T and group C.

Intra-operative shivering during regional anaesthesia especially in parturient undergoing caesarean section needs to be treated actively as shivering is not only troublesome but also increases the oxygen demand which can adversely affect both maternal and fetal outcome.

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CONCLUSION

Tramadol as compared to Clonidine is safe and effective in controlling the shivering in obstetric patients receiving spinal anaesthesia. Side effects were nil with tramadol, while patients received Clonidine were more sedated. Tramadol should be used for management of intra-operative shivering in regional anaesthesia for caesarean section.

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