Original Article

Indian Journal of Anesthesia and Analgesia
2017, 4 (4, Part-II), 1252-1267
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4417.54

A Comparative Study of the Effect of Clonidine and Tramadol on Post-Spinal Anaesthesia Shivering during Intraoperative Period

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Abstract

Introduction: Region anaesthesia is widely used and a safe anaesthetic technique. Shivering is frequently a known complication during regional anaesthesia. Shivering is a potentially serious complication. There are various methods available to control shivering during regional anaesthesia, which include non pharmacological methods and pharmacological methods using drugs. Drugs like tramadol, clonidine, are simple, cost-effective are useful for control of shivering. *Methodology:* The study was conducted in Gandhi Hospital, Secunderabad. All patients who developed post–spinal anaesthesia (intraoperative) shivering were randomly allocated to two groups: Group C (n=40) received clonidine 0.5 µg/kg (intravenously) IV, and group T (n=40) received tramadol 0.5 mg/kg IV. Standard monitoring of pulse rate was done, and non-invasive blood pressure (NIBP), oxygen saturation (SpO_2), body temperature (axillary) were recorded before the commencement of surgery and thereafter at every 5 minutes from the baseline i.e. subarachnoid block (SAB), for 30 min; and every 15 minutes, for the rest of the observation period. *Observation and Results:* In the present study, we found that clonidine is as effective as tramadol in treating post–spinal anaesthesia shivering, but the time interval from the commencement of treatment to cessation of shivering is quite less with clonidine (2.54±0.76 minutes) than with tramadol (5.03±1.02 minutes) (P=.0000001). The response rate was also higher in the clonidine group than in tramadol group, but the difference was not statistically significant (P=.03). *Conclusion:* In conclusion, both clonidine (0.5 µg/kg) and tramadol (0.5 mg/kg) effectively treated patients with post–spinal anaesthesia shivering, but tramadol took longer time to achieve complete cessation of shivering than clonidine, the difference being statistically significant. So we conclude that clonidine offers better thermodynamics than tramadol, with fewer side effects. The more frequent incidence of side effects of tramadol, like nausea, vomiting and dizziness, may limit its use as an anti-shivering drug.

Keywords: Post Spinal Anaesthesia Shivering; Tramodol; Clonidine; Better Thermodynamics.

Introduction

Regional anaesthesia (spinal anaesthesia) is widely used as a safe anaesthetic technique for both elective and emergency operations. Shivering is known to be a frequent complication, reported in 40 to 70% of patients undergoing surgery under regional anaesthesia[1,2] Shivering is a potentially serious complication, resulting in increased metabolic rate; increased oxygen consumption (up to 100-600%) along with raised carbondioxide (CO_2) production; ventilation and cardiac output; adverse postoperative outcomes, such as wound infection; increased surgical bleeding; and SSmorbid cardiac events. It causes arterial hypoxemia, lactic acidosis, increased intraocular pressure (IOP), increased intracranial pressure (ICP); and interferes with pulse rate, blood pressure (BP) And electrocardiographic (ECG) monitoring [3-5]. Shivering is very unpleasant, physiologically stressful for the patient undergoing surgery, and some patients find the accompanying cold sensation to be worse than the surgical pain. Though the mechanism of origin of shivering is not clear, various hypotheses have been proposed to explain its occurrence. Perioperative hypothermia is the primary cause, which occurs due to neuraxial anaesthesia–induced inhibition of thermoregulatory mechanism.

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Received on 23.08.2017, **Accepted on** 09.09.2017

Shivering occurs as a thermoregulatory response to hypothermia or muscle activity with tonic or clonic patterns, and various frequencies have been noticed. However,in the postoperative period, muscle activity may be increased even with normothermia, suggesting that mechanisms other than heat loss with subsequent decrease in the core temperature contribute to the origin of shivering. These may be uninhibited spinal reflexes, sympathetic over-activity, postoperative pain, adrenal suppression, pyrogen release and respiratory alkalosis [5]. Due to shivering and thermal discomfort, the quality of patient recovery suffers. Moreover,shivering per se may aggravate postoperative pain, simply by stretching of surgical incision.There are various methods available to control shivering during anaesthesia, which include non pharmacological methods and pharmacological methods using drugs which have anti-shivering properties. Non-pharmacological methods using equipment to maintain normal temperature of the body are effective but expensive and lack practicality, while the pharmacological methods using drugs like pethedine, tramadol, clonidine, doxapram, katenserin, nefopam, etc., are simple, cost-effective and easy to implement.

Aims and Objectives

The aim of this prospective double-blind randomized study was to compare the effects of clonidine with those of tramadol for control of shivering.

The following parameters will be compared between the two groups -

- Onset of shivering
- Severity of shivering
- Time interval from treatment to cessation of shivering
- Pulse rate changes intraoperatively
- Systolic blood pressure changes intraoperatively
- Diastolic blood pressure changes intra-operatively
- Side effects (if any)

Patients and Methods

Source of Data

The study was conducted in Gandhi Hospital, Secunderabad after obtaining approval from institutional ethical committee. A written informed consent was obtained from each patient. Eighty patients aged between 18 years and 50 years for elective abdominal, orthopaedic and gynaecological Surgeries were included in the study.

Method of Collection of Data

All patients who developed post–spinal anaesthesia intraoperative shivering were randomly allocated to two groups: Group C (n=40) received clonidine 0.5 μg/kg (intravenously) IV, and group T (n=40) received tramadol 0.5 mg/kg IV.

Inclusion Criteria

The following patients will be included in the study –

1. Patients of age between 18 and 45 years of both sexes.
2. Patients with American Society of Anaesthesiologists grade 1 and 2 physical status.
3. Patients posted for various elective abdominal, orthopaedic and gynaecological surgeries, e.g., inguinal herniorraphy, abdominal and vaginal hysterectomy,

K- nailing, dynamic hip screw (DHS), under spinal anaesthesia with no prior pre-medication, were included in this prospective double-blind randomized clinically controlled study.

Exclusion Criteria

Patients with the following features will be excluded from the study –

1. Patients with age less than 18 years and more than 50 years.
2. Patients with known hypersensitivity to clonidine and tramadol, known history of alcohol or substance abuse.
3. Patients with history of hyperthyroidism, cardiovascular diseases,
4. Patients with history of psychological disorder, severe diabetes or autonomic neuropathies
5. Patients with known urinary tract infection (UTI) were excluded.

Pre-Anaesthetic Evaluation

A thorough pre-anaesthetic evaluation will be

performed by taking detailed history and clinical examination.

In all the patients

- Height ,weight, basal heart rate, respiratory rate and blood pressure will be measured and recorded.
- Detailed physical examination of CVS, CNS, Per abdomen and RS .
- Examination of the spine.

Investigations

The following investigation were done.

1. Blood investigations: Hb%, BT, CT, Blood Urea, Serum creatinine, Serum electrolytes, Fasting blood sugar, Blood grouping and cross matching.
2. Urine: Albumin, sugar and microscopy
3. ECG and Chest x-ray PA view.

Preliminaries Included

1. Written informed consent
2. Intravenous access – starting of an intravenous line with 18G intravenous cannula.

Equipments

a For the procedure

A portable tray covered with sterile towels containing,

1. Disposable Syringe – 5 ml
2. 25 guage Quinke's needle
3. Bowl containing iodine
4. Sponge holding forceps.
5. Towels and towel clips.
6. Drug - 0.5% bupivacaine 3 ml.
7. Normal saline
8. Clonidine
9. Dexmedetomidineb) For emergency resuscitation

The anaesthesia machine, emergency oxygen source, working laryngoscope, appropriate size endotracheal tubes and breathing circuits.

- Working suction apparatus with suction catheter.
- Airways (oropharyngeal).
- Intravenous fluids. Anaesthetic agents
- Thiopentone sodium, diazepam, succinylcholine.

Resuscitation Drugs

- Hydrocortisone, atropine, adrenaline, aminophylline, mephentermine, calcium gluconate.

Position

The choice of position of the patient for performing the subarachnoid block depends on a number of factors- the proposed surgery being the most important. It can be done in lateral decubitus position or in sitting position.

Procedure

The patients were allocated to each group by computerized randomization.

Subarachnoid block was given with inj. Bupivacaine 0.5% (10-15 mg) at L 3-4or L 4-5 interspace using 25 gauge Quincke's needle, and blockage up to T 9-10 dermatome was achieved. All operation theatres in which the operations were performed maintained constant humidity (70%) and an ambient temperature of around 21°C to 23°C. Oxygen was administered to all the patients of both groups at a rate of 5 L/min with face mask, and patients were covered with drapes but not actively warmed. No means of active re-warming were used. Intravenous fluids and anaesthetic drugs were administered at room temperature. Preloading was not done in both the groups as we did not want intravenous fluid to influence the onset of shivering mechanism. Before beginning of spinal anaesthesia, standard monitoring procedures were established. Standard monitoring of pulse rate was done, and non-invasive blood pressure (NIBP), oxygen saturation (SPO_2), body temperature (axillary) were recorded before the commencement of surgery and thereafter at every 5 minutes from the baseline ie subarachnoid block (SAB), for 30 min; and every 15 minutes, for the rest of the observation period.

Definitions of Parameters

Shivering

Grading of shivering was done as per Wrench [32], 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

Hypotension: Patients whose blood pressure was recorded below i.e(>20% of baseline) were considered as hyotensive.

Bradycardia: Heart rate less than 50 beats per min (<50/min)

Sedation Score: Assessed with a four-point scale:

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

Recurrence of Shivering

Recurrence of shivering was noticed until the patient left the operation theatre. Patients 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, if required.

Statistical Analysis

Results were statistically analysed using Unpaired t test and Fisher exact test. A 'p' value of <0.05 was considered as significant. All the values are mentioned as Mean ± Standard Deviation.

Observation and Results

The prospective, randomized, comparative study was conducted in the Department of Anaesthesiology & Critical Care Gandhi Hospital, Secunderabad on 80 patients aged between 18-45 years posted for elective abdominal,orthopaedic and gynaeological surgeries. The purpose of study was to compare between Clonidine and Tramadol when given intravenously to control post anaesthesia spinal shivering interms of potency, efficacy, hemodynamic changes and complications / adverse effects.

There were no clinical or statistically significant differences in the demographic profile of patients and the two groups were comparable.

Age and Weight Distribution

The average age was 30.05±3.70 years in group C, and 28.92±3.48 years in group T.

Youngest patient in the study group was 23 years and oldest was 41 years. The average weights of the patients were 66.95±7.01 kgs in group C and 69.02± 7.512 kgs in group T respectively. There was no significant difference in age and weight between the two groups.

Types of surgeries

The two groups showed no statistical significant difference with respect to types of surgeries.

Gender Distribution

Both groups had predominantly male population, accounting for nearly ¾ of the total study population in each group. There was no significant difference between male and female of two groups with P value 1.0.

Duration of Surgery

The mean time for duration of surgery was 58.52± 5.08 min in group C whereas in group T the mean was 58.90±5.44min. This was statistically comparable with a p value of 0.582.

Onset of Shivering

The mean time of onset of shivering was 6.29 ±1.74 in group C when compared to 6.57±1.71 in group D. This was not clinically or statistically significant.

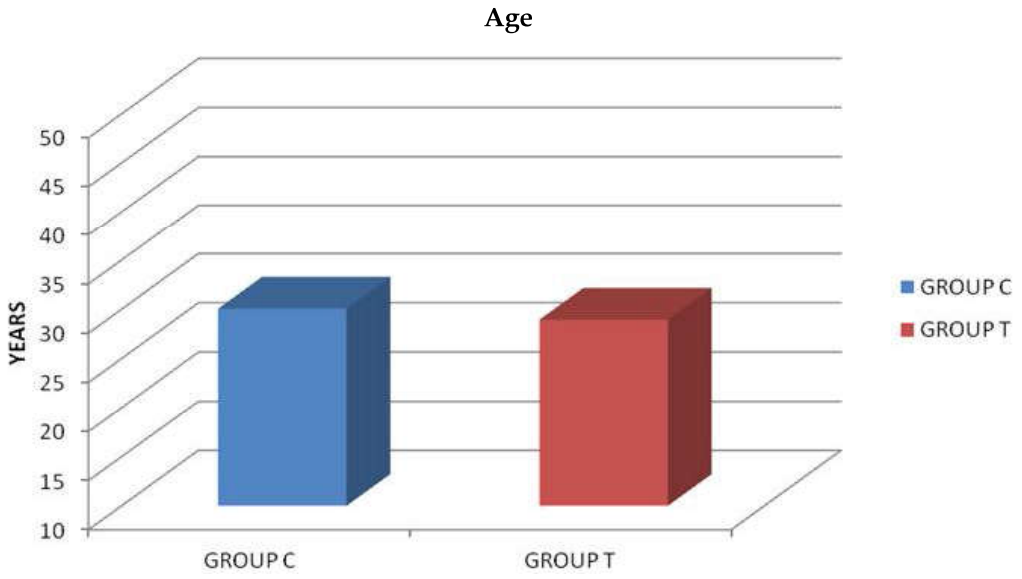
The grades of severity of shivering were 3.1 ± 0.59 in group C whereas in group T the mean was 2.90±0.44min. This was statistically comparable with a p value of 0.089.

The mean interval between the injection of drug (clonidine and tramadol) and the complete cessation of shivering was 2.525±0.598 and 5.025±1.025 minutes, respectively (P=.0000001).

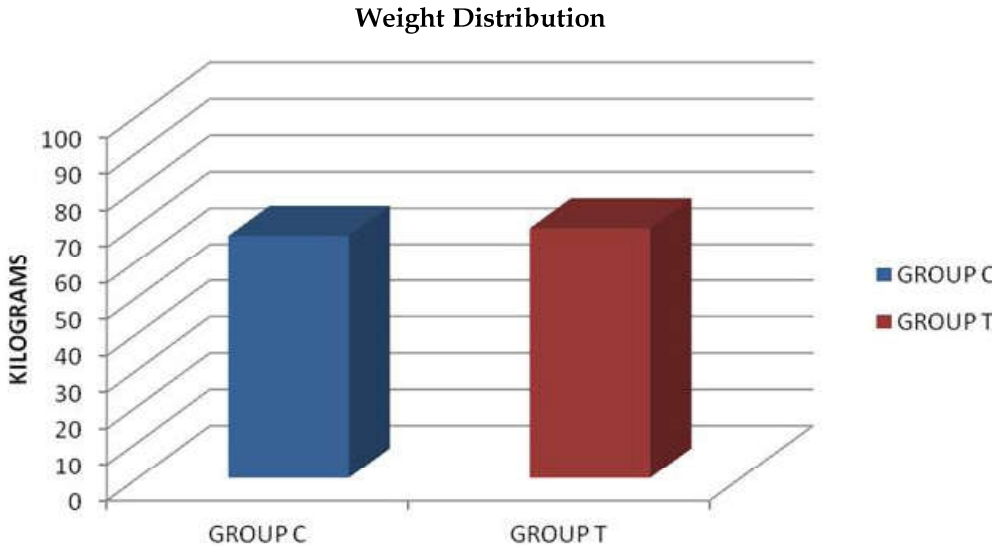
The time interval between administration of drug after onset of shivering and disappearance of shivering was significantly shorter in the clonidine group [Table 2] (P=.0000001).

Table 1: Comparison of age and weight distribution between the two groups (N=40)

		Group C	Group T	P Value
Age (years)	Mean	30.05	28.925	
	SD	3.70	3.48	0.163
Weight (in Kgs)	Mean	66.95	69.025	0.209
	SD	7.01	7.512	



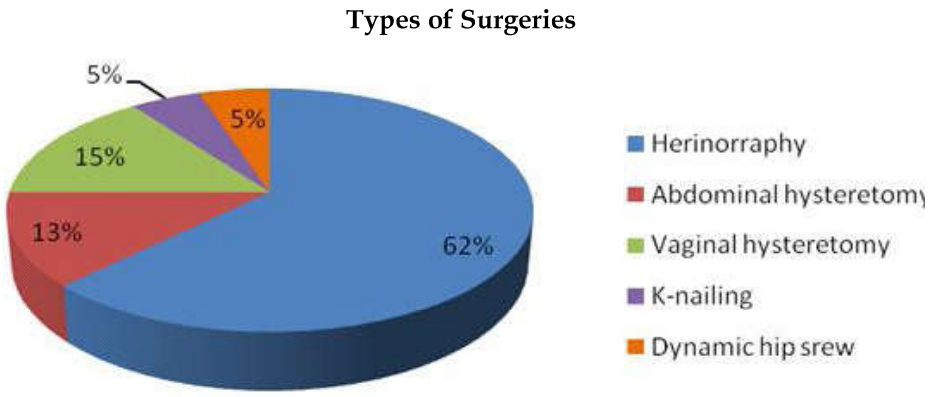
Graph 1: Age distribution



Graph 2: Weight distribution

Table 2: Types of surgeries : (N=40)

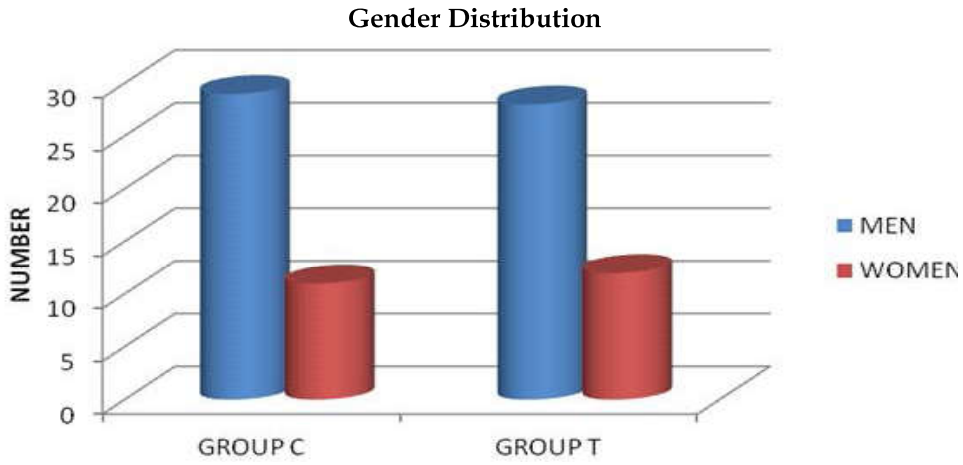
Type of Surgery	Group C	Group T
Herniorraphy	25	24
Abdominal hysterectomy	5	4
Vaginal hysterectomy	6	8
K-nailing	2	2
Dynamic hi screw	2	2



Graph 3: Types of surgeries

Table 3: Gender distribution between the two groups (N=40)

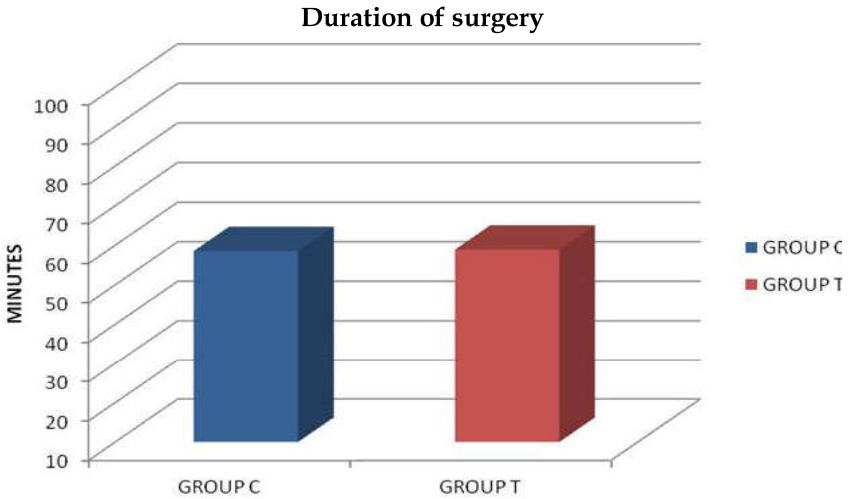
		Group C	Group T	Test	P Value
Gender	Male	29	28	Fischer's	1.0
	Female	11	12	Exact Test	



Graph 4: Gender distribution

Table 4: Duration of surgery in the two groups (N=40)

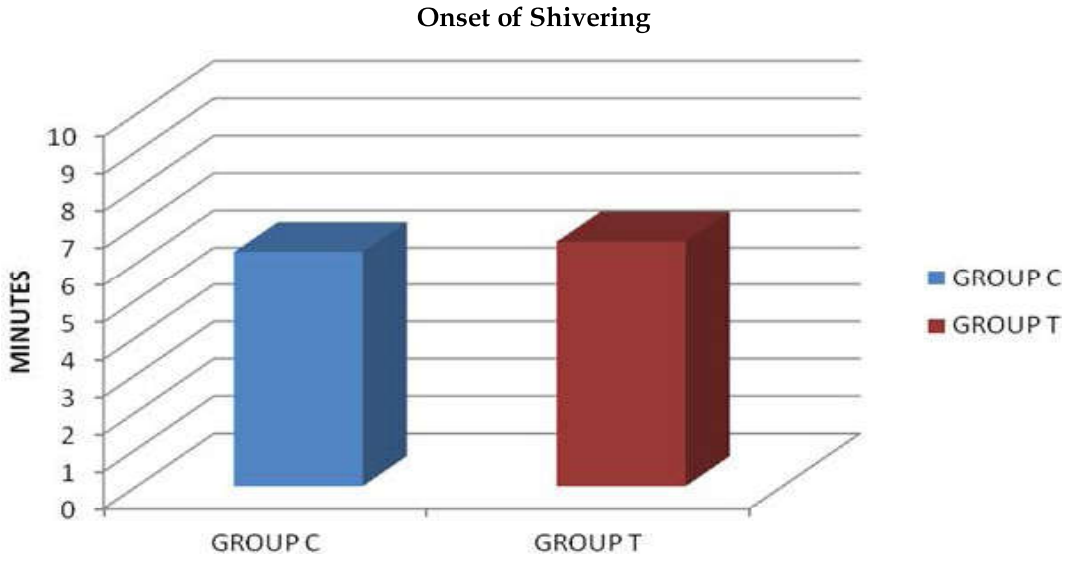
		Group C	Group T	Test	P Value
Duration of surgery (min)	Mean	58.52	58.90	Unpaired t test	0.582
	SD	5.08	58.44		



Graph 5: Duration of surgery

Table 5: Onset of shivering in the two groups (N=40)

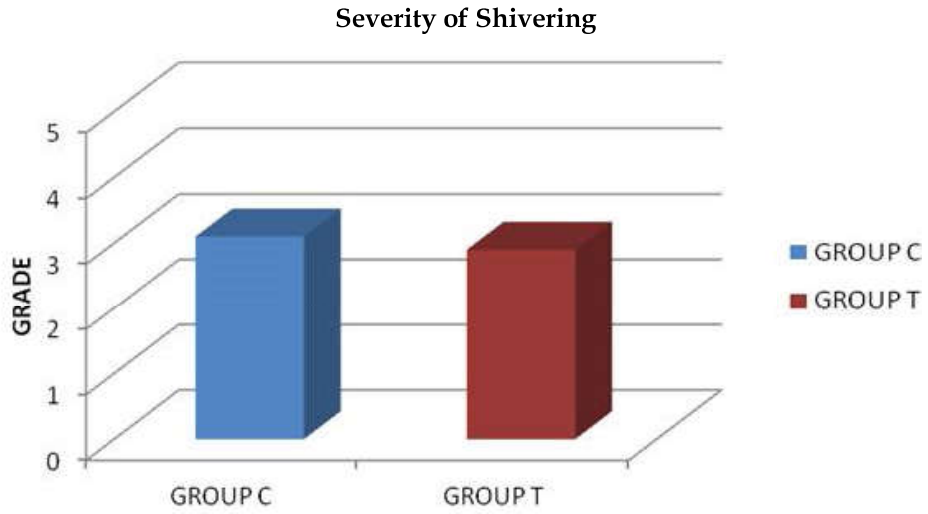
		Group C	Group T	Test	P Value
Time taken for the onset of shivering (min)	Mean SD	6.29 1.74	6.57 1.71	Unpaired t test	0.8660



Graph 6: Onset of shivering

Table 6: Severity of shivering in the two groups (N=40)

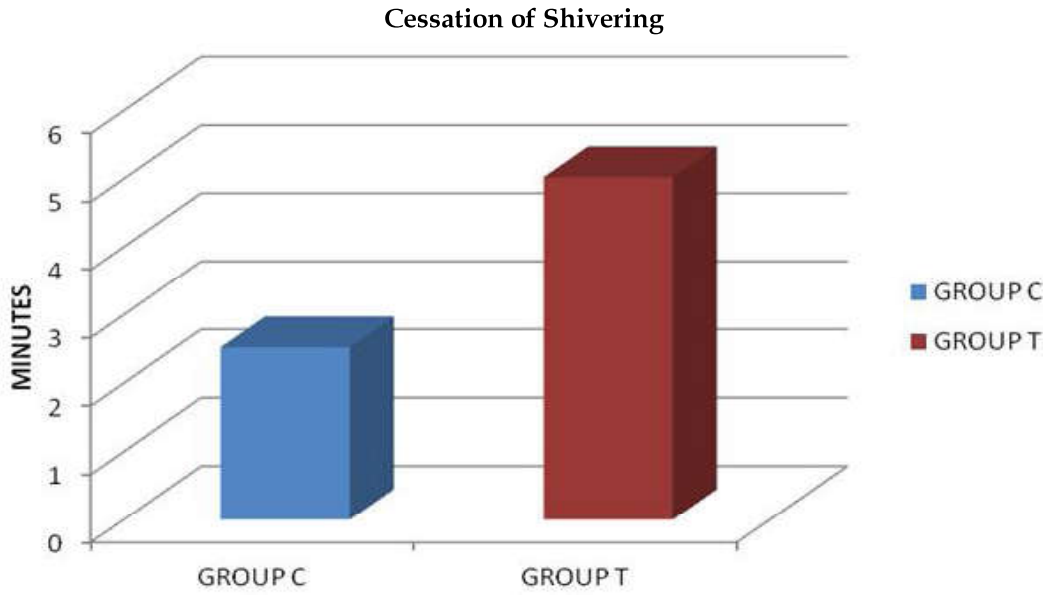
		Group C	Group T	Test	P Value
severity of shivering (grade)	Mean SD	3.1 0.59	2.9 0.44	Unpaired t test	0.0897



Graph 7: Severity of shivering

Table 7: Cessation of shivering in the two groups (N=40)

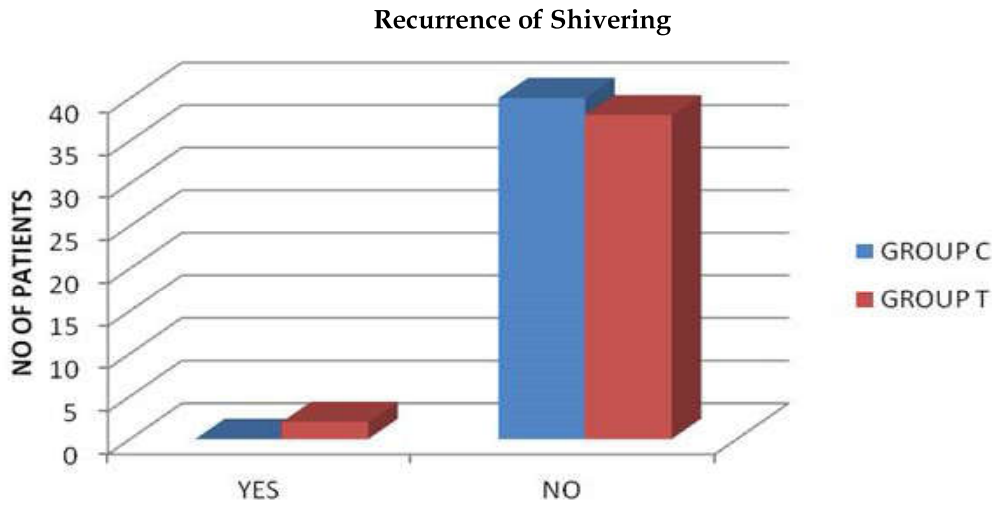
		Group C	Group T	Test	P Value
Cessation of shivering (min)	Mean SD	2.525 0.598	5.025 1.025	Unpaired t test	< 0.0001



Graph 8: Cessation of shivering

Table 8: Recurrence of shivering (N=40)

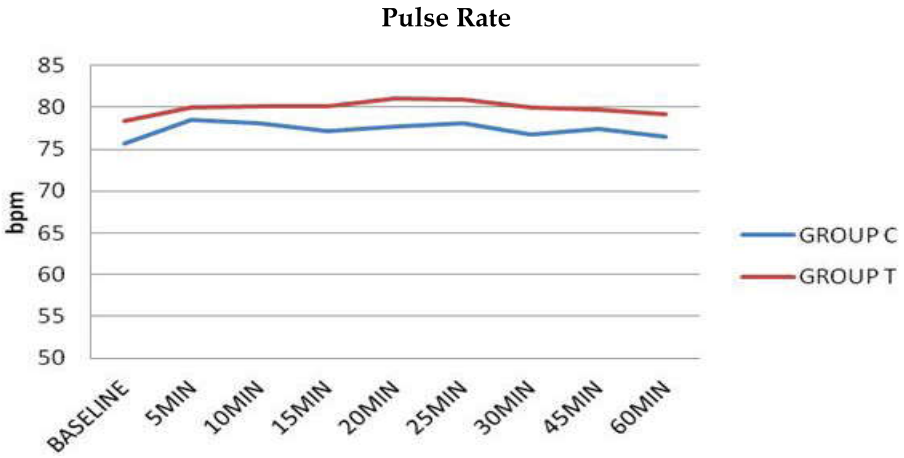
		Group C	Group T	Test	P Value
Recurrence of shivering	Yes	0	2	Fischer's Exact Test	0.49
	No	40	38		



Graph 9: Recurrence of Shivering

Table 9: Comparison of Pulse rate (beats per min) in the two groups (N=40)

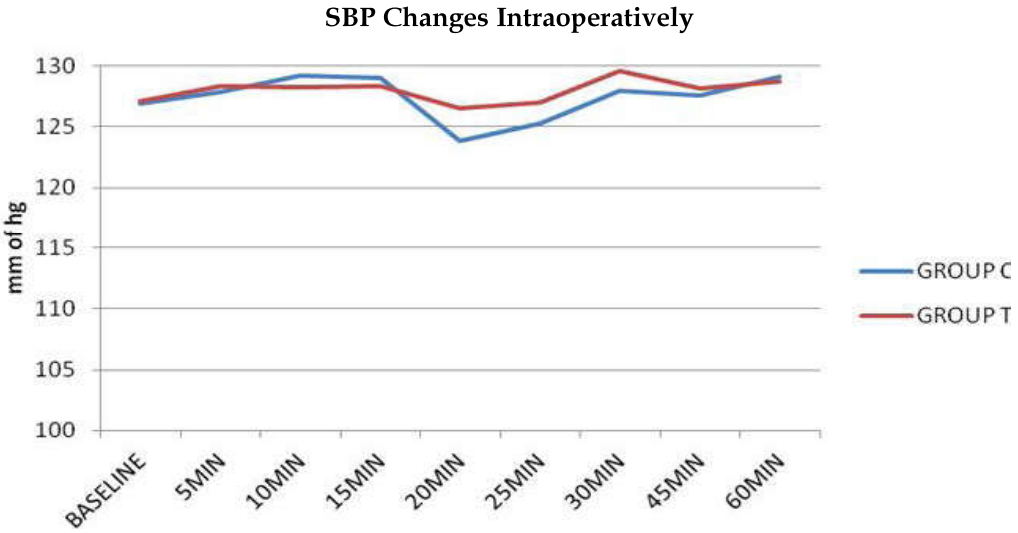
	Group C	Group T	Test	P Value
BASELINE	75.67 ± 6.09	78.37± 7.28		0.075
5 MIN	78.55 ± 6.95	80.05± 5.33		0.282
10 MIN	78.12 ± 6.36	80.07± 7.27		0.20
15 MIN	77.20± 6.28	8.12 ± 7.55	Unpaired t test	0.060
20 MIN	77.72 ± 6.99	81.02 ± 8.10		0.056
25MIN	78.15± 7.36	80.92 ± 6.88		0.086
30 MIN	76.82± 8.03	80.02 ± 6.83		0.051
45 MIN	77.40 ± 8.80	79.77 ± 7.39		0.190
60 MIN	76.50 ± 8.84	79.22 ± 9.41		0.186



Graph 10: Pulse rate changes intra-operatively

Table 10: Comparison of Systolic blood pressure changes in two groups (N=40)

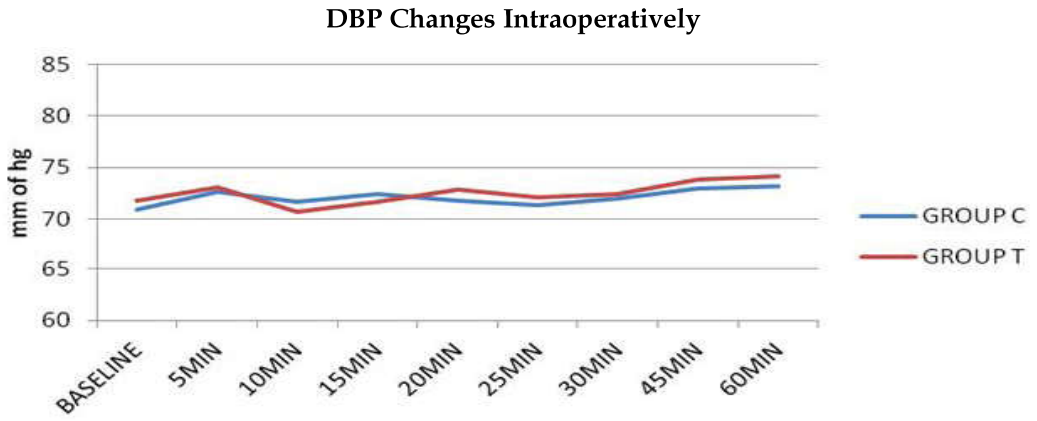
	Group C	Group T	Test	P Value
BASELINE	126.87 ± 7.18	127.07 ± 5.45		0.888
5 MIN	127.82 ± 6.28	128.32 ± 7.35		0.74
10 MIN	129.2 ± 5.85	128.2± 7.08		0.490
15 MIN	129.05± 7.64	128.32 ± 4.8		0.610
20 MIN	123.87 ± 11.46	126.57± 5.97	Unpaired t test	0.190
25 MIN	125.25 ± 7.19	127.02 ± 6.35		0.246
30 MIN	128 ± 6.70	129.62± 5.97		0.250
45 MIN	127.57 ± 6.52	128.12± 5.86		0.692
60 MIN	129.125 ± 6.53	128.70 ± 5.88		0.763



Graph 11: Systolic blood pressure changes intra-operatively

Table 11: Comparison of Diastolic blood pressure (mm of Hg) changes in the two Groups (N=40)

	Group C	Group T	Test	P Value
BASELINE	70.975 ± 4.82	71.775 ± 5.25		0.479
5 MIN	72.675 ± 4.89	73.05 ± 4.26		0.712
10 MIN	71.70 ± 5.16	70.75± 5.52		0.428
15 MIN	72.45± 5.14	71.65± 4.98		0.481
20 MIN	71.75± 5.98	72.90 ± 4.60	Unpaired t test	0.338
25 MIN	71.37± 5.49	72.10 ± 5.20		0.543
30 MIN	72 ± 5.16	72.47 ± 5.39		0.691
45 MIN	73.0 ± 4.88	73.87 ± 4.40		0.404
60 MIN	73.22 ± 5.19	74.12 ± 4.14		0.393



Graph 12: Diastolic blood pressure changes intra-operatively

The recurrence of shivering in group C and group D are statistically significant when compared with Fisher's exact test with p value 0.49.

Hemodynamic Parameters

There was no statistically significant difference in the pulse rate, systolic blood pressure and diastolic blood pressure between the two groups during all the periods of study

Discussion

Regional anaesthesia, either central neuraxial block or pheripheral nerve block, is a safe and very popular technique used for various surgeries. However, 40% to 70% of patients undergoing regional anaesthesia develop shivering, though it is also found to occur after general anaesthesia.

The mechanism which leads to shivering after regional anaesthesia is not very clear, but the probable mechanisms could be due to redistribution of heat from the core to the periphery secondary to peripheral vasodilatation [34]. It also decreases the shivering threshold by 0.6°C, triggering vasoconstriction and shivering (above the level of block) [35], and, by blocking the autonomic control to the affected region,

prevents vasoconstriction and shivering in the region of the block [36] and also due to the effect of cold anaesthetic drugs upon the thermosensitive receptors in the spinal cord [37,38]. There are many non-pharmacological and pharmacological methods used to prevent heat loss and decrease shivering. Non-pharmacological methods include radiant heat warmers, warming the operation theatre, blankets, warm IV fluids and using anaesthetic drugs at body temperature [39,40].

Parveen Goyal, Sandeep Kundra, et al. [41], performed study on Sixty-four patients belonging to ASA grade I and II were randomly allocated to either of the two groups. Group I received intravenous fluids at room temperature (22°C) and group II received intravenous fluids via fluid warmer (39°C). Core temperature was recorded at every 1 min for the first 5 min, followed by 10 min till the end of surgery using a tympanic thermometer. They found that the mean decrease in core temperature in group I was –2.184±0.413 and –1.934±0.439 in group II. The comparison of group I and II showed a statistically significant difference in mean core temperatures at times 5, 50, 60, 70, 80 and 90 min and immediately on arrival in the recovery room. A lower incidence of shivering was seen in group II patients, but the difference in the two groups was not statistically significant.

Rajeev Singh, Veena Asthana et., al. [42], conducted study on 40 male patients aged 50-85 years undergoing TURP under spinal anesthesia. Of which, 20 patients received irrigation fluid at room temperature 21°C and 20 patients received irrigation fluid at 37°C after random allocation. Core temperatures and hemodynamic parameters were assessed in all patients at preoperative, intra operative, and postoperative periods. Intraoperative shivering was also noted in both groups. They concluded that who underwent irrigation with fluid at room temperature Core temperature drop from 36.97°C in preoperative to 34.54°C in postoperative period with an effective difference of 2.38°C. Among patients who received warmed irrigation fluid at 37°C had core temperature drop from 36.97°C to 36.17°C and the effect of fall was 0.8°C. This difference was statistically significant ($P < 0.001$).

Shivering of Grades 1 and 2 was observed in nine patients, of Group 1 while only three patients had Grades 1 and 2 shivering in Group 2. The hemodynamic parameters were similar in the two groups and did not reach significant difference.

The present study was designed to standardise these possible compounding factors, while reflecting the common practice in our institution. The temperature in the operating room was maintained constant at 21°C to 23°C. IV fluids and drugs were given at room temperature. Axillary temperature was recorded at regular intervals intraoperatively.

In the present study, the factors that influence the occurrence of shivering, like temperature of IV fluids and drugs, were not tightly controlled, but this should not affect the validity of our study because the present study is focused on response to treatment used rather than incidence of shivering; and by randomization,both groups were subjected to similar degrees of influence of these factors.

Pharmacological methods to treat shivering include pethedine, tramadol, doxapram, ketanserin, nefopam, alfentanyl, doxapram, etc.

Abd El Azeem A. El Bakry, et al. [43], performed prospective double-blinded controlled study on 90 patients scheduled for TURP operations under spinal anesthesia. Patients were allocated into three groups: in the C group, patients were administered intravenous 10 ml normal saline before spinal anesthesia. In the P group, patients were administered 25 mg pethidine in 10 ml normal saline. In the D group, patients were administered 0.1 mg/kg dexamethasone in 10 ml normal saline. Core body temperature, mean arterial blood pressure, respiratory rate, oxygen saturation, incidence and severity of shivering, nausea, vomiting, and pruritus were recorded.

They concluded that the incidence and severity of shivering were low in the pethidine and dexamethasone groups compared with the control group ($P<0.05$), with no significant difference between the pethidine and dexamethasone groups ($P > 0.05$).

Anurag Tewari, Ira Dhawan et al [8], Conduted a comparative study evaluating the prophylactic efficacy of oral clonidine and tramadol for perioperative shivering in geriatric patients undergoing transurethral resection of prostate The patients were randomly allocated into three groups (40 patients each).

Group I received oral clonidine 150 mg, Group II received oral tramadol 50 mg, while Group III received a placebo. They found that in group I and II, 38 patients (95%) and 37 patients (92.5%) did not shiver, respectively. Although in the group III, 24 patients (60%) exhibited no grade of shivering, the shivering was of significantly severe intensity and lasted for a longer duration.

Velayudha S. Reddy, Sunil Chiruvella et al[9], performed a compartive study on Clonidine versus tramadol for post spinal shivering during caesarean section. In this prospective, a double blind, randomized study, 90 ASA grade I or II, parturients aged 18–35 years, undergoing caesarean section under spinal anaesthesia, who subsequently developed shivering grade 3 or 4, were randomized into two groups, to receive either clonidine or tramadol. There were significant differences in the response rate between the drugs ($P < 0.05$). Time taken from the starting of treatment to cessation of shivering was significantly less withthe tramadol group ($P < 0.05$), however, the frequency of nausea, vomiting, sedation and headache were also significantly more in the tramadol group.

Fidelis Anayo Onyekwulu, Edith Ebere Agu1 et al. [11], performed study on Efficacy of Intravenous Tramadol in the Control of Shivering following Spinal Anaesthesia for Caesarean Section.In the study 144 pregnant women were randomly allocated into three groups at the occurrence of shivering. Group T0.5 received 0.5 mg/kg of tramadol (n = 47), Group T0.25 received 0.25 mg/kg tramadol (n = 47) and Group TNS received 0.05 ml/kg of normal saline (n = 46). They conluded that Tramadol is effective in control of shivering during spinal anaesthesia in obstetric patients. Tramadol 0.5 mg/kg controlled shivering better than 0.25 mg/kg. Therefore, 0.5 mg/kg of tramadol can be used to manage shivering following caesarean section under spinal anaesthesia.

Geeta Mittal, Kanchan Gupta et al [13], Conducted study comparing dexmedetomidine and tramadol for post spinal anaesthesia shivering. This study was conducted in 50 American Society of Anaesthesiologists Grade I and II patients of either gender, aged between 18 and 65 years, scheduled for various surgical procedures under spinal anaesthesia. They observed that time taken for cessation of shivering was significantly less with dexmedetomidine when compared to tramadol. Nausea and vomiting was observed only in tramadol group (28% and 20%respectively). They concluded that although both drugs are effective, the time taken for cessation of shivering is less with dexmedetomidine when compared to tramadol. Moreover, dexmedetomidine has negligible adverse effects, whereas tramadol is associated with significant nausea and vomiting.

A limitation of this study is that we could not measure the core body temperature. For measurement of core body temperature, the probe needs to be put in the oesophagus or near the tympanic membrane. Both these are uncomfortable and unacceptable who has been given spinal anaesthesia. Rectal temperature monitoring was a possibility but was not tried.

In the present study, we compared the efficacy of clonidine and tramadol for treatment of shivering after spinal anaesthesia in patients undergoing various elective surgeries.

Clonidine is a centrally acting selective α2 agonist. Clonidine exerts its anti-shivering effects at three levels: Hypothalamus, locus coeruleus and spinal cord. At the hypothalamic level, it decreases thermoregulatory threshold for vasoconstriction and shivering, because hypothalamus has high density of α2 adenoceptors and hence is effective in treating the established post-anaesthetic shivering [25,26].

It also reduces spontaneous firing in locus coeruleus — a pro-shivering centre in pons.

At the spinal cord level, it activates the α2 adrenoreceptors and release of dynorphine, norepinephrine and acetylcholine [27]. The depressor effects of these neurotransmitters at the dorsal horn modulate cutaneous thermal inputs [28].

Clonidine is highly lipid-soluble and easily crosses the blood-brain barrier [44]. Due to these merits, interaction at the a 2 adrenoreceptors at spinal and supraspinal sites occurs within the central nervous system [45].

Aparna Bagle, Widya Thatte et al [7], performed study on Oral clonidine for shivering prophylaxis in patients undergoing elective urological surgeries under subarachnoid anesthesia which consists of 60 patients divided into two random groups. They found that inident of shivering was significantly less in Group C (10%) when compared with that of the Group P (40%) ($P < 0.01$). Patients in Group C had Grade 1 or 2 shivering while in the Group P patients experienced various grades of shivering ranging from Grades 1 to 4.

Israr-UL-Haq Lonea, Yasir Bashirb et al. [46], performed a prospective double-blind study on 120 elective patients after ethical clearance and after written informed consent was obtained from the patients who underwent urological surgeries. Patients were divided into two groups of 60 each: the study group and the placebo group.

Patients in the study group received an oral clonidine tablet of 150 μg 90 min before block.The severity of shivering and other hemodynamic parameters were noted and compared between the two groups.They found a statistically significant decrease in postblock shivering incidence as well as severity in the clonidine-treated group, with no signifi cant changes in hemodynamic and other parameters between the two groups and thus recommend its use.

Tramadol is an opioid analgesic with opioid action preferably mediated via μ (mu) receptor with minimal effect on kappa and delta binding sites. Tramadol also activates the mononergic receptors of the descending neuraxial inhibiting pain pathway. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both [47-49].

Dr. Aditi A. Dhimar, Dr. Mamta G. Patel et al. [50], conducted randomized, prospective study in 60 ASA grade I, II, or III patients, was designed to explore the efficacy and potency of Tramadol in comparison to Pethidine for control of shivering under regional anaesthesia. Patients received Tramadol or Pethidine in a dose of 1mg.kg-1I.V after the appearance of shivering. Disappearance and recurrence of shivering, as well as haemodynamics were observed at scheduled intervals. Onset of disappearance of shivering was found at 1 minute in Tramadol group (T)($p < 0.05$) and at 3 minutes in Pethidine group (P)($p < 0.05$). The complete disappearance of shivering took 5 minutes in T group while 20 minute in P group. Reccurence rate of shivering was 10% in T and 50% in P group patients respectively ($p < 0.05$). None of the patients had any complications except nausea and vomiting (6.6% and 20% in group T and P respectively, $p > 0.05$). Thus Tramadol and Pethidine were equally efficacious, but Tramadol was more potent with respect to control of shivering and its recurrence .They concluded that I.V Tramadol is qualitatively superior to Pethidine for control of shivering.

In the present study, we found that clonidine is as effective as tramadol in treating post–spinal anaesthesia shivering, bsut the time interval from the commencement of treatment to cessation of shivering is quite less with clonidine (2.54±0.76 minutes) than with tramadol (5.03±1.02 minutes) (P=.0000001).

The response rate was also higher in the clonidine group than in tramadol group, but the difference was not statistically significant (P=.03).

Usha Shukla, Kiran Malhotra, et., al. [51], evaluated the efficacy, potency and side effects of clonidine

as compared to tramadol in post–spinal anaesthesia shivering. In this prospective double-blind randomized controlled clinical trial, 80 American Society of Anaesthesiologists grade-l (ASAI) patients aged between 18 and 45 years scheduled for various surgical procedures under spinal anaesthesia, who developed shivering were selected.

The patients were divided into two groups: Group C (n=40) comprised of patients who received clonidine 0.5mg/kg intravenously (IV) and group patients who received tramadol 0.5 mg/kg IV. Grade of shivering, disappearance of shivering, haemodynamics and side effects were observed at scheduled intervals. Disappearance of shivering was significantly earlier in group C than in group T. Nausea, vomiting and dizziness were found to be higher in group T .While the patients in group C were comparatively more sedated (sedation level, 2; group C, 25%). They concluded that clonidine gives better thermodynamics than tramadol, with fewer side effects.

S. Kulshrestha, R.K. Mehta et al. [52], conducted a study to evaluate the efficacy, potency and side effects of clonidine as compared to tramadol in post spinal anaesthesia shivering. In this double blind comparative study, 90 American Society Anaesthesiologists grade I & II patients aged between 18-35 years scheduled for elective LSCS under spinal anaesthesia who subsequently developed shivering intra operatively were selected. Equal number of patients were allocated to receive either clonidine 50μg (Gr C) or tramadol 50mg (Gr T). Grade of shivering, disappearance of shivering, haemodynamics and side effects were observed at scheduled intervals.

The mean interval between the injection of drug and complete cessation of shivering was significantly earlier in group C than group T. Over all side effects were less in clonidine than tramadol, except sedation.They concluded that clonidine is more effective in cessation of shivering than tramadol with fewer side effects.

However there are some studies which do not support our findings like the study by

Prerna Attal, Akhilesh Chhaya et al. [53], which showed Tramadol is more effective in controlling post spinal anesthesia shivering than clonidine. Similarly *V.Aravind, M.Dhakshinamoorthy et al. [54]* also had findings contradicting our study.

The complications were found to be higher in case of tramadol compared to clonidine. In the present study, the incidence of nausea was higher in tramadol group compared to clonidine group. Similar differences were noted between the two groups in relation to vomiting and dizziness. In case of group C, 10 (25%) patients had sedation of grade 2; while in group T, it was 5 (12.5%) patients who had sedation. No patient in either group had sedation of grade 3 or 4. One patient of group C had dry mouth, which was not present ingroup T. Two patients of group T had recurrence of shivering in postoperative period, while no patient in clonidine group suffered recurrence of shivering.

These findings were similar to the findings of other researchers who compared clonidine with other drugs having anti-shivering properties [55,57].

Bradycardia occurred in 2 patients of group C, while 1 patient of group T suffered from bradycardia. Hypotension occurred in 3 patients of group C. On overall analysis, higher complication rates were noted in group T patients compared to group C patients.

It was noted in the present study that clonidine was quicker than tramadol in providing relief in shivering. Zavaherforoush et al [55] compared clonidine with pethedine and fentanyl for treating post–spinal anaesthesia shivering in elective Lower Segment

Caesarean Section (LSCS) and also found it to be offering better thermodynamics than pethedine.

Summary

This study "A Comparative Study of the Effect of Clonidine and Tramadol on Post- Spinal Anaesthesia Shivering during Intraoperative Period" was conducted in 80 patients of both sex, of age group 18-50 years admitted to Gandhi Hospital for for elective abdominal, orthopaedic and gynaecological surgeries, from 2015-2016.

Patients were randomized into two groups of 40 each (n=40), 57 of whom were male and 23 were female. Both the groups were comparable with respect to age, sex, weight, duration of surgery, type of surgery, volume of intravenous fluid administered and the duration of spinal block. The mean age of the patients in group C was 30.03±3.80 years; and patients in Group T, 28.8 ± 3.47 years (P=.137).

Shivering disappeared in 39 (97.5%) patients who received clonidine and 37 (92.5%) who received tramadol. Both the drugs were found to be effective

in reducing shivering. However, severity of shivering was unchanged in 1 (2.5%) patient of group C and 3 (7.5%) patients of group T. One patient in group C (severity of shivering unchanged) and 5 patients (3- severity of shivering unchanged; 2- recurrence of shivering) in group T were given rescue doses of clonidine or tramadol, respectively. Six (7.5%) patients out of a total of 80 patients received rescue doses. The mean interval between the injection of drug (clonidine and tramadol) and the complete cessation of shivering was 2.54±0.76 and 5.01±1.02 minutes, respectively (P=.0000001). Time for onset of shivering and severity of shivering were not statistically significantly different between the two groups.

However, the time interval between administration of drug after onset of shivering and disappearance of shivering was significantly shorter in the clonidine group (P=.0000001).

There was no statistically significant difference with respect to heart rate, mean blood pressure, axillary temperature and oxygen saturation between the two groups. Complication rates were significantly higher in group T than in group C [Table 3]. Nausea, vomiting and dizziness were higher in group T [nausea - 31; vomiting - 8; and dizziness - 22) than in group C. More patients of group C (10 patients) were sedated than of group T (5 patients).

Bradycardia occurred in 2 patients of group C and 1 patient of group T. In group C, 3 patients suffered from hypotension, and 1 patient complained of dry mouth, both of which were not present in group T.

Conclusion

In conclusion, both clonidine (0.5 μg/kg) and tramadol (0.5 mg/kg) effectively treated patients with post–spinal anaesthesia shivering, but tramadol took longer time to achieve complete cessation of shivering than clonidine, the difference being statistically significant. So we conclude that clonidine offers better thermodynamics than tramadol, with fewer side effects. The more frequent incidence of side effects of tramadol, like nausea, vomiting and dizziness, may limit it's use as an anti-shivering drug.

Further studies are needed to compare the effectiveness of various drugs in the treatment of shivering in patients undergoing surgery under spinal anaesthesia.

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