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Randomised Double Blind Comparative Study Of Dexmedetomidine And Tramadol For Control Of Post-Spinal Anesthesia Shivering

Dr Manish Kumar[1], Dr Homa Fatima[2], Dr Rakesh Kumar Singh[3], Dr. Malika Samina[4]
[1-4](Anesthesia, Katihar Medical College, India)

Abstract:
Background*: Regional anaesthesia is widely used and safe anaesthetic technique. It leads to Intra/ post-operative shivering. There are various methods available to control. Tramadol is one of the most widely used to control shivering, however it is also associated with nausea and vomiting. Dexmedetomidine, a congener of clonidine is an α-2 adrenoceptor agonist, commonly used for sedation, also known to have antishivering potential. Its use as an agent to treat and control post-spinal anesthesia shivering has been inadequately studied. Therefore, there is a search for the efficient drug that lacking of adverse effects. This study was conducted to compare the efficacy of dexmedetomidine and tramadol in the treatment of post spinal anesthesia (SA) shivering as well as to compare their side effect profile.,*
Materials and Methods*: A prospective randomized, and double-blind study was conducted in 80 ASA Grade I and II patients of either gender, aged between 18 and 65 years, undergoing various surgical procedure under spinal-anesthesia and developing shivering. The patients were randomized into two groups of n = 40 each to receive either dexmedetomidine - 0.5 µg/kg (Group D) or tramadol - 0.5 mg/kg (Group T) as an intravenous infusion on appearance of shivering. The time of onset, grade of shivering, time taken for cessation of shivering, response rate, and adverse effect were observed at scheduled intervals. SPSS-20 was used for statistical analysis, unpaired t-test for numerical data and chi-square test for categorical data.*
Results*: The time of onset of shivering in our study was higher in T group being 73 minutes as compared to D group being 72.4 minutes. The time taken for cessation of shivering was statistically significantly lower in D group being 178 seconds as compared to 275 seconds in T group in our study. 5% of the patients in the Dexmedetomidine group had nausea and vomiting while 15% patients had nausea or vomiting in the Tramadol group and the difference was statistically significant (p < 0.001).*
Conclusion: *Dexmedetomidine provides good outcomes as compared to tramadol with less associated effects. Tramadol (0.5 mg/kg) and dexmedetomidine (0.5µg/kg) both work well to treat post-spinal anesthetic shivering, although dexmedetomidine took less time to completely stop the shivering than tramadol. Furthermore, less side effects including nausea and vomiting are brought on by dexmedetomidine.*
Key Word: *Dexmedetomidine, Tramadol, Post Spinal Shivering, Spinal Anaesthesia*

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I. Introduction

Shivering is defined as an involuntary, repetitive activity of skeletal muscles. It is a common postanesthesia adverse event with an incidence of 40–70%.[1] Various mechanisms have been suggested for postanesthesia shivering. These include intraoperative heat loss, postoperative increased sympathetic tone, pain and systemic release of pyrogens.[2]

Though hypothalamic thermoregulation remains intact during regional anesthesia, it is associated with greater heat loss than general anesthesia which is attributed to various reasons like abnormal heat loss due to vasodilatation, impairment of shivering in the area of block and rapid intravenous (IV) infusion of cold fluids.[3] Shivering is not only physically distressing for the patient, but can have various other detrimental effects. It may lead to pain, patient discomfort, impede monitoring techniques, increase intraocular and intracranial pressures, double or even triple oxygen consumption and carbon dioxide production,[4] which might pose difficulties in patients with existing intrapulmonary shunts, fixed cardiac output or limited respiratory reserve. Various modalities have been used for the prevention and treatment of postanesthesia shivering. Dexmedetomidine, a centrally acting alpha 2-adrenergic agonist, has been used as a sedative agent and is known to reduce the shivering threshold. Various studies have been performed using dexmedetomidine in the prophylaxis of postoperative

shivering.[5] But until date, there are limited studies using dexmedetomidine in the treatment of postoperative shivering. Tramadol, an opioid receptor agonist, is an inhibitor of the re-uptake of serotonin (5-hydroxytryptamine) and norepinephrine in the spinal cord. This facilitates 5-hydroxytryptamine release, which influences thermoregulatory control. Presently it is a widely used drug for the control of shivering. But tramadol may cause nausea and vomiting which is very distressing for the patient. Hence the need to find a better drug which has comparable efficacy to tramadol and at the same time has less of side effects. The aim of the study was to compare the efficacy of dexmedetomidine and tramadol in the treatment of post-spinal anesthesia shivering as well as their side-effect profile.

II. Material And Methods

This prospective randomized controlled double blind study was carried out on patients of Department of general anesthesia at Katihar Medical College, Katihar, Bihar for 1 year after the approval from ethical committee. A total 80 adult subjects (both male and females) of aged ≥ 18, years were enrolled for in this study.

Study Design: Prospective randomized controlled study

Study Location: This was a tertiary care teaching hospital based study done in Department of general anesthesia at Katihar Medical College, Katihar, Bihar.

Study Duration: 12 Months, March 2023- February 2024.

Sample size: 80 patients.

Sample size calculation: A Sample size of total 80 cases with 40 in each group at 95% confidence and 80% power was adequate to verify the expected difference of 102(±23.14) in mean time for cessation of post spinal shivering in cases of both study group as per finding of a published study [8]. A total of 80 eligible subjects were recruited consecutively till sample size was achieved.

Subjects & selection method: The study population was drawn from patients who presented to of general anesthesia at Katihar Medical College, Katihar, Bihar between from March 2023- February 2024. Patients were divided into two groups (each group had 40 patients).
Group D (n=40) during shivering patient received inj. dexmedetomidine 0.5 mcg/kg i.v. diluted in 50 ml saline.
Group T (n=40) during shivering patient received inj. tramadol 0.5 mg/ kg diluted in 50 ml saline.
Allocation concealment was ensured using opaque sealed envelope method

Inclusion criteria:
The following criteria were included in the study:
1.Patients undergoing elective surgeries under spinal anaesthesia in whom any grade of shivering was noted
2.Age >18years
3.Those who gave informed and written consent to be part of the study
4.ASA Grade I/II.

Exclusion criteria:
The following criteria were excluded from the study:
1.Those who refused consent
2.Age <18years
3.ASA Grade III or above
4.Patients allergic to any of the drug used.
5. An initial core temperature >37.5C or <35.5C
6. Blood transfusion during surgery
7. Hypo- or hyperthyroidism
8. Psychiatric disorder
9. Pregnant women

Procedure methodology

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively. The questionnaire included socio-demographic characteristics such as age, gender, nationality, height, weight, and other clinical parameters.

Allocation concealment was ensured using opaque sealed envelope method for group allocation. Allocation was done by a person not involved directly in the research to avoid selection bias. Neither the anesthetist nor the patient was aware of the groups and the drugs used (Double blind). All patients were subjected to standard Pre anesthetic check-up before the surgery including detailed history, examination, vitals, routine investigations and markers. Patients heart rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), arterial oxygen saturation (SPO_2), shivering score, sedation score and temperature were measured at the beginning and 0,5,10,15,20,25,30 minutes after spinal anaesthesia and there after every 30 minutes. If any patient developed shivering of grade 3 or 4. He or she is randomized in any of 2 groups by sealed envelope method. IV tramadol 0.5mg/kg. in 50ml normal saline over 10 minutes (Group T) or IV dexmedetomidine 0.5 μg/kg.in 50 ml normal saline solution over 10 minutes (Group D) was given according to group allotted. If shivering continued after 15 minutes of study drug administration, dexamethasone IV injection (0.1 mg/kg) according to weight was given as a rescue drug and the treatment was considered to be ineffective. Such cases were excluded from the study.

Data Collection

• Shivering Score: Recorded pre-treatment and at regular intervals posttreatment (e.g., every 5 minutes for 30 minutes).
• Vital Signs: Blood pressure, heart rate, oxygen saturation monitored continuously.
• Sedation Score: Assessed every 5 minutes for 30 minutes post-drug administration.

Statistical analysis

The study compares time to shivering cessation, incidence of side effects, and severity of shivering using t-tests, chi-square, Fisher's exact, and nonparametric tests.

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann-Whitney test. Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

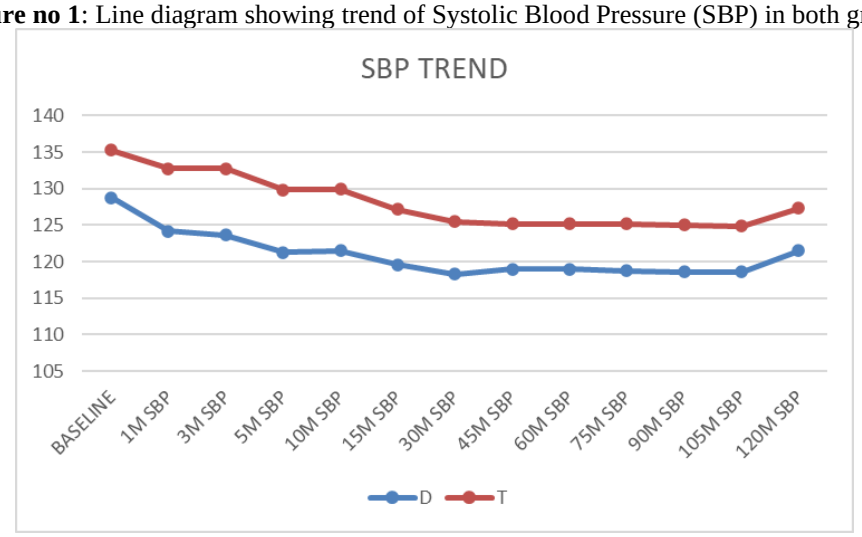
The baseline characteristics in both the study groups were comparable. The mean age was between 45 to 47 years and mean BMI was around 26. Similarly, the mean height was 1.62m for both the groups. The mean age of study participants in Dexmedetomidine group was lower than Tramadol group being 45.4 as compared to 47.3 years. But the difference was not statistically significant. The mean weight of D group was 68 kg as opposed to T group which was 69.9 kg. However, the difference was not statistically significant. The male and females were distributed unequally across the groups. Total males in study were 37 and females were 43. However, the distribution was similar across the groups. The mean BMI was 25.9 in D group and 26.68 in T group which was similar. The BMI in D group followed a normal distribution with maximum ranging between 25-30. The BMI in T group followed a normal distribution with maximum ranging between 27-31. The mean duration of surgery was 74.18 minutes in D group and 78.55 minutes in T group.

Table no 1: Descriptive statistics comparing details of shivering findings of both study groups

Details of Shivering	GROUP	N	Mean	Std. Deviation	Std. Error Mean	P-VALUE
GRADE OF SHIVERING	D	40	3.94732	.533466	.084348	.806
	T	40	3.97841	.592856	.093739	
TIME OF ONSET OF SHIVERING (min)	D	40	72.47231	.832083	.131564	.001
	T	40	73.03107	.573525	.090682	
TEMP AT ONSET OF SHIVERING (degree C)	D	40	35.97793	.554034	.087600	.637
	T	40	35.92083	.523682	.082801	
TIME TAKEN FOR CEASATION OF SHIVERING (Sec)	D	40	177.90	4.49	.71	.000
	T	40	275.14	2.60	.41	

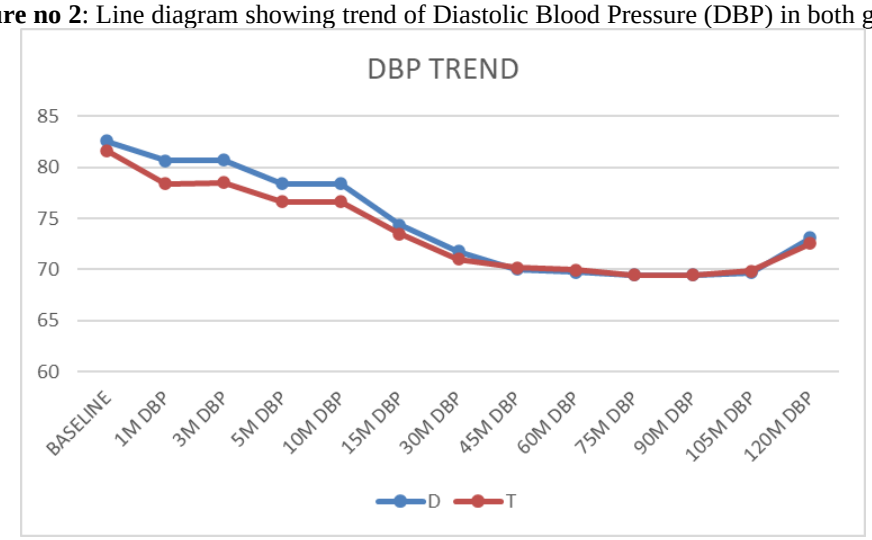
The grade and temperature at the onset of shivering was similar in both the groups. The time of onset of shivering was higher in T group being 73 minutes as compared to D group being 72.4 minutes. Also, time take to cessation of shivering was much lower in D group being 177 minutes as compared to 275 minutes in T group. (Table 1)

Figure no 1: Line diagram showing trend of Systolic Blood Pressure (SBP) in both groups



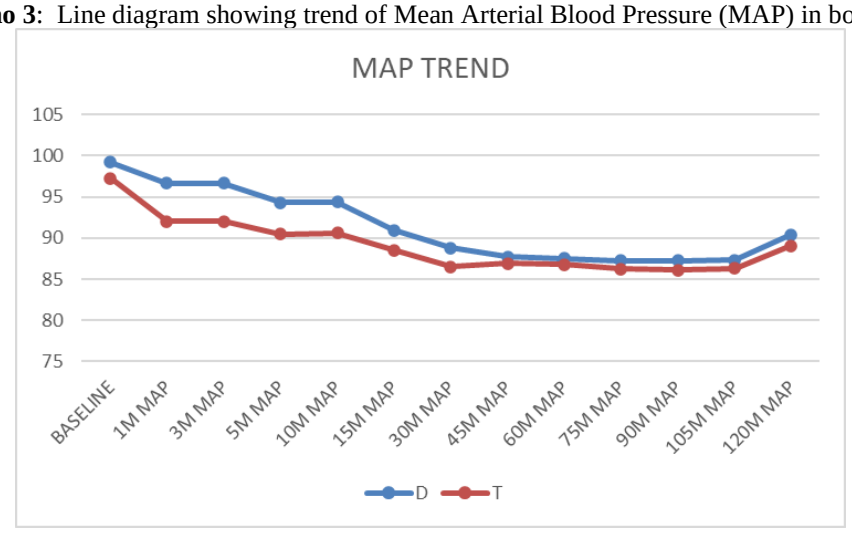
The mean systolic blood pressure was significantly higher in T group at all study intervals as compared to D group (p- value<0.05). (Figure 1)

Figure no 2: Line diagram showing trend of Diastolic Blood Pressure (DBP) in both groups



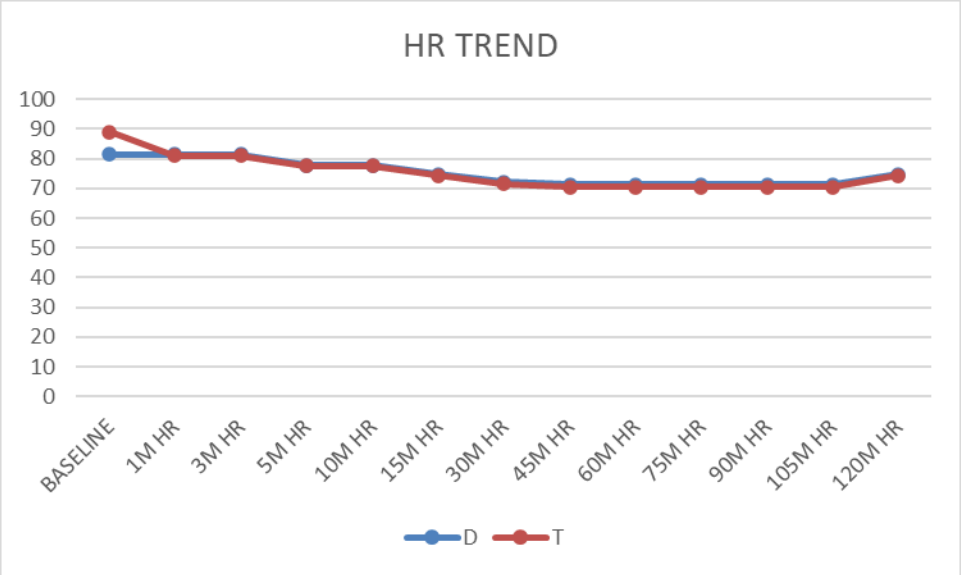
The mean diastolic blood pressure was similar to both groups during all the times of our study. (Figure 2)

Figure no 3: Line diagram showing trend of Mean Arterial Blood Pressure (MAP) in both groups



The mean arterial blood pressure was lower in T group at 1 minutes, 3 minutes, 5 minutes, 10 minutes, 15 minutes and 30 minutes. Rest of the time intervals the MAP was comparable. (Figure 3)

Figure no 4: Line diagram showing trend of Heart rate (HR) in both groups



The mean heart rate was comparable in both the study groups at all the time intervals. (Figure 4)

Table no 2: Descriptive statistics comparing mean time to recurrence of shivering in both study groups

	GROUP	N	Mean	Std. Deviation	Std. Error Mean	P-VALUE
TIME TO RECURRENCE OF SHIVERING (min)	D	4	71.17460	3.223844	1.611922	.031
	T	8	74.36239	1.295348	.457975	

The time to recurrence of shivering was statistically higher in Tramadol group being 74.3 minutes as compared to D group. (Table 2)

Table no 3: Comparison of frequency of recurrence of shivering observed during the study in both study groups

		GROUP		Total	p-value	95% CI
		D	T			
RECURRENCE OF SHIVERING	Absent	36	32	68	0.21	0.62-8.1
	Present	4	8	12		
Total		40	40	80		

The frequency of recurrence of shivering was similar in both the groups. It was 10 % in D group and 20% T group. (Table 3)

Table no 4: Comparison of frequency of side effects observed during the study in both study groups

		GROUP		Total	p-value	95% CI
		D	T			
BRADYCARDIA	Absent	32	35	67	0.36	0.17-1.9
	Present	8	5	13		
HYPOTENSION	Absent	35	37	72	0.45	0.13-2.55
	Present	5	3	8		
NAUSEA OR VOMITING	Absent	38	34	72	0.02	1.5-3.5
	Present	2	6	8		
Total		40	40	80		

The frequency of bradycardia was also similar across both the groups. It was 20% in D group and 12.5% in T group. The frequency of hypotension was 12.5% in D group and 7.5% in T group which was similar across the groups. The frequency of nausea and vomiting was 5% in D group and 15% in T group which was statistically higher in T group as compared to D group. (Table 4)

IV. Discussion

It is well recognized that shivering is a common side effect seen by individuals receiving regional anesthesia during surgery. One of the most popular medications for shivering control is tramadol; nevertheless, it is also linked to nausea and vomiting. Dexmedetomidine, a clonidine congener, is an α-2 adrenoceptor agonist that is frequently used for sedation and has the potential to prevent shivering. By inhibiting neuronal conductance, the new medication dexmedetomidine can lower central thermosensitivity and raise the shivering threshold [5,6]. Insufficient research has been done on its application as a treatment and management tool for shivering after spinal anesthesia. Therefore, the purpose of this study is to compare the effectiveness, hemodynamic alterations, and adverse effects of dexmedetomidine and tramadol in the management of post-spinal anesthetic shivering.

A total of 80 patients having shivering after spinal anesthesia were enrolled, out of which 40 received Dexmedetomidine (Group D) and 40 received Tramadol (Group T). The response rate, changes in hemodynamic parameters, time to cessation of shivering, frequency of recurrence of shivering and side effects (if any) were noted.

Similar to our research, hemodynamic aspects are found to be the standard range in both the groups in the study conducted by Bikumalla L, the frequency of bradycardia in Group D and Group T was 13% in 4 patients and 6% in 2 patients and in our study it was 20% and 12.5% respectively (7).

Crowley et al depicted that shivering is seen in 40 – 64% of the patients undergoing surgery under neuraxial anaesthesia (8). The present study showed an incidence of 15% of shivering in the study population. The time for control of shivering using dexmedetomidine in this study was 2.96 min. Kundra TS et al (9) showed the shivering was controlled using dexmedetomidinein 2.9 ± 0.23 min which is almost equal to the findings of the present study.

The time for control of shivering using tramadol was 4.61 min in the present study which is also comparable to Kundra TS et al (9) showing 4.61 (± 0.38) min and Shukla et al (10) showing 5.01 (±1.02) min. The difference in the time for control of shivering between dexmedetomidine and tramadol was statistically significant ($p < 0.001$) which is also reflected in Kundra TS et al (9). Twenty percentages of the patients in Tramadol group had recurrence of shivering whereas ten percent of the patients in the Dexmedetomidine group in our study had recurrence of shivering The difference was not statistically significant ($p > 0.05$). Kundra TS et al (9) also showed higher incidence of recurrence of shivering in Tramadol group (16%) compared to Dexmedetomidine group (6%).

The side effects of nausea and vomiting had a different distribution in the two study groups. 5% of the patients in the Dexmedetomidine group had nausea and vomiting while 15% patients had nausea or vomiting in the Tramadol group and the difference was statistically significant ($p < 0.001$). Kundra TS et al (9) also showed higher incidence of nausea and vomiting in Tramadol group of patients compared to Dexmedetomidine group of patients. The frequency of hypotension was 12.5% in D group and 7.5% in T group which was similar across the groups. In study by Bikumalla L (7) the frequency of nausea and vomiting in Group T was 26% in 8 patients and 23% in 7 patients. There was no occurrence of nausea and vomiting in Group D. similar findings were observed in study by Bharti P et al (11) were they found that frequency of Nausea and vomiting were significantly higher ("p-value" = 0.024) in Group T as compare to Group D, while the proportion of Hypotension and bradycardia were found significantly higher in group D as compare to Group.

Wang J et al., performed a meta-analysis of randomized controlled trials to compare dexmedetomidine with tramadol. They concluded that dexmedetomidine controls shivering better than tramadol, while also decreasing the incidences of recurrence (12). This was similar to the current study. The frequency of recurrence of shivering in our study was similar in both the groups. It was 10 % in D group and 20% T group. This finding was similar to findings of Bikumalla L (7) where the recurrence percentage of shivering was observed to be 20% in Group T and 6% in the Group D. the findings were also similar to study of Maheshwari et al (13) in which the recurrence percentage was to be 8 percent in T group, whereas the result found in the Group D was similar to the results of Bajwa et al (14) in this study the percentage of recurrence was found to be 5%.

In our study, hemodynamic aspects were found to be the standard range in both the groups. The frequency of bradycardia was 10 % in D group and 20% T group which was reverse to the findings of Bikumalla L (7) where they found bradycardia in Group D and Group T to be present in 13% ie 4 patients and 6% i.e. 2 patients. The difference in bradycardia was however not statistically significant. The higher incidence of bradycardia was found in the Group T.

In our study the difference of hemodynamic variable (mean heart rate mean diastolic blood pressure) remained non-statistically significance (>0.05) throughout the procedure in both dexmedetomidine and tramadol group. These observations were similar with the study of Geeta M. et al (15), Chauhan J et al (16) and Kundra TS et al (9) who reported that hemodynamic variability are remain stable throughout the procedure.

The time taken for cessation of shivering was statistically significantly lower in D group being 178 seconds as compared to 275 seconds in T group in our study. This was similar to the findings of Bharti P et al (11) who found that the mean time for cessation of shivering for Group D and Group T were 174.3±12.5 and

279.6±15.9 seconds respectively and there are significant ("p-value"<0.05) difference in between groups for mean time of cessation of shivering. These findings align with the study conducted by Geeta M et al (15) where they also observed that both drugs are effective to control the shivering and time taken for cessation of shivering was significantly less with dexmedetomidine (2.52 min) when compared to tramadol (5.92 min). Venkatraman et al. (17) also reported that dexmedetomidine require less time to cease post spinal anesthesia shivering than tramadol.

The time of onset of shivering in our study was higher in T group being 73 minutes as compared to D group being 72.4 minutes. Similar findings were reported in the study by Kundra TS et al (9) where the mean time for onset of shivering was 72.30 ± 41.37 minute for dexmedetomidine and 72.66 ± 41.64 in minute for tramadol. Additionally, study by Bharti P et al (11) also showed that the mean time for onset of shivering for Group D and Group T were 73.3±4.34 and 74.03±5.7, respectively similar to our study findings.

V. Conclusion

Dexmedetomidine provides good outcomes as compared to tramadol with less associated effects. Tramadol (0.5 mg/kg) and dexmedetomidine (0.5µg/kg) both work well to treat post-spinal anesthetic shivering, although dexmedetomidine took less time to completely stop the shivering than tramadol. Furthermore, less side effects including nausea and vomiting are brought on by dexmedetomidine. while compared to tramadol, the recurrence of shivering was significantly lower while using dexmedetomidine. More studies with different dosages of dexmedetomidine are required to solidify its position as a very effective anti-shivering medication.

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