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A Randomized Double Blinded Comparative Study on Efficacy of Intraoperative Dexmedetomedine versus Tramadol Intravenous Infusion in Prevention of Postoperative Shivering Following Spinal Anaesthesia

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Abstract

Introduction: Shivering is a frequent complication reported in 30 to 40% of patients undergoing surgery under regional anaesthesia. It increases oxygen consumption, hypercarbia and minute ventilation. It induces arterial hypoxemia, lactic acidosis, increased intra-ocular pressure, and interferes with patient monitoring and comfort. Most of the studies done in the past have been in the treatment of shivering rather than prevention. This study compared intravenous dexmedetomidine versus intravenous tramadol for prevention of shivering in patients who received spinal anaesthesia for various surgical procedures.

Aims and objectives: The aim of this study was to study and compare the efficacy of intravenous infusion of low dose dexmedetomidine (0.25mcg/kg) vs Tramadol (0.5mg/kg) in the prevention of postoperative shivering. Primary objective was prevention of shivering and Secondary objectives were sedation, hemodynamic changes and nausea and vomiting.

Materials and Methods: Prospective randomised double blinded comparative study was done on patients scheduled for elective surgery during June 2018-March 2019 in GKNM Hospital, Coimbatore. Patients were included as per criteria. Informed and written consent was obtained and randomized by computer. Group D received IV Dexmedetomidine of 0.25mcg/Kg dose and Group T received IV Tramadol of 0.5mg/kg. Data was collected and analyzed. Patients were evaluated post operatively by the investigator who was blinded to the group assigned.

Results: The mean age of the total population was 39.55 ± 11.73 years with male predominance in tramadol group. Dexmedetomedine was more effective in preventing shivering, 16 patients (40%) of group D had shivering compared to 24 patients (60%) of tramadol group. This difference though was not statistically significant, numerically showed that dexmedetomedine was better in prevention of shivering. The tramadol group had early onset of shivering in comparison to Dexmedetomedine group ($p<0.05$). Dexmedetomedine group had higher grades of sedation and incidence of nausea and vomiting was higher in tramadol group.

Conclusion: Dexmedetomedine even at a lower dose is comparatively a more effective drug for prevention of shivering with fewer side effects than tramadol in patients undergoing surgery under spinal anaesthesia.

Keywords: Dexmedetomedine; Tramadol; Prevention of postoperative shivering; Spinal anaesthesia.

Introduction

Spinal anaesthesia is widely used as a safe anaesthetic technique for both elective and emergency lower abdominal and lower limb surgeries. Shivering is a frequent complication reported in 30 to 40% of patients undergoing surgery under regional anaesthesia.[1]

Shivering can occur in patients receiving regional anaesthesia as well as those patients recovering from general anaesthesia. It causes patient discomfort and several undesirable physiologic consequences including increase in oxygen consumption, hypercarbia and increase in minute ventilation. It induces arterial hypoxemia, lactic acidosis, increased intra-ocular pressure, and interferes with patient monitoring.[1]

Shivering can be very unpleasant and physiologically stressful for the patients. Various methods are available for the control of shivering under anaesthesia. Non-pharmocological methods using equipments to maintain normothermia are effective but may be expensive and are not practical in all the settings. Pharmacological methods include administering various drugs like pethidine, clonidine, doxapram, tramadol, nefopam, etc.[2]

In homeothermic species, a thermoregulatory system coordinates defences against environmental temperature to maintain internal body temperature within a narrow range, thus optimizing normal body function.[2]

Thermoregulation

The processing of thermoregulatory response has three components: afferent thermal sensing, central regulation, efferent pathway. Afferent thermal sensing which includes receptors, C nerve fibres, Anterior Spinothalamic tract.[6,7] The nucleus raphe magnus and the subcoeruleus are responsible for the modulation of thermal afferent information.[9] Central regulation is by anterior hypothalamus and posterior hypothalamus. The anterior hypothalamus conducts the integration of afferent thermal information, whereas the posterior hypothalamus controls the descending pathways to the effectors. The pre-optic area of hypothalamus contains heat sensitive and cold sensitive neurons.[2,9] The efferent responses are characterized by- Altered behaviour, quantitatively the most effective mechanism, vasomotor response, consisting of vasoconstriction and pilo-erection in response to cold, vasodilatation and sweating in response to heat, shivering and increase in metabolic rate.[2,4,5,10]

Several hypotheses explain the occurrence of post anaesthetic shivering. These include perioperative hypothermia, postoperative pain, perioperative heat loss, the direct effect of certain anaesthetics, hypercapnia or respiratory alkalosis, the existence of pyrogens, hypoxia, early recovery of spinal reflex activity and sympathetic over activity.[11] The first clinical consequence of post anaesthetic shivering is discomfort and stressful sensation to the patient. Other consequences of post anaesthetic shivering increased pain caused by muscular contractions on the operated site and associated tension on suture lines. The main effect of post anaesthetic shivering is the increase in oxygen consumption (VO_2) by increase in metabolic demand. Rarely metabolic demand can exceed the capacity to deliver oxygen peripherally and result in anaerobic metabolism.[2,9,11]

Measures to combat shivering

Measures which reduce core hypothermia in turn reduce anaesthesia induced shivering. They include: Passive insulators like Cotton blankets, cloth or paper surgical drapes, disposable plastic drapes, and plastic bags. A single layer of an insulator reduces the heat loss by approximately 30%; unfortunately adding additional layers does not proportionately increase the benefit. Active warming systems: Convection warming system (Bair Hugger Unit), radiant heat system infra-red light, thermal ceiling lights can be used for warming body. Other measures like warming inspired air, warming intravenous fluids, blood and blood components before infusion can also be used. Maintaining warm post-operative environment (24^{o}C), are useful in preserving body temperature and reducing shivering.[2] Pharmacotherapy-biogenic monoamines, cholinomimetics, cations, endogenous peptides and possibly N-methyl-D-aspartate (NMDA) receptor antagonists. All these appear to modulate central thermoregulatory control mechanisms. The normal functions of these drugs are diverse and the predominant site of action of most of these drugs is difficult to establish.[2]

Pharmacology of Dexmedetomidine

Dexmedetomidine is a new alpha 2-agonist that received FDA approval in 1999 for use as a short-term (less than 24 h) sedative-analgesic in the intensive care unit.[6] Dexmedetomidine compared

to Clonidine is a much more selective alpha 2-adrenoceptor agonist, which might permit its application in relatively high doses for sedation and analgesia without the unwanted vascular effects from activation of alpha1-receptors. In addition, Dexmedetomidine is shorter-acting drug than clonidine and has a reversal drug for its sedative effect, Atipamezole.[12]

Presynaptic activation of the alpha2-A adrenoceptor in the Locus Ceruleus inhibits the release of norepinephrine (NE) and results in the sedative and hypnotic effects.[14] In addition, the Locus Ceruleus is the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. Stimulation of the alpha 2-adrenoceptors in this area terminates the propagation of pain signals leading to analgesia. At the spinal cord, stimulation of alpha 2-receptors at the substantia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P.[9] The spinal mechanism is the principal mechanism for the analgesic action of Dexmedetomidine even though there is a clear evidence for both a supraspinal and and peripheral sites of action.[2] Clonidine, the first developed and the most known alpha 2- agonist is considered as a partial alpha2-agonist since its alpha 2/alpha1 selectivity = 200, while the alpha 2/alpha 1 selectivity of dexmedetomidine is 1620 and hence is 8 times more powerful alpha 2-adrenoceptor than clonidine and is considered as a full alpha2 adrenoceptor agonist.[16] Dexmedetomidine-induced sedation qualitatively resembles normal sleep. The participation of nonrapid eye movement sleep pathways seems to explain why patients who appear to be deeply asleep from Dexmedetomidine are relatively easily aroused in much the same way as occurs with natural sleep.[14] Sedation induced by Dexmedetomidine is dose-dependent; however, even low doses might be sufficient to produce sedation. Dexmedetomidine may lack amnestic properties: more patients who received Dexmedetomidine for postoperative sedation were able to recall their ICU stay when compared to those receiving propofol for sedation.[17]

Peri-operative uses of Dexmedetomidine as premedication: Dexmedetomidine possesses anxiolytic, sedative, analgesic, antisialogogue and sympatholytic properties, which render it suitable as a premedication agent. Dexmedetomidine used intra-operative as adjunct to general anaesthesia, as adjunct to regional anaesthesia, in monitored anaesthesia care (MAC), or as a sole agent for total intravenous anaesthesia (TIVA).

III Use of Dexmedetomidine in the postoperative period: Dexmedetomidine special properties favour its use in recovery room. In addition to its sympatholytic effects, analgesic effects and decreased rate of shivering, the preservation of respiratory function allows the continuation of the dexmedetomidine infusion in the extubated, spontaneously breathing patient. The possibility of ongoing sedation and sympathetic block could be beneficial in reducing high rates of early postoperative ischemic events in high-risk patients undergoing non-cardiac surgery.[8]

Pharmacology of Tramadol

Tramodol is a centrally acting analgesic with a low affinity for opioid receptors. It is a synthetic analogue of codeine. It has a unique dual mechanism tramadol is a recemic mixture of 2 enantiomers. It has both opioid and non-opioid actions. It has a low affinity for opioid receptors. It acts as a selectiveμ-receptor agonist, but also binds weakly to Kappa and Delta receptors. Therapeutic efficacy: On intravenous administration - tramadol is equivalent to pethidine, $1/5^{th}$ as potent as nalbuphine, $1/10^{th}$ as potent as morphine.[2,13] The Advantages of tramadol are can be given through different routes - oral, parenteral etc, less respiratory depression, less dependence, abuse, tolerance, less secretion in the milk of lactating mother, freely available, no narcotic prescription restriction, comparatively cheap.

In the quest for safer and efficacious drug, we conducted a study comparing intravenous dexmedetomidine versus intravenous tramadol for prevention of shivering in patients who received spinal anaesthesia for various surgical procedures. Most of the studies done in the past have been in the treatment of shivering rather than prevention. A dose of dexmedetomidine of 0.5mcg/kg is more effective in the treatment of shivering but associated with reciprocal increase in hemodynamic instability. So to get the maximum benefit of the drug with the least of adverse effects, we chose the dexmedetomidine dose of 0.25mcg/kg.

Aims and objectives

The aim of this study was to study and compare the efficacy of intravenous infusion of low dose dexmedetomidine (0.25mcg/kg) vs Tramadol (0.5mg/kg) in the prevention of postoperative shivering. The outcomes analysed were:

1. Incidence of shivering after administration of drug

2. Time of onset of shivering after administration of drug

Primary objective: Prevention of shivering

Secondary objectives:

1. Sedation

2. Hemodynamic changes

3. Nausea and vomiting

Materials and Methods

Study area: Operation theatre and Postoperative ward. GKNM Hospital, Coimbatore.

Study population: After an informed written consent from the patients, those scheduled for elective surgery, meeting the following criteria were studied.

Study design: Prospective randomised double blinded comparative study.

Study duration: June 2018-March 2019.

Sample Size: Based on the article published by Lin Fern Et al[14], with an anticipated mean difference of time elapsed from treatment to cessation of shivering between two study groups as 3.1 and anticipated Standard deviation as 3.8 the minimum sample size per group was 40 with 90% power and 5% level of significance.

Statistical Data: Statistical analysis

Formula used $N = \frac{(Z\alpha + Z\beta)^2 \times 2\ SD^2}{MD^2}$

Z= Statistic at a level of significance

MD= Anticipated Mean Difference

SD= Anticipated standard deviation

Data was analysed using Mean+/-Standard deviation, Chi square test for association, comparison of means using T test, Anova for comparison between and within groups and diagrammatic presentation. The required sample size was 34 subjects in each group as per the above mentioned calculation. To account for a non-participation rate of 5% and loss to follow up of 5% another 4 subjects were included. Hence the final required sample size was 39 subjects in each group and was rounded off to 40.

Inclusion criteria:

1. Patients of either gender aged between 20 to 70 years.
2. American Society of Anesthesiologists (ASA) status I to II.
3. Patients undergoing surgery under spinal anaesthesia.

Exclusion criteria:

1. Patients not belonging to above mentioned age, BMI<18.5 or ASA grade.
2. Patients suffering from fever, drug allergy, thyroid disorders and neuromuscular diseases.
3. Surgeries expected to last more than 4 hours.
4. Patients who develop shivering even before administering spinal anaesthesia.
5. Patients requiring supplementation with general anaesthesia
6. Pregnancy
7. Patients requiring intraoperative bladder and uterine irrigation.

Methodology

Informed and written consent was obtained from all patients and were assigned to any of two groups by computer generated random numbers. Numbers from 1 to 80 were randomised and allocated into 2 groups

Group D: Dexmedetomidine 0.25mcg/kg intravenous infusion diluted to 20ml with normal saline was given over 10 minutes using a syringe pump after intiation of subarachnoid block.

Group T: Tramadol 0.5mg/kg intravenous infusion diluted to 20ml with normal saline was given over 10 minutes using a syringe pump after intiation of subarachnoid block.

Then these groups were written in a chart against number 1 to 80 and kept in a sealed envelope. Small cards with numbers 1 to 80 placed in a sealed box. On the day of surgery a person not involved in the study prepared the drug according to the card selected. 20ml syringes were used to draw the drug and normal saline was added to make a total volume of 20ml.The assigned drug was administered to patient after subarachnoid block. Patients were evaluated post operatively by the investigator who was blinded to the group assigned. At the end of the study all numbers were arranged in ascending order and the corresponding drug was revealed and written down in the proforma.

Anaesthesia technique

Operation theatre room temperature was kept in

between 22–260 C. Standard monitoring devices including ECG leads, sphygmomanometer cuff, and pulse oximeter were connected and baseline values were recorded and monitored intra-operatively and postoperatively. Baseline temperature was recorded using a mercury thermometer in the axilla placed in the vicinity of the axillary artery. All patients in our study group received spinal anaesthesia in left lateral position using 25G Whitacre needle via midline approach in the L_3-L_4 intervertebral space under strict aseptic precautions and local anaesthesia to skin. Following free flow of CSF, 2ml to 3ml of 0.5% Bupivacaine (hyperbaric) was injected depending on the requirement of surgery. Patients were administered 5 litres oxygen by Hudson transparent face mask and were adequately covered by surgical drapes.

Patients were closely monitored for a period of 4 hours in postoperative ward for shivering and side effects such as nausea and vomiting, bradycardia, hypotension, dizziness, respiratory depression and sedation score was recorded. The vitals were recorded every 10 minutes in the intra-operative period, every 10 minutes for 1 hour in the postoperative period and then every half an hour for 4 hours in the postoperative period. Bradycardia (<50 beats/min), hypotension (<20% of baseline value) and vomiting was treated with atropine, ephedrine and metoclopramide respectively in titrated doses when required. Any shivering intra-operatively or postoperatively inspite of administration of drug were treated with external warming devices and reassurance. None of the patients required blood transfusion during or after the surgery.

Crossly and Mahajan scale of shivering[2]

0 – No shivering

1 – Piloerection or peripheral vasoconstriction, but no visible shivering

2 – Muscular activity in only one muscle group

3 – Muscular activity in more than one muscle group, but not generalised

4 – Shivering involving the whole body.

Sedation score will be assessed with a four point scale as per Filos[2]

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

Statistical methods

Intra-operative heart rate, diastolic blood pressure, systolic blood pressure, SpO_2 was considered as primary outcome variables. Grade of shivering, nausea, vomiting and GOS (grade of sedation) were considered as secondary outcome variables. Study group (tramadol vs dexmedetomedine) was considered as primary explanatory variable.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagram and pie diagram.

All quantitative variables were checked for normal distribution within each category of explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-wilk test was also conducted to assess normal distribution. Shapiro wilk test p value of >0.05 was considered as normal distribution.

For normally distributed quantitative parameters the mean values were compared between study groups using independent sample t-test (2 groups). For non-normally distributed quantitative parameters, medians and interquartile range (IQR) were compared between study groups using Mann Whitney u test (2 groups).

Categorical outcomes were compared between study groups using Chi square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used.) P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.

Results

A total of 80 subjects were included in the final analysis. In our study, both the groups had 40 patients in each group. The mean age of subjects in tramadol group was 39.55 ± 11.73 years and it was 39.48 ± 10.33 years in dexmedetomedine group (p-0.976). In tramadol group, 25 (62.5%) participants were male and 15 (37.5%) participants were female. In dexmedetomedine group, 20 (50%) participants were male and 20 (50%) participants were female (p-0.26). The mean weight of subjects in tramadol group was 64.45 ± 11.91 kg and it was 60.60 ± 5.82

kg in dexmedetomedine group (p-Value 0.07). In tramadol group, 34 (85%) participants were ASA grade I and 6 (15%) participants were ASA grade II. In dexmedetomedine group, 32 (80%) participants were ASA grade I and 8 (20%) participants were ASA grade II. The difference in the proportion of ASA grade between study groups was statistically not significant p- value 0.556. The mean Surgery duration of subjects in tramadol group was 65.75 ± 14.12 (min) and it was 61.91 ± 12.83 (min) in dexmedetomedine group (p- value –0.207). (Table 8).

In tramadol group the mean time interval from the time of administration of drug to onset of shivering was 40.63 ± 6.38 (min), in dexmedetomedine group 44.69 ± 6.18 (min), the difference was statistically significant with p value–0.053. (Table 8).

In tramadol group, 24 (60%) participants had shivering. In dexmedetomedine group, 16 (40%) participants had shivering and started intraoperatively for all patients, so shivering was prevented in 60% of patients in dexmed group and 40% of patients in tramadol group after the administration of drug. The difference in the proportion of occurrence of shivering between study groups was statistically not significant p value 0.074. (Table 1 and Fig. 1).

In tramadol group, 24 patients out of total 40 had shivering, where 9 patients had grade 2 and 15 patients had grade 3 shivering. In dexmedetomedine group 16 patients out of total 40 had shivering, where 9 patients had grade 1 and 7 patients had grade 2 shivering. The degree of shivering was more in tramadol group compared to dexmedetomidine. (Table 2 and Fig. 2).

The mean Intra-operative heart rate at baseline of tramadol group was 84.1 ± 10.42 (bpm) and 83.95 ± 10.32 (bpm) in dexmed group. The mean difference between two groups was statistically not significant p value 0.949. (Table 3 and Fig. 3).

The mean post-op heart rate at 90 mins of tramadol group was 86.83 ± 8.21 and it was 83.48 ± 6.2 min dexmed group. The mean difference between two groups was statistically significant p value 0.003. (Table 4 and Fig. 4).

Table 1: Comparison of occurrence of shivering between the study group (N=80).

Occurrence of shivering	Study group		Chi square	P-value
	Tramadol (N=40)	Dexmed (N=40)		
Yes	24 (60%)	16 (40%)	3.200	0.074
No	16 (40%)	24 (60%)		

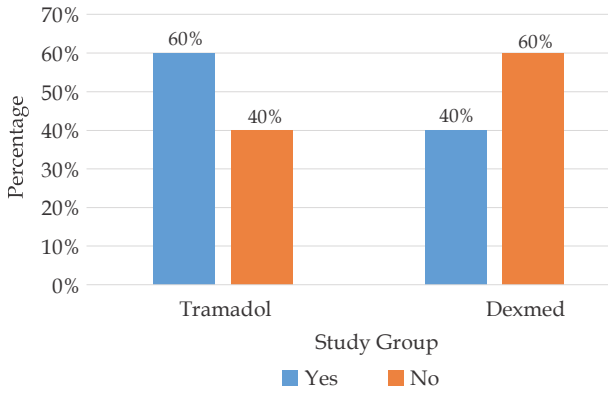

Fig. 1: Clustered bar chart of Comparison of occurrence of shivering between the study group (N=80).

Table 2: Comparison of grade of shivering between the study group (N=80).

Grade of shivering	Study group	
	Tramadol (N=40)	Dexmed (N=40)
0	16 (40%)	24 (60%)
1	0 (0%)	9 (22.5%)
2	9 (22.5%)	7 (17.5%)
3	15 (37.5%)	0 (0%)

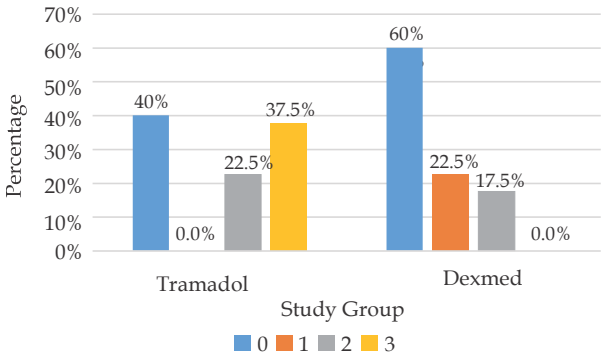

Fig. 2: Clustered bar chart of Comparison of grade of shivering between the study group (N=80)

Table 3: Comparison of mean of intra-op heart rate between the study groups (N=80).

Intra-op Heart rate (bpm)	Study group		P value
	Tramadol (N=40) (Mean± SD)	Dexmed (N=40) (Mean± SD)	
Baseline	84.1 ± 10.42	83.95 ± 10.32	0.949
5 min	94.83 ± 12.58	83.9 ± 9.01	<0.001
10 min	94.3 ± 10.98	83.85 ± 8.94	<0.001
20 min	92.18 ± 13.4	82.9 ± 8.24	<0.001
30 min	91.03 ± 11.93	82.35 ± 8.37	<0.001
40 min	89.13 ± 11.18	82.68 ± 8.09	0.004
50 min	90.85 ± 10.08	83.95 ± 7.81	<0.001
60 min	91.28 ± 10.28	82.72 ± 7.15	<0.001
70 min	92.08 ± 7.78	82.58 ± 5.52	<0.001
80 min	91.28 ± 8.21	82.88 ± 6.43	<0.001

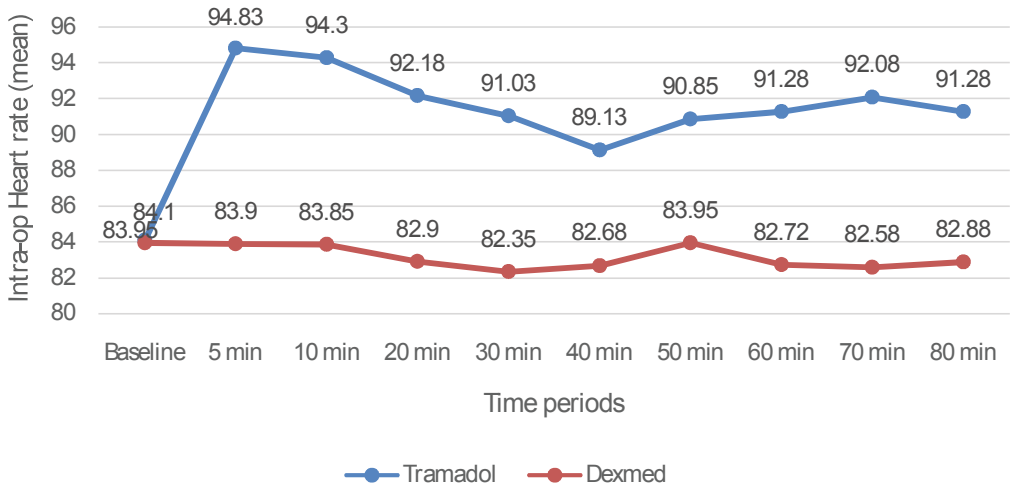

Fig 3: Comparative line diagram of comparison of mean of intra-op heart rate between the study groups (N=80).

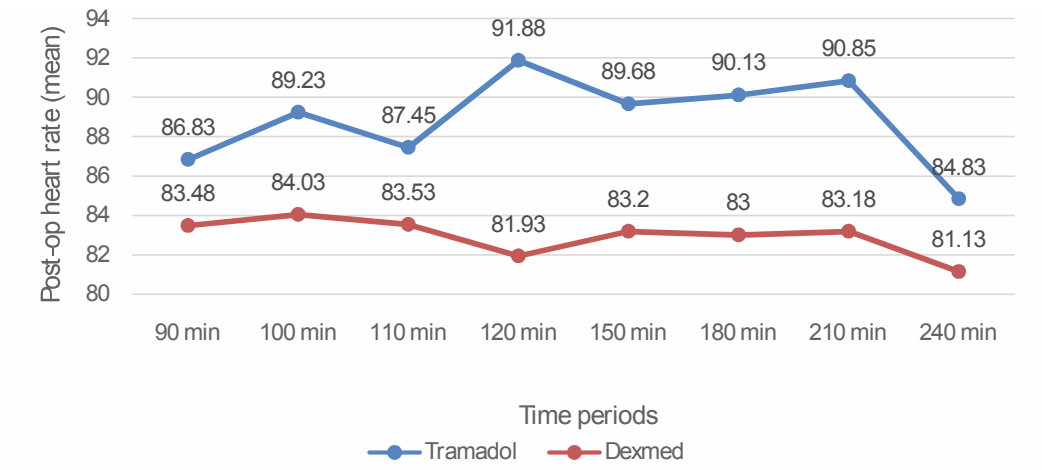

Fig 4: Comparative trend line diagram of comparison of mean of post-op heart rate between the study group (N=80).

Table 4: Comparison of mean of post-op heart rate between the study group (N=80).

Post-op Heart rate (bpm)	Study group		P value
	Tramadol (N=40) (Mean± SD)	Dexmed (N=40) (Mean± SD)	
90 min	86.83 ± 8.21	83.48 ± 6.2	0.043
100 min	89.23 ± 9	84.03 ± 5.54	0.003
110 min	87.45 ± 6.73	83.53 ± 5.13	0.004
120 min	91.88 ± 12.77	81.93 ± 6.39	<0.001
150 min	89.68 ± 9.33	83.2 ± 7.05	<0.001
180 min	90.13 ± 9.94	83 ± 7.06	<0.001
210 min	90.85 ± 11.48	83.18 ± 6.59	<0.001
240 min	84.83 ± 11.09	81.13 ± 6.09	0.068

Table 5: Comparison of nausea between the study group (N=80).

Nausea	Study group		Chi square	P-value
	Tramadol (N=40)	Dexmed (N=40)		
Yes	13 (32.5%)	6 (15%)	3.382	0.066
No	27 (67.5%)	34 (85%)		

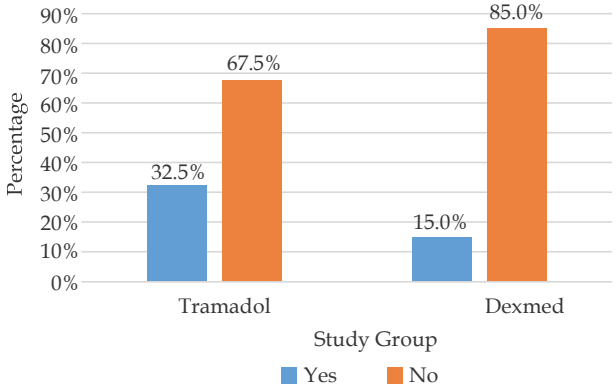

Fig. 5: Clustered bar chart of comparison of nausea between the study group (N=80).

Table 6: Comparison of vomiting between the study group (N=80).

Vomiting	Study group		Chi square	P-value
	Tramadol (N=40)	Dexmed (N=40)		
Yes	8 (20%)	5 (12.5%)	0.827	0.363
No	32 (80%)	35 (87.5%)		

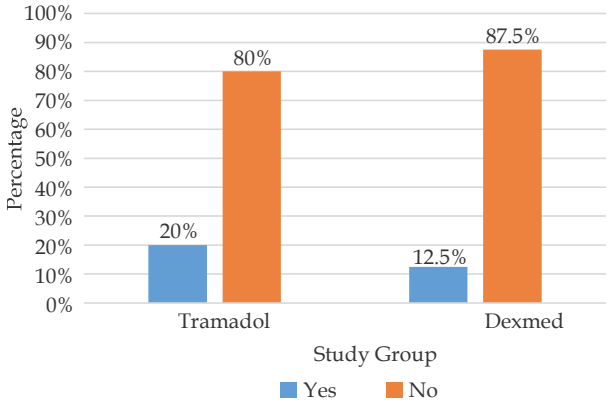

Fig. 6: Clustered bar chart of Comparison of vomiting between the study group (N=80).

In tramadol group, 13 patients had nausea. In dexmedetomedine group, 6 patients had nausea; the difference was not statistically significant with p value 0.066. In tramadol group, 8 patients had vomiting. In dexmedetomedine group, 5 patients had vomiting. The difference was statistically not significant with p value–0.363. (Fig. 5, 6 and Table 5, 6).

In tramadol group, 24 patients had grade 1 and 16 patients had grade 2 shivering. In dexmedetetomedine group, 35 patients had grade 2 shivering and 5 patients had grade 3 shivering. The degree of sedation was higher in dexmedetomedine group compared to tramadol group though we could not apply any statistical test. (Table 7 and Fig. 7).

Table 7: Comparison of GOS (Grade of Sedation) between the study group (N=80).

GOS	Study group	
	Tramadol (N=40)	Dexmed (N=40)
1	24 (60%)	0 (0%)
2	16 (40%)	35 (87.5%)
3	0 (0%)	5 (12.5%)

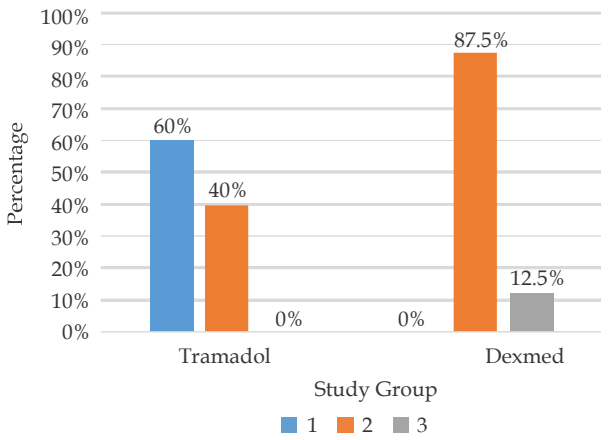

Fig. 7: Clustered bar chart of Comparison of GOS (Grade of sedation) between the study group (N=80).

Table 8: Tables of various variables and respective p values.

Parameter	Study group		P value
	Tramadol (N=40) (Mean± SD)	Dexmed (N=40) (Mean± SD)	
Age (years)	39.55 ± 11.73	39.48 ± 10.33	0.976
Sex	Male- 25 (62.5%) Female–15 (37.5%)	Male- 20 (50%) Female- 20 (50%)	0.260
Weight(kg)	64.45 ± 11.91	60.60 ± 5.82	0.070
ASA grade	Grade I -34 (85%) Grade II- 6 (15%)	Grade I- 32 (80%) Grade II- 8 (20%)	0.556
Surgery duration (min)	65.75 ± 14.12	61.91 ± 12.83	0.207
Temperature (Celsius)	37.18 ± 0.36	37.19 ± 0.49	0.917
Time interval to onset of shivering after administration of drug(min)	40.63 ± 6.38	44.69 ± 6.18	0.053

There was no statistically significant difference between two groups with regards to blood pressure (SBP and DBP) in both intra-operative and post operative period (p value >0.05). There was no statistically significant difference between two groups in intra-operative SPO_2 and also post-operative SPO_2.

Discussion

Postoperative period is associated with variable incidence of shivering. Around 30–40% of patients undergoing spinal anaesthesia will experience shivering. Drugs like Dexmedetomedine, pethidine, tramadol, nefopam,clonidine are traditionally being used to prevent and treat postoperative shivering, but these are associated with undesirable side effects like respiratory depression, hemodynamic instability, nausea and vomiting.

Most of the studies done in the past have been in the treatment of shivering rather than prevention. In a quest to address the issue of postspinal shivering, we conducted a study comparing the efficacy of dexmedetomedine and tramadol administered immediately after subarachnoid block in the prevention of shivering.

Dexmedetomedine decreases the vasoconstriction and shivering threshold by acting on central thermoregulation system. Tramadol is a synthetic opioid, which acts by inhibiting reuptake of norepinephrine and serotonin and activates descending inhibitory spinal pathways. The incidence of shivering may be associated with many factors including age, duration of surgery, type of surgery and also type of anaesthesia. These factors

can interefere with interpretation of the results of the study. So we designed the study in such a way that these factors were well balanced between both study groups. The anaesthetic technique was standarised, patient related variables were also standardised. The demographic variables between both groups are comparable to eliminate the confounding variables which could interfere with the interpretation of the superiority of one drug in a particular dosage over the other in the prevention of shivering.

Tanveer singh kundra, Parminder kaur et al[21] conducted a prospective observational study on the minimum dose of dexmedetomedine required for cessation of postspinal anaesthesia shivering. They studied the time taken for abolition of shivering in 90 patients having shivering who received different doses from 1mcg/kg,0.5mcg/kg and 0.25mcg/kg, 30 in each group and concluded that minimum dose required for control of shivering was 0.25mcg/kg to 0.29mcg/kg. Lim Fern et al[14] conducted a study on the treatment of shivering and had concluded that a dose of dexmed 0.5mcg/kg though more effective in the treatment of shivering was associated with reciprocal increase in hemodynamic instability. So to get the maximum benefit of the drug with the least of adverse effects, we chose to the dexmed dose of 0.25mcg/kg.

In our study, group T patients were administered tramadol of 0.5mg/kg. Lim Fern et al, Geeta Mittal et al[7,3] studied the effect of tramadol in treatment of postoperative shivering, both the studies used 0.5mg/kg of tramadol, hence the dose of tramadol 0.5mg/kg used in the present study was based on optimal dose used in previous studies. Our study group consisted of total 80 patients, 40 patients in each group and the outcomes were compared in terms of, efficacy in prevention of shivering and adverse effects like sedation, nausea, vomiting and hemodynamic instability.

Efficacy in the prevention of shivering

In the present study, shivering was prevented in 40% of patients in tramadol group and 60% of patients in dexmedetomedine group and these patients did not have shivering in postoperative period as well. Shivering occurred in 16 patients (40%) of dexmedetomedine group compared to 24 patients (60%) of tramadol group. This difference though was not statistically significant, numerically showed that dexmedetomedine was better in prevention of shivering. In a similar study conducted by Tanveer singh et al[21] with 0.25mcg/kg of dexmedetomedine given for treatment, 41% of patients had shivering, which was comparable to our study.

In a study conducted by Samsettin Bozgeyik et al[19], the incidence of shivering of grade <2 was 96.6% as against 100% in our study and the incidence of shivering of grade >2 was 3.4% as against 0% in our study. Burhanettin usta et al[18] conducted a study on comparing the efficacy of normal saline and dexmed 0.5mcg/kg on prevention of post-operative shivering .They concluded that 10% of patients had shivering in their study which is less than incidence in our study, one of the contributing factor could be use of 0.5mcg/kg of dexmed in their study.

In our study, 24 patients (60%) of tramadol had shivering. In a study conducted by Samsettin Bozgeyik et al[19], a fixed dose of 100 mg tramadol was administered to all patients in the group pre-emptively. The incidence of shivering with grade of shivering <2 was 90% as against 62.5% in our study and grade of shivering >2 was 10% as against 37.5% in our study. But it is not possible to compare their results as their study design is based on fixed dose of tramadol that is 100mg for all patients. The overall higher incidence of shivering in our study inspite of pre-emptive administration can be attributed to, including the lower grades of shivering also unlike other studies.

Sedation

In our study, in dexmedetomedine group all patients were sedated with 87.5% of grade 2 and 12.5% of grade 3 sedation. This is comparable to similar study done by Burhanettin usta et al[19] in which also all the patients in the dexmedetomedine group were sedated, but the sedation score was 3 to 5 in their study which could be due to higher dose (0.5mcg/kg) of dexmedetomedine used. The study results are also similar to study done by Semsettin et al, Tanveer et al and Rajagopal venkataraman et al[19,21,and 20] all of which report a higher incidence of sedation with dexmed at different doses.

In our study 40% of patients were sedated in the tramadol group and all had grade 2 sedation. This is close to the study results of Rajagopal venkataraman et al[20], though the tramadol dose was higher in their study. But the results are contradictory to that of study done by aditi dhimar et al[15] which found 0% sedation with the same dose of tramadol.

Nausea and vomiting

In our study, incidence of nausea and vomiting was 15% and 12.5% in dexmedetomedine group respectively .The incidence of nausea and vomiting was 32.5% and 20% in tramadol group respectively. This correlates with the study of Geeta mittal et al[3], which gives closer incidence with same dose of tramadol. Overall the incidence of nausea and vomiting appears higher in both the groups in our study compared to other studies, which could be due to patient and surgical factors.

Hemodynamic parameters

In our study, both the groups had stable hemodynamics and none of the patients in both the groups had significant bradycardia or hypotension after the administration of the drug (tramadol or dexmedetomedine) respectively. Tanveer Singh Kundra, Paraminder Kaur et al[21] conducted a study on minimum dose of dexmedetomedine required to treat postoperative shivering and concluded that minimum dose required was 0.25mcg/kg and there was no significant bradycardia and hypotension noted in their study. Same dose of dexmedetomedine (0.25mcg/kg) was used in our study as well. Many other studies have reported some incidence of bradycardia and hypotension in both the groups, more with dexmed groups which could be due to the higher doses used.

Time interval from administration of drug to onset of shivering

In tramadol group of our study, the mean time interval from administration of drug to onset of shivering was 40.63 ± 6.38minutes. In dexmedetomedine group 44.69 +/– 6.18minutes from the time of administration of the drug, the difference was statistically significant with P value–0.053.Burhanettin Usta et al (18) conducted a comparative study on prevention of postoperative shivering with dexmedetomedine versus saline and concluded that time to onset of shivering from administration of drug was longer in dexmedetomedine group compared to saline group.

Conclusion

In our study A Randomized Double Blinded Comparative Study On Efficacy of Intraoperative Dexmedetomedine Versus Tramadol Intravenous Infusion In Prevention of Postoperative Shivering Following Spinal Anaesthesia our Primary outcome measure was prevention of shivering and secondary outcome measures were sedation, nausea, vomiting and hemodynamic stability. The demographic parameters of all patients in two groups were comparable. There was no statistically significant difference between Group D and group T in terms of patient characteristics. The prevention of shivering was better in group D but not statistically significant. The incidence and grade of sedation was more in dexmedetomedine group. The incidence of nausea and vomiting was higher in group T when compared to group D which was statistically insignificant. There was in fall in heart rate in group D compared to group T but none of the patients in both.

Dexmedetomedine even at a lower dose is comparatively a more effective drug for prevention of shivering with a better side effect profile than tramadol in patients undergoing surgery under spinal anaesthesia. Time interval between administration of drug and onset of shivering was longer in dexmedetomedine group compared to tramadol group and was statistically significant with p value–0.053.

Limitations

The limitations to our present study were;

1. Temperature was not checked in the intraoperative and postoperative period hence we could not make a correlation on the influence of hypothermia on shivering.
2. Axillary temperature was checked rather than core body temperature preoperatively.
3. Small sample size was taken.
4. The results cannot be extrapolated for long duration surgeries.

Recommendations

1. A larger study population would have higher statistical power so as to come to definite conclusion.
2. Intraoperative temperature monitoring could have thrown a better light on those cases where hypothermia was the causative agent of shivering.
3. The estimation of blood loss and volume replacement should be considered since it

can be one of the contributing factors for shivering.

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