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COMPARISON OF DEXMEDETOMIDINE, TRAMADOL AND PETHIDINE IN THE PREVENTION OF INTRAOPERATIVE SHIVERING IN PATIENTS UNDERGOING SURGERY UNDER SPINAL ANESTHESIA

Anaesthesiology

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ABSTRACT

Background: Shivering is an uncomfortable experience to many patients which occurs perioperatively.[1] It increases oxygen consumption, carbon dioxide production and catecholamine production.[2] Pethidine has been used for the prevention and treatment of shivering for many decades. Tramadol has shown its efficacy in the treatment of shivering, but tramadol has many adverse effects.[3] Dexmedetomidine has also shown anti shivering properties.[4] This study was undertaken to evaluate which out of the three drugs, dexmedetomidine, tramadol and pethidine is most efficacious in preventing intraoperative shivering after administration of spinal anaesthesia. **Methodology:** The study was conducted on 129 adult consented patients between 18-65 years of age with ASA grade I/II undergoing spinal anaesthesia. Patients were divided into 3 groups, Group D received injection Dexmedetomidine 0.5µg/kg, Group P received injection Pethidine 0.5mg/kg and Group T received injection Tramadol 0.5mg/kg just 10 minutes prior to spinal anesthesia**.** Shivering was monitored by a grading system modified by Wrench.[5] Patients were monitored for a period of 120 minutes or till the end of the surgery whichever was longer. **Results:** In the dexmedetomidine group, significantly lesser number of patients shivered compared to pethidine group and tramadol group. Pethidine group had lower incidence of shivering when compared to tramadol group. Rescue drug for the treatment of shivering was required in lesser number of patients in the dexmedetomidine group as compared to pethidine group and tramadol group. The requirement of rescue drug for control of shivering did not vary significantly between pethidine group and tramadol group. **Conclusion:** Dexmedetomidine is most effective and comparably superior to Pethidine and Tramadol in preventing intra-operative shivering after spinal anaesthesia. Pethidine is superior to Tramadol in preventing intraoperative shivering after spinal anaesthesia.

KEYWORDS

Dexmedetomidine, Pethidine, Tramadol, Shivering, Spinal Anesthesia

INTRODUCTION

Shivering is defined as an involuntary, oscillatory muscular activity that augments metabolic heat production. It is an uncomfortable experience to many patients which occurs perioperatively during the surgery.[1] Human core temperature ranges from 36.5°C to 37.5°C. Anterior hypothalamus integrates thermal inputs from different tissues and compares this peripheral information with a threshold value. As the body temperature falls below this set point, it produces responses to warm the body and when the temperature becomes higher than the set point, it triggers reflexes to cool down the body.[2,3] Spinal anaesthesia impairs this thermoregulatory system by inhibiting vasoconstriction. Spinal anaesthesia results in redistribution of core heat from the trunk (below the level of block) to the periphery.[4,5] Both these effects predispose patients undergoing spinal anaesthesia to hypothermia and shivering.

Studies have shown that even mild hypothermia can triple the incidence of adverse cardiac outcomes and increase surgical blood loss. Shivering increases oxygen consumption, carbon dioxide production, catecholamine production, lactic acidosis, intraocular pressure and intracranial pressure.[6]

Treatment of shivering consists of non-pharmacological and pharmacological methods. Non-pharmacological methods include external heating like use of blankets, forced air warmers and warmed fluids, maintaining operating room temperature etc. Pharmacological agents which are used to treat shivering include meperidine, tramadol, clonidine, dexmedetomidine, alfentanil, ketanserin, magnesium sulphate, nefopam. Meperidine/pethidine is the drug which is being used for the prevention and treatment of shivering for many decades. Many studies on tramadol show its efficacy in the treatment of shivering. However, tramadol produces adverse effects like nausea, vomiting, dizziness which cause discomfort to the patient.[7,8] Dexmedetomidine is a selective α2 adrenergic agonist and has 1600 times greater selectivity for the α2 adrenoceptor compared with the α1 receptor. It produces sedation, anxiolysis, hypnosis, analgesia, sympatholysis and has anti shivering properties as well.[9]

Research has been carried out to study the efficacy of various drugs to control intraoperative shivering after spinal anaesthesia, however not much research has gone into studying the efficacy of these drugs in preventing shivering after spinal anaesthesia. Hence this research work was undertaken to evaluate which out of the three drugs, dexmedetomidine, tramadol and pethidine is most efficacious in preventing intraoperative shivering after administration of spinal anaesthesia.

METHODS

The study was conducted on 129 adult consented patients of both sexes with ASA grade I/II who were undergoing lower limb and infra-umbilical surgeries under spinal anaesthesia after obtaining clearance from ethical committee of the institution. Patients with known hypersensitivity/allergy to study drugs, those who had cardio-pulmonary, renal or hepatic impairment, those with history of substance abuse, patients with convulsions or psychiatric disorder and pregnant, lactating women were excluded from the study.

After shifting the patients to the operation theatre, monitors were connected and baseline vital parameters were noted, intravenous access was secured and preloading was done with Lactated Ringer's solution at 10ml/kg over 15 minutes. The operation room temperature was maintained at 25°C. All the patients were covered by a single layer of surgical drapes, exposing only the surgical site.

All the patients received injection ondansetron 4mg intravenously before the infusion of the study drugs. The study drugs were then infused in 100ml normal saline by a blinded observer over 10 minutes via a three way adapter just before administrating spinal anaesthesia. Patients in group D received injection dexmedetomidine 0.5µg/kg, those in group P received injection pethidine 0.5mg/kg and those in group T received injection tramadol 0.5mg/kg as study drug.

Taking aseptic measures spinal anaesthesia was administered using 3ml of 0.5% bupivacaine with a 25 gauge spinal needle. Patients were monitored for a period of 120 minutes or till the end of the surgery whichever was longer. Shivering was monitored by modified grading system of Wrench.[5]

Data Collection

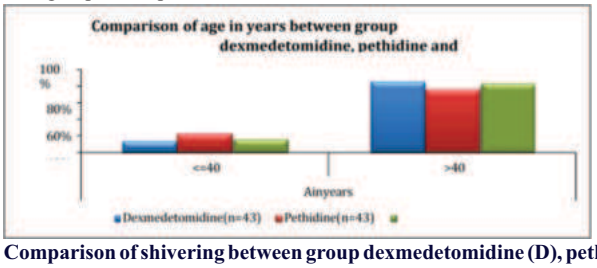
Sample size was calculated based on a previous study comparing the anti shivering effects of dexmedetomidine, tramadol and pethidine. We defined a relevant clinical difference of 20% in frequency of intra operative shivering among three groups with reference to the previous study. Thus sample size of 43 patients per group provided an 80% power for detecting a significant difference between any two groups at an alpha level of 0.05.

Categorical variables are presented in number and percentage and continuous variables are presented as mean +/- SD and median. Normality of data was tested by Kolmogorov Smirnov test. If the normality was rejected then non-parametric test was used. Quantitative variables were compared using Kruskal Wallis test between the three groups & Mann Whitney test was used for

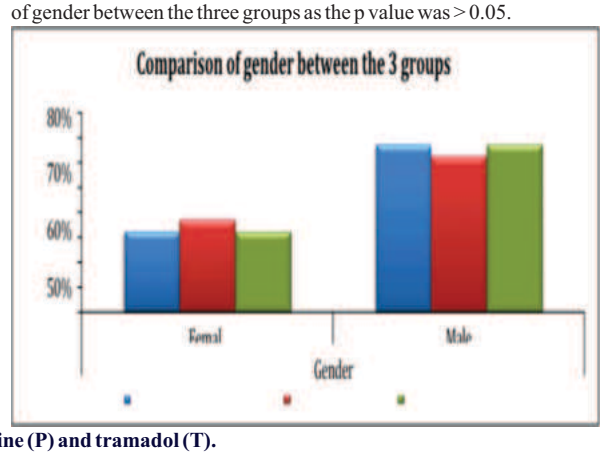
comparison between two groups. Qualitiative variables were compared using Chi-Square test/Fisher's exact test. A p value of < 0.05 was considered statistically significant. The data was entered in MS EXCEL spreadsheet and analysis was done using SPSS version 21.0

RESULTS AND OBSERVATIONS

Majority of the patients in all the three age groups were more than 40 years of age; 86.05% in dexmedetomidine group, 76.74% in pethidine group and 83.72% in tramadol group. While13.95% of patients in dexmedetomidine group, 23.26% of patients in pethidine group and 16.28% of patients in tramadol group were less than 40 years of age. No significant difference was seen in the distribution of age between the 3 groups as the p value was >0.05.



Majority of patients were males in all the three groups; 67.44% in dexmedetomidine group, 62.79% in pethidine group and 67.44% in tramadol group. On the other hand proportion of females was 32.56% in dexmedetomidine group, 37.21% in pethidine group and 32.56% in tramadol group. No significant difference was seen in the distribution of gender between the three groups as the p value was > 0.05.



Comparison of shivering between group dexmedetomidine (D), pethidine (P) and tramadol (T).

Shivering	Dexmedeto- midine (n=43)	Pethidine (n=43)	Tramadol (n=43)	Total	Pvalue
At 0 minute	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value
At 5 minutes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value
At 10 minutes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value
At 15 minutes	0 (0%)	4 (9.30%)	11(25.58%)	15(11.63%)	0.001, D vs P:0.116, D vs T:0.0005, P vs T:0.086
At 30 minutes	2 (4.65%)	10 (23.26%)	15 (34.88%)	27 (20.93%)	0.001, D vs P:0.026, D vs T:0.0007, P vs T:0.235
At45 minutes	2 (4.65%)	9 (20.93%)	14 (32.56%)	25 (19.38%)	0.003, D vs P:0.049, D vs T:0.002, P vs T:0.223
At60 minutes	1 (2.33%)	1 (2.33%)	9 (20.93%)	11(8.53%)	0.003, D vs P:1 D vs T:0.015 P vs T:0.015
At 75 minutes	0 (0%)	0 (0%)	1 (2.33%)	1 (0.78%)	1,D vsP:No pvalue, DvsT:1 PvsT:1
At 90 minutes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value
At 105 minutes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value
At 120 minutes	0 (0%)	0 (0%)	0 (0%)	0 (0%)	No p value

None of the patients shivered at 0, 5 and 10 minutes in all the three groups.

At 15 minutes significant difference was seen when the three groups were overall compared for shivering incidence as the p value was < 0.05. Significant difference was seen in the distribution of shivering incidence at 15 minutes when dexmedetomidine group was pair- wise compared to tramadol group as the proportion of patients who developed shivering at 15 minutes in dexmedetomidine group was 0.00% which was significantly lower than 25.58% patients who developed shivering in tramadol group. Rest of the pair wise comparisons were not significant statistically.

Significant difference was seen in the overall distribution of shivering incidence at 30 minutes when the three groups were compared as the p value was 0.001. When dexmedetomidine group was pair-wise compared to pethidine and tramadol groups separately, significant difference was seen in the distribution of shivering incidence at 30 minutes as proportion of patients in dexemedetomidine group who shivered was significantly lower than the proportion of patients who shivered in both pethidine group and tramadol group. However, when pethidine group and tramadol group were compared pair-wise, no significant difference was seen in the distribution of shivering incidence at 30 minutes.

Significant difference was seen in the overall distribution of shivering incidence at 45 minutes when the three groups were compared as the p value was 0.003. When dexmedetomidine group was pair-wise compared to both tramadol and pethidine groups separately significant difference was noted for the incidence of shivering, but when pethidine and tramadol groups were compared head to head for shivering incidence no significant difference was observed. Significant difference was seen in the overall distribution of shivering incidence at 60 minutes when the three groups were compared as the p value was 0.003. When dexmedetomidine group was compared to pethidine group, no significant difference was seen in the distribution of shivering incidence at 60 minutes as comparably similar proportion of patients shivered in both the groups. However, significant difference was seen in the distribution of shivering incidence at 60 minutes when tramadol group was pair-wise compared to both dexmedetomidine and pethidine groups separately as the proportion of patients in tramadol group who shivered at 60 minutes was significantly higher as compared to that of dexmedetomidine group and pethidine group.

No significant difference was seen in the distribution of shivering incidence at 75 minutes, between group dexmedetomidine, pethidine and tramadol. None of the patient had shivering at 90, 105 and 120 minutes in all the three groups.

Comparison of rescue drug between group dexmedetomidine (D), pethidine (P) and tramadol (T)

Rescue drug	Dexmedeto-midine (n=43)	Pethidine (n=43)	Tramadol (n=43)	Total	P value	Test performed
No	41 (95.35%)	33 (76.74%)	28 (65.12%)	102 (79.07%)	0.002 D vs P:0.026 D vs T:0.0007 P vs T:0.235	X^2 test,12.085 D vs P:Fisher Exact test D vs T:Fisher Exact test P vs T:X^2 test,1.41
Yes	2 (4.65%)	10 (23.26%)	15 (34.88%)	27 (20.93%)		
Total	43 (100%)	43 (100%)	43 (100%)	129 (100%)		

Significant difference was noted in the distribution of rescue drug requirements between dexmedetomidine, pethidine and tramadol groups (p value<0.05). Proportion of patients in dexmedetomidine group who needed rescue drug was 4.65% which was significantly lower as compared to pethidine group (23.26%) and tramadol group (34.88%). Rescue drug was administered to 23.26% of all patients in pethidine group which was comparable with 34.88% in tramadol group (p value>0.05).

DISCUSSION

One of the least addressed and distressing complaints in patients after administration of spinal anaesthesia is shivering during surgery and in immediate postoperative period. Shivering causes discomfort, agitation, increased oxygen consumption, increased catecholamine production, increased intracranial and intraocular pressures.

Pethidine is a synthetic opioid which is time tested gold standard drug for the control of shivering. Tramadol is a semi synthetic opioid which controls shivering but it has a high incidence of vomiting which is

estimated to be approximately 70%. [9,10] So, all the patients in our study were given ondansetron 4mg intravenously irrespective of the study group prior to administration of the study drug. Dexmedetomidine, a selective α 2 agonist produces arousable sedation, hypnosis, anxiolysis and has antishivering properties

We formulated a prospective, randomized, double-blinded, comparative study to find out which of the three drugs, dexmedetomidine, tramadol and pethidine more effectively prevented intraoperative shivering after the administration of spinal anaesthesia. The dosages used in our study were the same as used in a previous study by Lim Fern et al[11] who compared 0.5 mcg/kg of dexmedetomidine, 0.5 mg/kg of tramadol and 0.5 mg/kg of pethidine administered intravenously in the treatment of post- neauraxial anaesthesia shivering. We wanted to ascertain that at the similar dosages which of the three agents were better at preventing post-spinal anaesthesia shivering intraoperatively.

The incidence of shivering was significantly less in dexmedetomidine group compared to pethidine group at 30 minutes and 45 minutes after spinal anesthesia, when the dexmedetomidine group was compared to tramadol group the incidence was significantly less in dexmedetomidine group than tramadol group at 15 minutes, 30 minutes, 45 minutes and 60 minutes after spinal anaesthesia. Pethidine was relatively better at preventing shivering after spinal anaesthesia than tramadol as the incidence of shivering at 60 minutes was significantly less in pethidine group when compared to tramadol group.

Our findings concurred with the study findings of Lim fern et al[11] who observed that 0.5 mcg /kg of dexmedetomidine had superior anti-shivering effects than 0.5 mg/kg of pethidine and 0.5 mg/kg of tramadol. However, they also observed that both tramadol and pethidine group had similar anti-shivering effects in contrast to the findings of our study. The reason for this difference could have been because in their study, the drugs were administered after the patients shivered for treating shivering while we administered the drugs to prevent intraoperative shivering after spinal anesthesia. Similar observations to our findings were also made by Ameta N et al[12], who found that 0.5 mcg/kg of dexmedetomidine was superior to 0.5 mg/kg of tramadol in preventing shivering after spinal anesthesia. Abdel-Ghaffar HS et al[13] also found that 0.5mcg /kg and 0.3 mcg /kg of dexmedetomidine had better anti-shivering effects than 0.4 mg/kg of pethidine in patients undergoing surgeries under spinal anesthesia. Our observations concur with the findings of Sharma M et al[14] that 0.5 mg/kg of pethidine provides better antishivering effect than 0.5 mg/kg of tramadol in patients undergoing surgery under sub-arachnoid block. However, our study findings were in contrast to the observations of Bozgeyik et al[15] who found that dexmedetomidine and tramadol were equally efficient in the prevention of shivering after spinal anaesthesia. The tramadol dose used in this study was 100 mg while we used tramadol at a dose of 0.5 mg/kg which could be responsible for the differences in findings. Philip et al[16] noted that tramadol had better anti shivering effects than pethidine in contrast to our observations which is because they used 1 mg/kg of tramadol in their study while we used 0.5 mg/kg of tramadol in our study.

RESCUE DRUG

Pethidine was used as a rescue drug for the treatment of shivering in our study as in a systematic quality assessment of published anti-shivering protocols by Choi et al[17] skin warming and pethidine use were the most commonly cited strategies. Using pethidine as a rescue drug, which is also one of our study drug, did not affect the results of our study, as the primary objective of our study was to assess incidence of shivering after spinal anesthesia which was assessed before the administration of rescue drug.

In our study, the need for rescue drug was significantly lesser in the dexmedetomidine group as compared to pethidine group and tramadol group. The proportion of patients needing rescue drug for treating shivering was less in pethidine group as compared to tramadol group although the difference was non-significant. Similar observations were made by Usta B et al[18], Yong-Shin-Kim et al[19] who in their study found that prophylactic administration of dexmedetomidine was associated with less requirement of rescue drug for control of shivering.

CONCLUSION

From our study it may be concluded that 0.5 mcg/kg of dexmedetomidine is more effective and comparably better than both 0.5 mg/kg of pethidine and 0.5 mg/kg of tramadol for the prevention of intraoperative shivering developing after spinal anesthesia when administered intravenously prior to subarachnoid block and 0.5 mg/kg of intravenous pethidine is superior to 0.5 mg/kg of intravenous tramadol in the prevention of intraoperative shivering after spinal anaesthesia.

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