

The Effects of Preemptive Tramadol and Dexmedetomidine on Shivering During Arthroscopy

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ABSTRACT

Background: Shivering, the rate of which in regional anesthesia is 39% is an undesired complication seen postoperatively. **Aims:** This study aims to compare the ability of preventing the shivering of preemptive tramadol and dexmedetomidine during the spinal anesthesia (SA). **Methods:** A total of 90 patients with American Society of Anesthesiologists physical status I-II, aged 18-60 years and undergoing elective arthroscopic surgery with SA were divided into three groups randomly. After spinal block, 100 mg tramadol in 100 ml saline was applied in group T- ($n = 30$) and 0.5 µg/kg dexmedetomidine in 100 ml saline was applied in group D- ($n = 30$) and 100 ml saline was administered in group P- ($n = 30$) in 10 min. The hemodynamics, oxygen saturation, tympanic temperature, shivering and sedation scores were evaluated and recorded intraoperatively and 45 min after a postoperative period. **Results:** In group T and D, shivering scores were significantly lower when compared with group P in the intraoperative 20th min ($P = 0.01$). Sedation scores in group D were significantly higher than the baseline values ($P = 0.03$) and values in group T and P ($P = 0.04$). **Conclusions:** Preemptive tramadol and dexmedetomidine are effective in preventing the shivering under SA. In addition, dexmedetomidine was superior in increasing the level of sedation which is sufficient to prevent the anxiety without any adverse effects.

Key Words: Arthroscopic surgery, dexmedetomidine, shivering, spinal anesthesia, tramadol

INTRODUCTION

The shivering associated with neuraxial anesthesia is normally thermoregulatory, as evidenced by the precedence of thermoregulatory vasoconstriction and as is mostly the case with the shivering observed after general anesthesia (GA).^[1,2]

The shivering after anesthesia leads to feelings of discomfort in the patient as well as an increase in oxygen consumption, carbon dioxide production, catecholamine excretion, cardiac output and intraocular pressure and complications such as tachycardia and hypertension. In addition to this,

shivering may inhibit accurate monetarization by causing artifacts in the monitor.^[1,3-5] In the studies carried out so far, the effectiveness of many drugs toward prevention and treatment of shivering after anesthesia has been established. These drugs include tramadol,^[3] meperidine, opioids, doxapram and serotonin antagonists.^[1]

Clonidine, centrally acting alpha2-adrenergic agonist, has been reported to prevent perioperative shivering possibly by acting on the hypothalamic alpha2-adrenergic receptors.^[6] The clonidine use has brought forward the use of another alpha2 agonist, dexmedetomidine in the treatment of shivering. Dexmedetomidine is a powerful and highly selective, alpha2-adrenoceptor agonist with a large pharmacological effect spectrum. In another study carried out with the healthy volunteers, the group exposed to intravenous (iv) dexmedetomidine infusion was compared with the placebo group and it was observed that dexmedetomidine decreased vasoconstriction and shivering threshold and had no clear effect on sweating threshold.^[7] The effectiveness of dexmedetomidine on shivering was demonstrated when

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used in sedative doses in volunteers and as premedication in patients who would receive GA.^[8] However, research on its effectiveness over shivering in spinal anesthesia (SA) is lacking.

The effectiveness of tramadol, which is a central effective analgesic with its weak opioid features, has also proved to be effective in the treatment of shivering after GA,^[9] yet research on the effectiveness of tramadol over the shivering of patients under SA is lacking. This study aims to compare the effects of dexmedetomidine and tramadol given prophylactically on shivering, which may be seen in patients under SA and may disturb them.

METHODS

This study was conducted in Gaziantep University, Faculty of Medicine, Anesthesiology and Reanimation Department, as randomized and double-blind, placebo-controlled. In order to conduct the study, written consent of Gaziantep University Faculty of Medicine Ethics Committee was taken on February 19th under the decision numbered 02-2009/42. A day prior to the surgery, patients were given detailed and comprehensible information about the operation and their written consent was taken.

Ninety patients to undergo elective arthroscopic surgery in Orthopedics and Traumatology Department participated in the study. Their ages ranged between 18 and 60 years and they were in the American Society of Anesthesiologists I-II risk group.

Patients who were allergic to the drugs patients used and had active infection, neurological disorders, abnormal coagulation tests, serious cardiac, renal or hepatic failure, respiratory and endocrinal system disorders with a tympanic body temperature above 36.5°C fewer than 5°C and those who were noncooperative were excluded from the study

The cases who were not applied premedication prior to operation were applied electrocardiography from standard DII derivation, heart rate (HR), peripheral oxygen saturation (SpO₂), monitorization (with Siemens SC 7000 monitor) of non-invasive mean arterial blood pressure (MAP) after being brought to the operation room. IV cannulation was maintained with 18 gauge (G) cannula and 500 ml 0.9% NaCl infusion was applied to the cases prior to SA and saline to be effective at 10 ml/kg/h was used. The saline solutions had not been warmed before administration. This was a non-warming strategy for this study. The room temperature was kept at 24°C and all the

drugs and solutions used were kept at room temperature. Isobaric levobupivacaine (Chirocaine[®], Abbott), 3 ml was used for SA, after keeping at room temperature for 15 min.

The spinal block was realized in the lateral decubitus position after the skin was disinfected with 10% povidon iodine and 15 mg isobaric levobupivacaine was applied to the subarachnoid space from the L4 to L5 intervertebral space for 1 min by means of 25 G quincke spinal needle. Following the spinal block application, patients were divided into three groups randomly. Prior to the operation, 100 mg Tramadol (Contramal[®], Abdi Ibrahim, iv) was applied to Group T (Tramadol) in 100 ml saline and 0.5 µg/kg Dexmedetomidine (Precedex[®], Meditera, iv) was applied to Group D (Dexmedetomidine) in 100 ml saline so as to last 10 min; 100 ml saline was applied to Group P (Placebo) with infusion so as to last 10 min. Patients were not provided with active heating and after the spinal block they were covered with two sterile sheets.

After the subarachnoid injection, the sensory block level was assessed in the middle line by means of pin prick test (by touching dermatomes with a 22 G sharp needle point) at the 2nd, 4th, 6th, 8th, 10th, 15th min. When the sensory block level was assessed and reached T12 level, the surgeon was permitted to start. Care was taken so that the sensory block level did not exceed T8.

An anesthetist different from the person who was knowledgeable about the patient group and medicine and who prepared the study solutions performed the observation and assessment of patients.

The cases' MAP, HR, SpO₂, shivering score, sedation score, tympanic body temperature at the beginning and 0, 5, 10, 15, 20 and 30 min after the SA were observed and recorded. In the postoperative 45-min period, HR, SpO₂, non-invasive MAP pressure values were observed. The shivering scores, sedation scores, tympanic body temperatures in the postoperative 0, 15th, 30th, 45th, min were observed and recorded.

Patients' tympanic temperature was measured from the tympanic membrane by means of GENIUS 2 Thermometer (Tyco, ABD, 2008). A five point scale was used in the assessment of the patients' shivering level; zero point: No shivering, one point: Piloerection without observable muscle activity, one or more peripheral cyanosis without any other reason, two points: Continuity of observable muscle activity in a muscle group, three points: Continuity of observable muscle activity in more than one muscle group, four points: Muscle activity covering the whole body.^[10]

The sedation level of the patients was assessed by means of Ramsay sedation scale; one point: Worried, agitated or unpeaceful, two points: Cooperative, oriented and calm, three points: Responds to oral warnings, four points: Snoozing, gives lively response to hitting between the eye brows or loud noise, five points: Snoozing, slowly responds to hitting between the eye brows or loud noise, six points: Snoozing, no response.^[11]

It was planned that the decrease of patients' MAP below 60 mmHg was to be considered to be hypotension, the decrease of HR below 50/min as bradycardia and the decrease of SpO₂ below 90% at room temperature to be considered as respiratory depression.

It was also planned that 0.5 mg atropine was to be used if bradycardia developed in patients; one ampule ephedrine was to be diluted with 0.9% NaCl₂ to 10 ml to make 2 mg iv accompanied by iv liquid replacement if hypotension developed; metoclopramid (Primperan[®], Biofarma) was to be given in the case of nausea-vomiting; basic life support was to be maintained and 1 mg/kg dose of iv methyl prednisolone (Prednol-L[®], M. Nevzat) and iv application of antihistaminic pheniramine maleate (Avil[®], Sandoz) were to be applied in the case of anaphylactic or allergic reaction.

The cases, which had a shivering score of three and over at the end of the 20th min were regarded to be non-responding to present treatment and planned to be treated with iv 25 mg meperidine (Aldolan[®], Gerot Pharmazeutika Wien).

Observation of the cases in the postoperative period was performed by a third anesthetist who did not know which medicine was used. The cases with shivering scores of one or zero, sedation scores of one or two and stable hemodynamic parameters were sent to the service.

Statistical Analysis

Statistical Package for Social Sciences for Windows 11.0 statistics program was used in the assessment of the parameters studied. The demographic features of each group were compared by means of variance analysis. In order to analyze and compare the between-groups parametric data (comparison of MAP, HR, tympanic temperature) one-way ANOVA was used. The shivering score and sedation score were compared by means of Kruskal-Wallis test. All data were expressed as mean ± standard deviation, percentage or median (minimum-maximum). The statistical significance level was determined to be meaningful at $P < 0.05$. We did not calculate the sample size. However, for purposes of the power calculation, a 25% increase in the shivering was considered to be significant.

RESULTS

No statistically-significant difference was recorded among the groups in terms of demographic characteristics [Table 1]. There was no significant difference between the groups in terms of MAP and HR. When the shivering scores in the intraoperative 20th min were compared, the number of patients whose shivering score was two and less was significantly lower in Group T and D in comparison with Group P [$P = 0.01$, Table 2].

From the intraoperative 30th min and postoperative 0, 15th, 30th, 45th min, shivering scores were under three in all three groups and an additional dose of meperidine treatment was not necessary. Sedation scores at intraoperative 5, 10, 15, 20, 30th min in group D were significantly higher than the baseline values ($P = 0.03$) and values in group T and P [$P = 0.04$, Table 3]. When the postoperative sedation scores in the 30th and 45th min were compared, no significant difference was observed between the groups. Although the sedation scores were significantly higher in Group D, they were three and below in all patients in the intraoperative and postoperative periods.

When the tympanic temperature values at the 5th, 10th, 15th, 20th, 30th min were compared with the baseline values, they were found to be significantly low in all groups [$P = 0.04$, Figure 1]. When the tympanic values at the 0, 5th, 10th, 20th and 30th min were compared between groups no difference

Table 1. The demographic data and mean sensory block level at 15th min

	Group T (n = 30)	Group D (n = 30)	Group P (n = 30)
Age (years)	41.9±12.7	41.8±12.0	40.3±13.0
Gender (F/M) (n)	10/20	11/19	10/20
Weight (kg)	73.0±9.5	76.6±8.8	71.0±9.3
Height (cm)	169.9±6.4	170.6±6.7	170.1±6.07
Duration of Operation (min)	44.9±11.6	44.0±10.3	41.9±10.0
ASA I/II	15/15	14/16	13/17
Mean Sensory Block at 15 th min	T8(T6-T11)	T9(T7-T10)	T10(T8-T12)

Table 2. The shivering score at intraoperative 20th min and the number of the patients given meperidine

Shivering Score	Group T (n = 30)	Group D (n = 30)	Group P (n = 30)	p
≤2	27(%90)	29(%96,6)	24(%80)	NS
>2 (the Number of the Patients Given Meperidine)	3 [†] (%10)	1 [†] (%3,4)	6(%20)	0.01

[†]p, when compared with group P; NS: Non Significant

was found [Figure 1]. The postoperative tympanic temperature at 0, 15th, 30th, 45th min were significantly lower than the baseline values in all groups [$P = 0.04$, Figure 2]. There was no significant difference among the groups regarding tympanic temperature at the 0, 15th, 30th, 45th min [Figure 2].

The side effects observed in patients in the intraoperative period were similar. Nausea-vomiting was treated with 10 mg metoclopramid. Hypotension was treated with 5 mg ephedrine. Bradycardia was treated with 0.5 mg atropine.

DISCUSSION

Shivering is considered to be a body response to hypothermia; for this reason, it is essential that the body temperature be maintained within the normal limits.^[1] Old age, applied block height^[12], the temperature of the local anesthesia used, temperature of iv liquids^[1], room temperature^[13] are significant

risk factors in the development of hypothermia under regional anesthesia (RA).

GA, many agents have been used in the treatment of shivering.^[14] Although opioids are effective in the treatment of shivering, their use in repeated doses increases the risk of respiratory depression.^[15] Wrench *et al.*,^[16] reported the minimum meperidine dose as 0.35 mg/kg for preventing shivering after GA. In this study, a low dose 25 mg, iv, the effectiveness of which was proven in many studies, was used in the treatment of the patients who did not respond to dexmedetomidine and tramadol treatment with a shivering score of three and above.

Central adrenergic receptors have an important place in the modulation of shivering after anesthesia.^[17] The importance of clonidine, which is an adreno receptor agonist, in the treatment and prevention of shivering has been well-established in various studies.^[18,19] It is thought that dexmedetomidine decreases shivering by lowering shivering threshold temperature.^[7] Dexmedetomidine was used in various studies in order to prevent the post anesthetic shivering related to GA at doses of 1 µg/kg^[17,20] and 0.5 µg/kg^[21] and found to be effective. Since the half duration of dexmedetomidine elimination was short (2 h) and had a single dose application, long-term postoperative follow-up was not found to be necessary.

Tramadol's effect mechanism in the treatment of shivering is not clearly known. Tramadol is a racemic mixture composed of two isomers, R and L having different activity spectrum. R Tramadol shows weak affinity to R tramadol µ receptors, 5-OH triptamine inhibits "re-uptake" of noradrenaline and eases its excretion. L tramadol inhibits "re-uptake" of noradrenaline.^[22,23] These findings lend support to the view that the effectiveness of tramadol in shivering treatment may be related to serotonergic and/or

Table 3. The comparison of the intraoperative and postoperative sedation scores and shiverings of the groups

	Group T (n = 30)	Group D (n = 30)	Group P (n = 30)	p
Sedation Score during Intraoperative 20 th min	1 (1-2)	2 (1-3)*	1 (1-2)	0.04
Sedation Score during Postoperative 15 th min	1 (1-2)	2 (1-3)*	1 (1-2)	0.04
The Shivering Score during Intraoperative 30 th min	1 (0-2)	1 (0-2)	1 (0-2)	NS
The Shivering Score during Postoperative 15 th min	0 (0-1)	0 (0-1)	0 (0-2)	NS

*p, when compared the Group D with Groups T and P; NS: Non Significant
Data are presented as median (minimum-maximum)

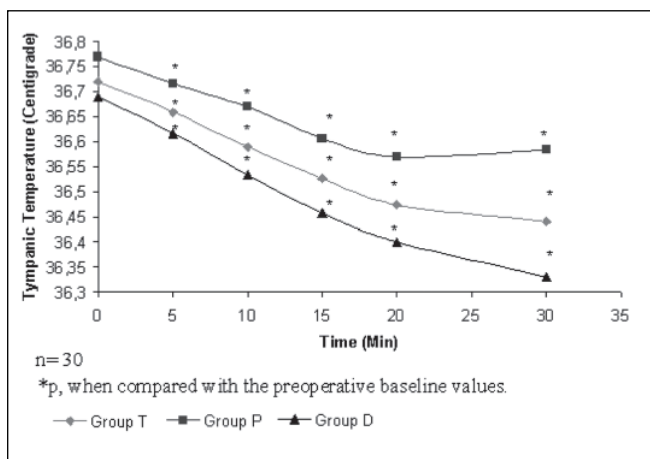


Figure 1: The Intraoperative Tympanic Temperature of the Groups

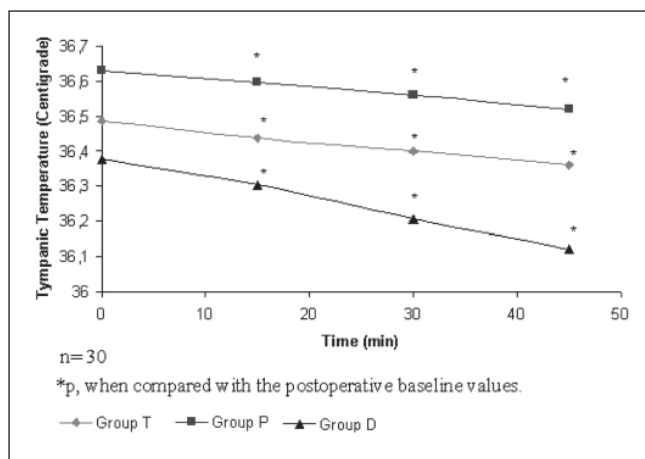


Figure 2: The Postoperative Tympanic Temperature of the Groups

noradrenergic activity. Some studies have reported that shivering, which may arise due to RA can be prevented with iv 0.25, 0.5 and 1 mg/kg tramadol.^[18,24] In this study, shivering scores at the 20th min were significantly lower in dexmedetomidine and tramadol group in comparison with the placebo group.

Some studies also report that dexmedetomidine had hypothermic effects.^[7] In this study, although the intraoperative and postoperative tympanic temperature values were significantly lower than basal values, loss of temperature in all three groups did not reach levels that endangered life functions. The reason why the tympanic temperature decreased in the dexmedetomidine group was not very significant in comparison with previous studies might be that the dexmedetomidine was maintained at lower doses in this study. Or the patients without any medications suppressing the thermoregulation should have been hypothermic. Furthermore the majority of the previous studies were conducted with patients under GA and there was a greater decrease in sympathetic nervous system activity and body metabolic rate under GA in comparison with SA. Furthermore, in this study, the mean sensory block levels of the patients who were applied SAHesia were T8-10 dermatomes, which may be related to less sympathetic blockage.

It was reported that although intraoperative hypothermia presents a major risk factor for shivering after hypothermic anesthesia, shivering may also arise in normothermic patients after surgery.^[18] In this study, similar results were found. When the loading dose of dexmedetomidine is applied, hypotension and bradycardia may be seen. Some studies report that the cardiovascular side effects may be reduced to a minimal level by decreasing the initial dose.^[25,26]

Previous studies have shown that tramadol used at doses of 0.5-1 mg/kg prevents post anesthetic shivering and does not form a significant difference on the arterial blood pressure.^[3,27] In studies where iv 1 mg/kg dose of tramadol was used under epidural and GA in the treatment of post-anesthetic shivering, no clear change was observed in the HR.^[2,24] In this study, the reasons for considering the cardiovascular side effects to be at low rates is that the drug doses were decreased, that there was a slow infusion of 10 min, that the mean sensory block level was T8-10 in the SA application and the fact that it was not at a high level may be related to the fact that the sympathetic tonus was not lowered much.

In Jaakola study^[28] in Intravenous regional anesthesia cases where iv 1 µg/kg dexmedetomidine was used in premedication and in another study where dexmedetomidine

was used in order to prevent post-anesthetic shivering at a loading dose of 1 µg/kg, respiratory depression was not reported.^[20] In studies where tramadol was used in shivering treatment, it was reported that tramadol applied at a dose of iv 1 mg/kg^[2,3,24] and 2 mg/kg^[29] did not lead to a significant decrease in the mean SpO₂ values.

In this study, it was observed that the cases to which iv 0.5 µg/kg dexmedetomidine was applied, sedation could reach Ramsay three level and this level was significantly higher than that of other groups and this low sedation level may have removed anxiety in patients. In studies where iv 1-2 mg/kg^[29] and 3 mg/kg^[22] tramadol was given at the end of operation in post-anesthetic shivering treatment, it was reported that sedation levels were not significantly influenced. In the present study the sedation score of the patients in group T were similar to patients in group P.

The most important problem in tramadol use is nausea and vomiting.^[23] Studies on the prevention or treatment of post-anesthetic shivering have reported that nausea and vomiting increased with iv 1 and 2 mg/kg tramadol and the number of nausea and vomiting cases decreased through a 2-min slow infusion application.^[3,29] The reason why nausea and vomiting in tramadol group in this study were not higher than that of other groups was accounted for by 10-min slow infusion. In addition, it was observed that the low dose dexmedetomidine used in this study had no increasing effect on nausea and vomiting.

CONCLUSION

Low dose dexmedetomidine and tramadol given preemptive in order to prevent shivering that may occur in the SA was found to be effective. In addition, as a major advantage of dexmedetomidine, it removes anxiety without any adverse effects.

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