

Effects of Oral Tizanidine Premedication on Pain and Hemodynamic Responses after Spinal Needle Skin Puncture

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Background: Although a variety of methods have been suggested to reduce stress, anxiety and pain intensity due to spinal needle skin puncture, their adverse effects restrict their widespread administration. In this study we evaluated the effects of oral Tizanidine on the reduction of pain caused by spinal needle puncture and hemodynamic responses.

Methods: In this double blind randomized clinical trial, 52 patients who were scheduled for elective surgeries under spinal anesthesia were recruited. They were randomly allocated in 2 groups of case and control. In the case group 4mg oral Tizanidine was administered to patients one hour before surgery while control group received placebo. Heart rate, systolic and diastolic blood pressure were recorded exactly before spinal needle puncture and 1, 3 and 5 minutes after spinal anesthesia.

Results: The mean average of pain score was significantly lower in case group ($p < 0.001$). Also hemodynamic variables, in terms of heart rate and diastolic blood pressure, were statistically different between two groups ($p=0.04$ and $p=0.02$); however, the difference between systolic blood pressure was not significant between two groups.

Conclusion: Premedication with 4mg oral Tizanidine produced stability in blood pressure and heart rate during surgery and reduced pain intensity caused by needle puncture.

Keywords: Tizanidine; premedication; spinal anesthesia; pain; hemodynamic response

Among the techniques of regional anesthesia, spinal anesthesia is a common practice that is used in genitourinary, lower limb and caesarean section surgeries. The advantages of this method are mentioned as easy performance, producing postoperative analgesia and reducing the incidence of deep vein thrombosis after hip surgery [1]. One of the most important contraindications of spinal anesthesia is patient refusal that mostly happens due to the fear of pain caused by spinal needle puncture. The pain intensity can be reduced by using oral α_2 agonists such as clonidine, infiltration of local anesthetics like lidocaine 2% or intravenous injection of opioids and sedatives like midazolam [1]. However, some adverse effects are reported [1]. NMDA receptors which are mainly located in posterior horn of spinal cord are categorized among pain transmitter receptors [2-3]. Tizanidine is imidazole derived α_2 agonist which reduces excitatory amino-acid release and thereby

decreases the stimulation of NMDA receptors [4]. Despite of structural similarities with Clonidine, cardiovascular adverse effects like hypotension and severe bradycardia are rare and transitory with Tizanidine administration [5-9]. In this study, we evaluated the effects of oral Tizanidine on the reduction of pain caused by spinal needle puncture and hemodynamic responses.

Methods

This double-blinded randomized clinical trial surveyed patients with ASA class I and II who underwent elective surgeries under spinal anesthesia and was approved by Tehran University of Medical Sciences ethics committee. The cases of patient refusal, more than one puncture attempt, positive history of psychological disorders or any opium addiction were excluded from the study. For calculating 30% of difference with 80% power and 10% lost-follow-up, 26 patients for each group was estimated as appropriate sample size. Prior to the surgery, all the patients were informed about the investigation and a written consent was obtained. Included patients were divided into 2 groups, Case and Control, by block randomization. An hour before surgery, 4 mg oral Tizanidine was administered to case group, while the other group was treated with placebo. Upon entering the operating room, vital signs were recorded and all the patients underwent standard monitoring such as ECG, pulse oximetry and non-invasive blood pressure monitoring

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(NIBP). Crystalloid solution at the rate of 5 ml/kg was infused for patients' hydration. In addition, heart rate and blood pressure were recorded exactly before needle puncture. Spinal anesthesia was performed in lateral position and midline approach through L4-L5 or L5-S1 intervertebral space with 25 gauge Quincke needle by an expert anesthesiologist. Pain intensity caused by needle puncture was evaluated with Numerical Rating Scale (NRS) that was completely described to patients (zero belongs to no pain and 10 belongs to the most severe pain ever). Hemodynamic responses were assessed by evaluating heart rate and systolic and diastolic blood pressures one hour prior to spinal anesthesia, exactly before needle puncture and 1, 3 and 5 minutes after spinal anesthesia.

Results

52 patients (42 males, 10 females) with the mean age of 41.7 ± 15.6 (ages between 19 to 72) years were enrolled in the study, 26 in case group (76.9% males, 23.1% females) and 26 in control group (84.6% males, 15.4% females). The mean age of the patients was reported 41.8 ± 17.8 years in cases and 41.6 ± 13.4 years in controls. The mean average of pain scores on the basis of NRS were reported 2 in case and 3 in control groups which were statistically significant ($P < 0.001$). Recorded heart rate and blood pressure are shown in (Table 1) at 5 different time points: T1: an hour prior to spinal anesthesia, T2: exactly before needle puncture, T3: 1 minute after spinal anesthesia, T4: 3 minutes after spinal anesthesia and T5: 5 minutes after spinal anesthesia.

In this study, the average of hemodynamic variables at all time points were compared using repeated measures ANOVA. There were significant differences between two groups in terms of heart rate and diastolic blood pressure, (respectively $P=0.04$ and $P=0.02$); however, the difference between systolic blood pressure among two groups was not statistically significant. Also in comparison of two groups, patient satisfaction of spinal anesthesia due to prepared analgesia, was significantly higher in Tizanidine-treated cases ($P=0.03$).

Discussion

Regarding the results of this survey, prescription of oral Tizanidine as premedication in patients undergoing spinal anesthesia significantly reduced the pain caused by needle puncture and also increased the level of satisfaction of anesthesia due to prepared analgesia ($P=0.03$). In addition, the mean of heart rate and diastolic blood pressure in patients treated with Tizanidine was significantly lower than controls receiving placebo. Although, in the terms of systolic blood pressure the difference was not statistically significant. In 1995, the effects of Clonidine and Tizanidine were surveyed in 63 patients who underwent spinal anesthesia. According to the results, patients receiving α_2 agonists had more stable hemodynamic variables and needed less analgesic agents [10]. These results are in accordance with our study. In 2004, by studying 40 patients undergoing epidural anesthesia, it was reported that blood pressure and pain score assessed by VAS in patients receiving Tizanidine were significantly lower than controls. However, contrary to of our survey, there was no significant difference among

heart rate between two groups [11]. Our study population was based on patients undergoing spinal anesthesia. In some studies the effects of Tizanidine on hemodynamic changes observed in patients undergoing general anesthesia and needing direct laryngoscopy and intubation has been reported [5,12]. In the study performed in 2002 on 52 patients, Tizanidine prescription significantly decreased blood pressure fluctuation caused by laryngoscopy/intubation and reduced the amount of midazolam and sevoflurane MAC [12]. In addition, in 2013 another study showed that Tizanidine significantly reduced the heart rate and blood pressure changes in patients under general anesthesia. Also the incidence of shivering and propofol dosage decreased in patients receiving Tizanidine [5].

Table 1- The comparison of hemodynamic variables between two groups

		Case	Control	P Value
Heart rate	T1	76.2 ± 11.9	78.1 ± 5.5	0.2
	T2	80.6 ± 13.4	85.4 ± 7.7	0.1
	T3	79.6 ± 11.7	89 ± 8.1	0.1
	T4	78.5 ± 12.6	84.5 ± 5.9	0.03
	T5	77.2 ± 13.7	82.1 ± 5.8	0.02
Diastolic blood pressure	T1	76.4 ± 9.5	78.1 ± 5.5	0.59
	T2	79.2 ± 9.4	84.9 ± 7.01	0.01
	T3	79.1 ± 8.5	89 ± 8.1	0.009
	T4	78.5 ± 12.6	71.4 ± 6.7	0.01
	T5	71.4 ± 7.1	73.2 ± 6.8	0.3
Systolic blood pressure	T1	126 ± 12.8	121 ± 9.5	0.14
	T2	132.4 ± 13.1	133.5 ± 7.3	0.72
	T3	133.3 ± 16.5	138.1 ± 8.3	0.2
	T4	124.3 ± 14.7	122.3 ± 9.8	0.5
	T5	119.8 ± 16.6	115.4 ± 12.9	0.2

Conclusion

Using oral Tizanidine as a premedication, yielded stability in blood pressure and heart rate during surgery and decreased the pain caused by needle puncture. Considering its short duration of action, Tizanidine's use as a premedication can be recommended for sedation and stabilization of hemodynamic responses during the operations. Although it is suggested to design and perform other studies with different population in different surgeries under various types of anesthesia techniques. It seems that more supplementary surveys are needed to determine the optimum dosage of Tizanidine.

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