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CONSEQUENCE OF ORAL TIZANIDINE ON PROTRACTION OF INTRATHECAL LIDOCAINE

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Abstract:

Objective: *In order to prolong the duration of intrathecal lidocaine, various drugs are used along with it. Due to the promising effects of tizanidine on central nervous system, it can be assumed that tizanidine can have a positive effect on increasing the anesthesia duration too. Thus, we aimed to investigate the effect of oral tizanidine on the duration of lidocaine spinal anesthesia.*

Methods: *This double-blind clinical trial was conducted on 40 male patients waiting for elective leg surgery with the age range of 20-60 years in the Anesthesia Unit II department of Mayo Hospital Lahore for one-year duration from May 2019 to May 2020. We used simple random sampling and our participants were assigned into 2 groups (placebo and oral tizanidine receivers). Spinal anesthesia with 1 mg/kg of hyperbaric lidocaine 5% was performed in both groups. In tizanidine group, patients received 4 mg of oral tizanidine one hour before spinal anesthesia. Sensory block was examined by pin prick test and all anesthetic duration including start block until reduction of sensory level was calculated at 2 lower dermatomes.*

Results: *Findings showed that oral tizanidine compared to placebo can cause a 10-15minute increase in patients' lidocaine spinal anesthesia. Therefore, the average anesthesia time for tizanidine group increased meaningfully (P= 0.03). In addition, tizanidine can sedate patients during surgery (P= 0.00) or in recovery (P= 0.003).*

Conclusion: *Based on the results, tizanidine increased the duration of lidocaine so oral tizanidine can be used to prolong the duration of lidocaine spinal anesthesia.*

Keywords: *Tizanidine, Intrathecal lidocaine, Spinal anesthesia*

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INTRODUCTION:

Subarachnoid anesthesia is considered one of the neurobasal blocks (while centroceratids is an injectable drug) sympathetic block, sensory, and motor block. Spinal Anesthesia is one of the common methods used in operations; However, due to time constraints and because the anesthetic time of these drugs is not enough to complete the operation, additive drugs are often used to increase the duration of the operation. Vasoconstrictors are one of these supplements and the most appropriate adrenaline is 0.1 and 0.2 mg and phenylephrine is 2 mg.

These drugs reduce blood flow in the spinal cord and then reduce the elimination of the local anesthetic solution and cause anti-nociception by stimulating alpha-adrenergic receptors. Most researchers believe that adding vasoconstrictors to a local anesthetic solution can be dangerous for phenylephrine and adrenaline, which are considered particularly strong vasoconstrictors and can lead to a decrease in blood intake from the spine. In some studies, increased temporary neurological symptoms were reported after the addition of tetracene phenylephrine and epinephrine. In addition, the addition of adrenaline subarachnoid adrenaline can increase nerve damage to lidocaine. In addition, a local anesthetic solution in patients with diabetes can increase the risk of nerve damage anemia, adding this drug.

Other drugs include local anesthetic solutions for the breakdown of acetylcholine added, the release of nitric oxide into the spinal cord, thereby increasing block time and density. Neostigmine is one of the drugs that has been asked about the use due to nausea and prolonged motor overload along with local anesthetic drugs. The addition of opioids to local anesthetics increases the effects and reduces postoperative pain. However, the use of these drugs is not common in terms of delaying the release of a hospital patient and causing patients to be hospitalized in terms of breathing suppression.

Like clonidine, an alpha-2-adernorseptor agonist, which is mainly used as a relaxation with a central tizanidine effect. Clonidine derivatives can cause certain effects such as relaxation, anxiety, and pain reduction; lowering blood pressure and creating fewer bradycardia. Tizanidine has a direct effect on the spinal cord and prevents the release of "amino acid simulation"" (NMDA receptor stimulant) and its preventive actions are actually known.

The side effects of tizanidine are primarily associated with dosing and include drowsiness, fatigue, weakness, headache, bradycardia, low blood pressure and digestive and liver disorders. This drug is available on Iranian markets in the form of 2 and 4 mg tablets. It is absorbed by the digestive system and reaches the maximum plasma shaking within 1-2 hours; and its rejected half-life is 2-4 hours.

Currently, fewer side effects of sub-arachnoid anesthesia, easy performance, patient satisfaction and emergency anesthesia are largely taken into account in operations limited to the lower extremities and pelvis. Therefore, various drugs have been used to prolong the time of anesthesia and improve quality. The benefits of tizanidine, especially in terms of hemodynamics and stability of the cardiovascular system, replace clinics; and with regard to the recommendations contained in previous studies, taking into account the use of oral triple tablets to prolong neuropathic anesthesia.

METHODS:

This study was a randomized, double-blind clinical trial held in the Anesthesia Unit II department of Mayo Hospital Lahore for one-year duration from May 2019 to May 2020. Sampling was straightforward and the study involved 40 men aged 20-60 years awaiting elective leg surgery. These patients were not prohibited from taking tizanidine and performing spinal anesthesia. Initially, they were visited and consulted before entering the operating room, and those who did not sign a consent form were omitted from the study. After establishing the necessary criteria, patients were placed in one of two research groups. Patients with cardiovascular diseases, liver and kidney diseases, people using drugs and alcohol, and people taking antihypertensive and beta-blocking drugs were excluded. One hour before surgery, patients took oral tizanidine or placebo (in packages similar to the original drug) with 30-50 ml of water. Upon arrival in the operating room, patients were placed in operating beds, and their electrocardiography, pulse oximeter, non-aggressive blood pressure and sedation levels were monitored and assessed. All patients received 7 cm3 / kg of crystalloid bell liquid as intravascular equilibration volume. Subsequently, in a sitting position, subarachnoid anesthesia was performed with 1 mg / kg of 5% hyperbaric lidocaine using a 23-gauge Quincke needle in the third and fourth or fourth and fifth lumbar steps; all sterilization conditions were complied with. Immediately after the injection, patients were asked to lie on their backs and their electrocardiography, pulse oximeter, blood pressure, heartbeat, and sedation (based on Kulka's criteria) were re-monitored by a blind anesthesiologist.

Kulka Criterion:
0= awake

1= sleepy or sedate who awakes easily
2= sleepy who reacts quickly to verbal stimulus
3= sleepy who reacts to verbal stimulus with a short delay
4= unconscious

The duration of anesthesia (expressed in minutes) was measured from stabilization of anesthesia in the highest sensory dermatome to recovery of anesthesia to the two lower dermatomes and recovery of blockade by reducing the area of anesthesia to four lower dermatomes. The area of anesthesia was examined by pin puncturing after intervertebral injection. If the patient's systolic blood pressure was less than 90 mm / silver, ephrin was used to correct it, and if the patient had nausea, vomiting or heart rate below 50 pulses / min, 0.6 mg of venous atropine was prescribed. After collecting the information, the data was recorded in SPSS version 12. The t-test and the Mann-Whitney U test were used to compare the data. For the qualitative variables, the chi-square test was used accordingly. 0.05 was considered a significant level.

RESULTS:

Demographic indicators such as age, weight, as well as basal blood pressure and heart rate in both groups showed no significant differences between the two groups (Table 1). The results showed that oral tizanidine, compared to placebo, can increase the spinal anesthesia of lidocaine by 10-15 minutes, so that the mean duration of anesthesia for the tizanidine and placebo groups was 57 ± 16 and 47 ± 11 minutes, respectively (increased significantly, P = 0. 03). However, the stability of spinal anesthesia in the tizanidine and placebo groups was 8 ± 2.9 and 7 ± 2.5 minutes, respectively (no statistically significant difference) (Table 2). Unlike the placebo group, tizanidine did not cause any significant hemodynamic disturbances. The changes in blood pressure and heart rate in both groups were not related to any particular time, and there was no significant correlation in both groups with regard to the time of occurrence of these changes (whether before, during or after surgery) (Figures 1 and 2).

Table 1. Comparison of general indexes in both groups

Examined index	Treatment group (mean ±SD)		*P* value
	Placebo	Tizanidine	
Weight (kg)	68.1±7	67.7±5	0.8
Age (y)	33.1±12	31.1±10	0.6
Basic blood pressure (mm Hg)	125.81±13	127.79±10	1
Average basic blood pressure (mm Hg)	95.24±11	94.97±12	0.09
Average blood pressure during surgery (mm Hg)	84.7±19	89.3±17	0.08
Average basic heartbeat (beat/min)	88.9±18	85.85±12	0.05

Table 2. Comparison of spinal anesthesia in various treatment groups (min)

Examined index	Treatment group (mean ±SD)		*P* value
	Placebo	Tizanidine	
Beginning point	7.2±2.5	8.0±2.9	0.35
Reduction of sensory block to 2 dermatomes	46.5±11.0	56.6±16.0	0.03
Reduction of sensory block to 4 dermatomes	72.4±14.0	60.7±13.0	0.01
Recovery duration	26.5±11.0	19.6±9.0	0.05

Another finding of this research is that, tizanidine can sedate patients during surgery (P= 0.00) or in recovery (P= 0.003); it also decreases the need for using sedation and venous sedatives. These results were statistically very valuable and meaningful (Table 3).

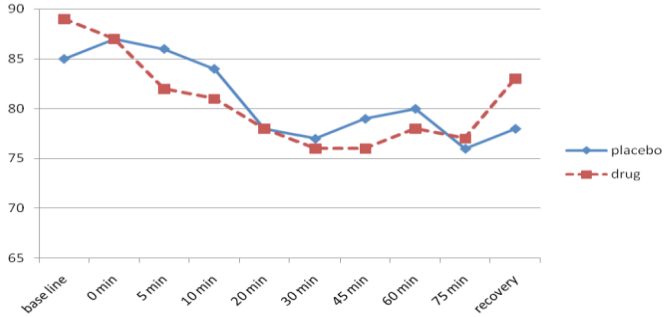

Figure 1. The trend of heartbeat changes (number/minute) in both groups

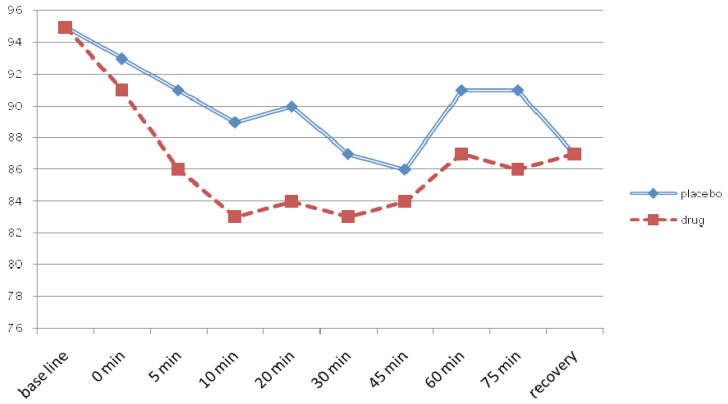

Figure 2. The trend of average blood pressure changes (mm Hg) in both groups.

Table 3. Comparison of variables frequency (class ASA, sedation, atropine and ephedrine consumption)

Variable	Placebo (n=20)		Drug (n=20)		*P* value
	No.	%	No.	%	
Class ASA I	18	90	18	90	1
II	2	10	2	10	1
Sedation before surgery	0	0	4	20	0.1
Sedation during surgery	1	5	15	75	0
Sedation in recovery	0	0	8	40	0.003
Ephedrine consumption	1	5	2	10	1
Atropine consumption	4	20	3	15	1

No increase was reported in the use of venous liquids, atropine and ephedrine in those who had used tizanidine. None of the patients in this study showed a special problem during anesthesia or after it. We also evaluated the side effects of drug (e.g. bradycardia, nausea, reduced blood pressure, headache, and sleepiness) in both groups. We did not observe a significant difference between groups.

DISCUSSION:

The results of these studies showed that the consumption of oral tizanidine one hour before the procedure may prolong spinal anesthesia with lidocaine. By having a sedative and sedative effect, this drug reduced patients' anxiety and anxiety during surgery and increased their relaxation during surgery and convalescence, thereby reducing the use of venous sedatives. Moreover, the use of tizanidine under spinal anesthesia with lidocaine did not change the requirements for atropine, ephedrine and venous fluids. Spinal anesthesia is one of the common methods used in surgery; however, due to time constraints and because the duration of anesthesia with these drugs is not sufficient to complete the operation, additional drugs are usually used with them to extend the duration of the operation. However, the use of these drugs in intervertebral injections can cause cardiovascular problems. In a 1995 study in Japan on gynecological patients undergoing spinal anesthesia with tetracaine, the effects of oral tizanidine and clonidine were compared. The results showed that both drugs could prolong spinal anesthesia with tetracaine, while tizanidine had fewer side effects and resulted in better hemodynamic stability. In this study, tizanidine potentiated the effects of lidocaine and did not cause homodynamic effects. In another study, which was conducted in 2008, intervertebral lidocaine was added to local anesthetics. The results showed an increase in the frequency of hypotension episodes, but no bradycardia was observed. No bradycardia or hypotension were found in the studies in patients. Asgari et al. They studied the effect of sub-diaphragmatic infiltration of 1% lidocaine at the beginning of surgery combined with spinal anesthesia to reduce pain, but unlike previous studies, their results showed that the mean pain intensity in patients was not significant and the addition of lidocaine 1% did not affect worsening of pain. In the present study, spinal anesthesia was performed with 1 mg / kg of 5% hyperbaric lidocaine. In a 2001 study by Gabriel and Gordin in the United States, clonidine, along with local anesthetics, increased sensory blockade regardless of the starting point. In our study, tizanidine had no effect on the starting point and the duration of anesthesia was extended. In another study by Miettinen et al., The sedative

effect of 12 mg of oral tizanidine was comparable to 50 µg of clonidine, but the effect of clonidine was longer; but the decrease in diastolic blood pressure with clonidine was greater than with tizanidine. In these studies, oral tizanidine was introduced as a suitable substitute for clonidine during surgery. Rupani et al. Showed that preoperative oral tizanidine improves the intensity of postoperative anesthesia without exacerbating side effects. Their results are consistent with this study. In this study, the side effects of tizanidine, such as hypotension, bradycardia, nausea, headache, and somnolence in the placebo and tizanidine groups were not significantly different, while patients' relaxation was greater based on Kulka's criterion.

CONCLUSION:

In this study, the effect of oral tizanidine on the duration of lidocaine in spinal anesthesia was examined. It was shown that tizanidine increased the duration of lidocaine more than placebo; homodynamic change in both groups was not significant. It is suggested that various doses of tizanidine and various times of prescription prior to operation should be examined.

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