Original Article

J Babol Univ Med Sci
22; 2020. P: 181-187

The Effect of Oral Tizanidine on Bleeding and Quality of Surgical Field During Endoscopic Sinus Surgery

A. Mahoori (MD)[1], B. Gholamveisi (MSc)[2], M. Golmohammadi (MD)[1], Sh. Pashaei Khoei [1], Sh. Sane (MD)*[1]

1.Department of Anesthesiology, School of Medicine, Urmia University of Medical Sciences, Urmia, I.R.Iran

2.Department of Operating Room, Faculty of Nursing and Midwifery, Kurdistan University of Medical Sciences, Sanandaj, I.R.Iran

3.

J Babol Univ Med Sci; 22; 2020; PP: 181-187

Received: Jun 11st 2019, Revised: Jul 28th 2019, Accepted: Dec 14th 2019.

ABSTRACT

BACKGROUND AND OBJECTIVE: Intraoperative bleeding during endoscopic sinus surgery compromises the surgeon's vision for surgery at the surgical field. Since tizanidine causes contraction of peripheral blood vessels and hypotension, which together reduce blood flow to nasal mucosa, this study was performed to evaluate the effect of oral tizanidine on the quality of vision at the surgical field during endoscopic sinus surgery.

METHODS: This double-blind clinical study was performed on 60 patients. Patients were randomly divided into two groups by computer randomization software (2.0) and received 6 mg tizanidine and placebo before the surgery. During the operation, the quality of the operation field was evaluated and scored by the surgeon based on Boezaart scale. Pain score in recovery and 6 hours after surgery and intraoperative hemodynamic parameters were assessed.

FINDINGS: The quality of the surgical field based on the Boezaart scale was significantly better in the group receiving tizanidine (p=0.04). Pain score in recovery was 2.83±1.17 in the case group and 4.53±1.56 in the control group (p=0.001). Pain score 6 hours after surgery in the case group was 3.23±1.22 and in the control group was 4.13±1.33 (p=0.008). Mean arterial blood pressure (p=0.03) and heart rate (p=0.19) during surgery were lower in the tizanidine group.

CONCLUSION: The results of the study showed that tizanidine as a perioperative medication before endoscopic sinus surgery improves the quality of vision at the surgical field and provides a better hemodynamic profile for patients.

KEY WORDS: *Tizanidine, Endoscopic Sinus Surgery, Bleeding, Arterial Blood Pressure*.

Please cite this article as follows:

Mahoori A, Gholamveisi B, Golmohammadi M, Pashaei Khoei Sh, Sane Sh. The Effect of Oral Tizanidine on Bleeding and Quality of Surgical Field During Endoscopic Sinus Surgery. J Babol Univ Med Sci. 2020; 22: 181-7.

***Corresponding Author: Sh. Sane (MD)**

Address: Department of Anesthesiology, Imam Khomeini Hospital, Urmia University of Medical Sciences, Urmia, I.R.Iran

Tel: +98 44 33468967

E-mail: shahryarsane@yahoo.com

[DOR: 20.1001.1.15614107.1399.22.1.24.6]

[DOI: 10.22088/jbums.22.1.181]

Introduction

Endoscopic sinus surgery has become a common procedure in the field of ENT, which is used in nasal polyp surgeries, recurrent or chronic sinusitis, control of nasal bleeding, pressure relief in the orbital cavity (graves ophthalmopathy), removal of foreign body, treatment of sinus mucosa and many other cases (1-4). Despite advances in surgery and anesthesia techniques, bleeding during endoscopic sinus surgery is still a persistent problem (4, 5); a small volume of bleeding can impair the surgeon's vision and as a result, prolong the surgery time or even lead to incomplete surgery (4). There are various techniques to improve vision of the field of sinus surgery, the most common of which are cochlear implant, topical injection of vasoconstrictors, and controlled blood pressure reduction (6). Topical vasoconstrictors may cause hemodynamic instability or even ischemic heart problems (7). Controlled blood pressure reduction exposes the patient to more anesthetic drugs and consequently more complications. Eventually, none of these methods are able to properly control bleeding (8).

Alpha-2 receptor agonists are important in the terms of anesthetics and analgesics (9). These drugs can also be used as antihypertensive drugs. Side effects such as severe bradycardia and hypotension have been reported (10-13). Alpha-2 agonists can reduce the flow of nasal mucus and affect the volume of bleeding as previously studied in animal models (14). Tizanidine is an oral alpha-2 receptor agonist and has fewer cardiovascular side effects, which makes tizanidine a drug of interest for anesthesia (15).

Wawrzyniak et al. examined the effect of clonidine as a pretreatment agent on the quality of surgical vision in endoscopic sinus surgery and found that pretreatment with clonidine before endoscopic sinus surgery shortens the surgery duration and improves the quality of surgical vision (16). The use of alpha-2 receptor agonists may allow the surgeon to establish the appropriate hemodynamics and surgical field in these surgeries and be able to influence the surgical procedure, the duration of surgery and in turn the duration of anesthesia, and at the same time be able to influence analgesia and sedation in the postoperative period. This was the reason for choosing this topic for the present study. Tizanidine has also been used as a drug for premedication and research on it is very limited. In this study, the effect of preoperative oral tizanidine on the volume of bleeding and the quality of the surgeon's vision in the surgical field in endoscopic sinus surgery was investigated.

Methods

This randomized clinical trial was approved by the Research Ethics Committee of Urmia University of Medical Sciences with the code IR.UMSU.REC.1395.299 and with the registration number of the clinical trial IRCT20160430027677N12 after obtaining informed consent from the research units in operating room B of Imam Khomeini Hospital. The study was performed on 60 patients. Patients in the age group of 25 to 55 years, ASA Class I and suffering from chronic sinusitis were included in the study. According to the study of Mohseni et al., based on the comparison of Mean ± SD, bleeding of 216±67 cc in the clonidine-receiving group and 276±78 cc in placebo group, 80% power, 1% error, and one-tailed test, the sample size was considered 29 people in each group. Overall, 60 people were analyzed; 30 people in each group. STATA10 software was used to determine the sample size (14).

Patients with heart problems such as contraindications in hypertensive patients, hepatic and renal insufficiency, and known hypersensitivity to tizanidine, systolic blood pressure above 160 and diastolic blood pressure above 90 or heart rate below 50 at preoperative visit were excluded from the study. Patients receiving anticoagulants, beta-blockers, calcium channel blockers, or digoxin were also excluded. Patients were randomly divided into two groups receiving 6 mg oral tizanidine (manufactured by ACTOVERCO Iran, Karaj) and placebo by computer randomization software (2.0). Randomization of patients was performed by a table of random numbers.

The patient, surgeon and anesthesiologist were unaware of the type of drug used. Medications were administered to patients 90 minutes before entering the operating room. 3 to 5 minutes before surgery, 1 mg midazolam and 2 µg per kg body weight fentanyl and 1.5 mg/kg body weight intravascular lidocaine were injected as premedication. After using 5 liters per minute oxygen 100% for 5 minutes, induction of anesthesia was done through injection of 1.5 mg/kg body weight propofol, 0.1 µg/kg body weight remifentanil and 0.5 mg/kg body weight atracurium and intubation was performed. Controlled hypotension of intravenous infusion of serum nitroglycerin (TNG) was used to maintain an average blood pressure of 55 mm Hg. To maintain normocapnia, the patient was placed under anesthesia with controlled mechanical ventilation mode with 10 breaths per minute and a volume of 10 ml per kg body weight. At the end of anesthesia, the muscle

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]

relaxant effect was reversed with neostigmine and atropine. Prior to induction of anesthesia, patients received 3 ml of isotonic crystalloid per kilogram of body weight. During surgery, maintenance fluids were given according to the weight of the patients and bleeding was compensated with Ringer's lactate solution with 3:1 ratio. One anesthesia and surgery team was responsible for all patients.

Based on the protocol of this study, local vasoconstrictors were not used for any of the patients. All patients were in the reverse Trendelenburg position by 10 degrees during surgery. Intraoperative bleeding was estimated by the anesthesiologist in charge of the patient at the end of the surgery. The amount of bleeding was estimated by measuring the amount of blood in the suction device and the gases used (25 g per impregnated gas) (4, 16). The quality of the surgical field was measured by a surgeon who was unaware of the patient's intervention based on the Boezaart scale (no bleeding: 0; severe bleeding requiring continuous suction: 5) (17). The surgeon's satisfaction with the control of bleeding and the quality of the operation field was assessed with a five-point Likert scale (Very bad: 1, Bad: 2, Medium: 3, Good: 4, Excellent: 5).

Hemodynamic indices were recorded every 15 minutes. Postoperative pain was assessed using a visual analog scale (zero: painless and 10: the worst pain he/she has ever experienced) and before anesthesia, the patients were explained how to evaluate pain (18). The incidence of pain in recovery and 6 hours after surgery was assessed and recorded. In case of postoperative pain and a score above 4, 50 micrograms intravenous fentanyl was injected. Data were analyzed using SPSS V.21 statistical software. In this study, Chi-square test was used to evaluate qualitative variables such as gender, and for quantitative variables in two groups, independent t-test was used for normal data and Mann-Whitney test was used for abnormal data. Kolmogorov-Smirnov test was used to confirm the normality of the data. Repeated Measures Anova test was also used for data analysis, while $p<0.05$ was considered significant.

Results

In this study, the two groups were not statistically different in terms of demographic characteristics and duration of surgery (Table 1). The mean score of recovery pain was 2.83±1.17 in the study group and 4.53±1.56 in the control group (p=0.001). The mean pain score 6 hours after surgery was 3.23±1.22 in the study group and 4.13±1.33 in the control group (p=0.008). The mean bleeding level was 229.83±19.98 in the study group and 281.50±16.89 cc in the control group. (p=0.001) (Table 2). The quality of the surgical field and the surgeon's satisfaction with the bleeding control based on Boezaart scale showed a significant difference between the two groups (p=0.04). The median rank of surgeon satisfaction with the surgical field was 4 in the tizanidine group versus 3 in the placebo group (Table 3). There was no significant difference between the mean heart rate at the recorded times between the placebo and tizanidine groups (p=0.19) but there was a significant difference in the mean arterial blood pressure (p=0.03) (Table 4).

Table 1. Demographic characteristics of patients in the two groups

Variable	Tizanidine Mean±SD Or N(%)	placebo Mean±SD N(%)	P. value
Age (years)	38.26±8.92	42.33±8.09	0.07
Gender			
male	18(60)	20(66.7)	0.39
female	12(40)	10(23.3)	
BMI (kg/m^2)	23.76±2.37	24.43±2.02	0.24
Surgery time (minutes)	102.80±13.50	95.83±18.52	0.10

Table 2. Distribution of absolute and relative frequency of pain and bleeding in the two groups

Level of pain	Tizanidine Mean±SD	placebo Mean±SD	P. value
The average pain score during recovery	2.83±1.17	4.53±1.56	0.001
The average pain score 6 hours after surgery	3.23±1.22	4.13±1.33	0.008
Bleeding (ml)	229.83±9.98	281.50±16.89	0.001

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]

Table 3. Surgical field scale (based on Boezaart scale) and surgeon satisfaction in the two groups

Scale	Tizanidine N(%)	placebo N(%)
Surgery field*		
1	3(100)	0(0)
2	22(57.9)	16(42.1)
3	4(26.7)	11(73.3)
4	1(25)	3(75)
Surgeon Satisfaction*		
1	2(40)	3(60)
2	3(42.9)	4(57.1)
3	5(26.3)	14(73.7)
4	14(63.6)	8(36.4)
5	6(85.7)	1(14.3)

***p= 0.04**

Table 4. Comparison of mean heart rate between the two study groups over 90 minutes

Time	Mean arterial pressure		heart beat	
	Tizanidine	placebo	Tizanidine	placebo
	Mean±SD		Mean±SD	
0	97.11±11.41	99.77±11.25	79.30±11.42	82.76±9.89
15	95.04±10.91	98.81±10.69	75.83±11.45	78.26±10.08
30	89.72±10.31	92.24±12.36	76.40±10.34	78.63±13.22
45	89.71±10.90	94.62±11.05	74.20±11.40	76.33±8.47
60	91.77±8.31	93.23±9.73	77.60±12.41	75.26±14.19
75	89.07±8.44	93.04±11.08	73.50±9.32	77.93±7.05
90	87.09±7.62	94.18±9.87	72.83±8.02	77.53±8.86
P	0.03		0.19	

Discussion

The results of this study showed that preoperative oral tizanidine can affect hemodynamic changes, bleeding, quality of surgical field and surgeon satisfaction and mean postoperative pain score. In this study, bleeding and the surgeon's satisfaction with the bleeding control in patients receiving tizanidine were better and this difference was statistically significant. Mean blood pressure during surgery was significantly lower in the tizanidine group. In the tizanidine group, the mean pain score in recovery and 6 hours after surgery was lower and statistically different.

Wawrzyniak et al., in a study that examined the quality of surgical field of view during endoscopic sinus surgery while using clonidine as a pretreatment agent, found that clonidine pretreatment prior to endoscopic sinus surgery shortened the time of surgery and improved the quality of the surgeon's field of vision (16). We used tizanidine in our study and achieved similar results.

In a study, Mohseni et al. examined the effect of preoperative oral clonidine on bleeding and quality of surgical field in sinus endoscopy. They concluded that oral administration of 0.2 mg clonidine before surgery effectively reduced bleeding during sinus endoscopic surgery (14). Wawrzyniak et al., who examined the improvement in surgeon's field of vision during endoscopic sinus surgery after the use of clonidine as a pretreatment agent, showed that the use of clonidine as a pretreatment before endoscopic sinus surgery can provide better quality of surgical field and more favorable hemodynamic condition (19). These results are consistent with what we obtained in our study.

Tabari et al. examined the effects of oral tizanidine on hemodynamic responses (during surgery) in direct laryngoscopy under general anesthesia. In general, the difference between blood pressure and heart rate, after induction of anesthesia, after intubation and tube removal was lower in the tizanidine group. Hemodynamic examination in our study indicates that the mean blood pressure was lower in the tizanidine group and consequently the quality of the surgical field was better and the bleeding was lower. Blood pressure changes were also less and more stable in this group (20).

This study showed that 6 mg oral tizanidine before surgery can be effective in improving the overall surgical and hemodynamic status and postoperative pain. However, this difference was not significant between the study groups. Given that limited studies have been conducted in this regard, new clinical methods with different approaches and integration of clinical knowledge and experience to generalize the results of evidence-based clinical studies will play an important role in the treatment and survival of patients (21). Therefore, it is recommended that more studies be conducted with more samples and different doses of tizanidine be used in this regard.

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]

Acknowledgment

We would like to thank the Deputy of Research and Technology of Urmia University of Medical Sciences and Dr. Iraj Mohebbi for their help in carrying out this project.

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]

References

1.Baker AR, Baker AB. Anaesthesia for Endoscopic Sinus Surgery. Acta Anaesthesiol Scand. 2010;54(7):795-803.

2.Amorocho MR, Sordillo A. Anesthesia for Functional Endoscopic Sinus Surgery: A Review. Anesthesiol Clin. 2010;28(3):497-504.

3.Ankichetty SP, Ponniah M, Cherian V, Thomas S, kumar K, Jeslin L, et al. Comparison of Total Intravenous Anesthesia Using Propofol and Inhalational Anesthesia Using Isoflurane for Controlled Hypotension in Functional Endoscopic Sinus Surgery. J Anaesthesiol Clin Pharmacol. 2011;27(3):328-32.

4.Kazemi Haki B, Eftekhari J, Alizadeh V, Tizro P. Comparison of Hemodynamic Stability, Bleeding, and Vomiting in Propofol-Remifentanil and Isoflurane-Remifentanil Techniques in Septorhinoplasty Surgery. Jentashapir J Heal Res (Jentashapir J Cell Mol Biol). 2014;5(3):125-30.

5.Wormald P-J, Athanasiadis T, Rees G, Robinson S. An Evaluation of Effect of Pterygopalatine Fossa Injection With Local Anesthetic and Adrenalin in the Control of Nasal Bleeding During Endoscopic Sinus Surgery. Am J Rhinol. 2005;19(3):288-92.

6.Riegle EV, Gunter JB, Lusk RP, Muntz HR, Weiss KL. Comparison of Vasoconstrictors for Functional Endoscopic Sinus Surgery in Children. Laryngoscope. 1992;102(7):820-3.

7.Eftekhari J, Kazemi Haki B, Tizro P, Alizadeh V. A Comparison to Facilitate Insertion of the Laryngeal Mask: Term of Recovery and Postoperative Nausea and Vomiting After Anesthesia With Propofol- Atracurium and Thiopental-Atracurium. Acta Med Iran. 2015;53(2):117-21.

8.Dahmani S, Brasher C, Stany I, Golmard J, Skhiri A, Bruneau B, et al. Premedication With Clonidine Is Superior to Benzodiazepines. A Meta Analysis of Published Studies. Acta Anaesthesiol Scand. 2010;54(4):397-402.

9.Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine Injection Into the Locus Ceruleus Produces Antinociception. Anesthesiology. 1996;84(4):873-81.

10.De Vos H, Bricca G, De Keyser J, De Bacher J-P, Bousquet P, Vauquelin G. Imidazoline Receptors, Non-Adrenergic Idazoxan Binding Sites and A2-Adrenoceptors in the Human Central Nervous System. Neuroscience. 1994;59(3):589-98.

11.Hamilton CA. The Role of Imidazoline Receptors in Blood Pressure Regulation. Pharmacol Ther. 1992;54(3):231-48.

12.Guyenet PG, Cabot JB. Inhibition of Sympathetic Preganglionic Neurons by Catecholamines and Clonidine: Mediation by an Alpha-Adrenergic Receptor. J Neurosci. 1981;1(8):908-17.

13.Adinehmehr L, Salimi S, Majedi MA, Alizadeh A, Sane S. Comparison the Effects of Oral Tizanidine and Tramadol on Intra- and Post-operative Shivering in Patients Underwent Spinal Anesthesia. Adv Biomed Res. 2018;7:140.

14.Mohseni M, Ebneshahidi A, Asgarian-omran S. The Effect of Oral Clonidine Premedication on Blood Loss and the Quality of the Surgical Field During Endoscopic Sinus Surgery: A Placebo-Controlled Clinical Trial. J Anesth Pain. 2012;2(8):152-7. [In Persian]

15.Miettinen TJ, Kanto JH, Salonen MA, Scheinin M. The Sedative and Sympatholytic Effects of Oral Tizanidine in Healthy Volunteers. Anesth Analg. 1996;82(4):817-20.

16.Wawrzyniak K, Kusza K, Cywinski JB, Burduk PK, Kazmierczak W. Premedication With Clonidine Before TIVA Optimizes Surgical Field Visualization and Shortens Duration of Endoscopic Sinus Surgery - Results of a Clinical Trial. Rhinology. 2013;51(3):259-64.

17.Hassani V , Alimian M, Farhadi M, Zaman B, Mohseni M. Surgeon Satisfaction During Endoscopic Management of Cerebrospinal Fluid Rhinorrhea: A Comparison Between Propofol-Remifentanil and Isoflurane-Remifentanil Anesthesia. J Minim Invasive Surg Sci. 2012;1(2):62-6.

18.Sane S, Aghdashi MM, Kazemi Haki B, Gholamveisi B, Rajabzadeh M, Golabi P. The Effect of Pregabalin on the Prevention of Succinylcholine-Induced Fasciculation and Myalgia. J Perianesth Nurs. 2020;35(3):255-9.

19.Wawrzyniak K, Burduk PK, Cywinski JB, Kusza K, Kazmierczak W. Improved Quality of Surgical Field During Endoscopic Sinus Surgery After Clonidine Premedication--A Pilot Study. Int Forum Allergy Rhinol. 2014;4(7):542-7.

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]

20.Tabari M, Alipour M, Esalati H. Evaluation of Oral Tiazinidine Effects on [intraoperative] Hemodynamic Responses During Direct Laryngoscopy Under General Anesthesia. Iran Red Crescent Med J. 2013;15(7):541-6.
21.Kazemi Haki B, Moaddab SR, Rafii MR, Eftekhari M, Lebadi S, Ghorbaniyan N, et al. The Effect of Sodium Selenite on the Acute Phase Protein Response and Plasma Variables in Patients Admitted in ICU. Jentashapir J Health Res (Jentashapir J Cell Mol Biol). 2017;9(2):e65647.

[DOR: 20.1001.1.15614107.1399.22.1.24.6]
[DOI: 10.22088/jbums.22.1.181]