

ORIGINAL
ARTICLE

Effect of phenylephrine spray on closed reduction of nasal fractures in patients under general anesthesia

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Abstract

Introduction: As the most anterior part of the face, the nose is more prone to trauma than other parts of the face, thereby making it the most common facial fracture site. Closed reduction has long been used as the standard treatment of the nasal fracture, which can be performed outpatiently or inpatiently. Bleeding due to the fracture can be minimized by adopting certain strategies before the realignment of the nasal fracture. One of these strategies is to use phenylephrine spray before surgery. This study aimed to evaluate the effect of phenylephrine spray in closed reduction of nasal fractures.

Methods: A total number of 200 patients with nasal fracture – who were admitted to the ENT department of Vali-e-Asr Hospital in 2014 and 2015 – were incorporated in this clinical trial via simple randomization method. The patients were assigned into case and control groups. The case group received phenylephrine spray twice: 30 minutes before the surgery and before anesthesia. The control group did not receive phenylephrine spray. To evaluate the efficiency of the spray, data concerning intraoperative and postoperative bleeding, pain intensity, blood pressure, and the need for tampon in both groups were recorded. The data were compared in the SPSS software version 18 using T-test and Chi-Square test at a confidence level of 95%.

Results: The average age of the participants was 25.12±13.73 years and the majority were men (n=127; 63.5%). The mean systolic pressure of the patients in the case group was significantly higher than that of the patients in the control group (P=0.02). Furthermore, the bleeding volume during surgery in the cases was significantly lower than that of the controls (P=0.01). However, postoperative bleeding volume, pain intensity, and the need for tampon were not significantly different in the groups.

Conclusions: By reducing the intraoperative bleeding, phenylephrine spray can play an important role in decreasing the complications caused by surgery. However, it is not recommended for the patients with heart diseases because it increases systolic pressure.

Key Words: Phenylephrine; Closed Fracture Reduction; Anesthesia; Fractures; Bone; Intraoperative Complications

Introduction

As the most anterior facial organ, the nose is more prone to trauma than other facial parts and it

is the most common fracture site of the face. Although these fractures mainly involve the nasal bones, they are often neglected by the patient (1).

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Depending on the severity of the trauma and its direction, the nasal fracture may be single, multiple, with or without displacement. Nasal fractures account for more than 50% of all facial fractures in adults (2). The examination of nasal fractures during a five-year period showed that these fractures had increased by 45.3% in the elderly, in most of which the orbit cavity had also been involved (3). The study by Hanba et al. (2016) showed an increased risk of nasal fractures in postmenopausal women, and also revealed that these fractures were significantly different in terms of age, sex, and race (4). The main causes of nasal fractures are road accidents, sports injuries, and physical conflicts (5).

The realignment of nasal fractures is performed upon local or general anesthesia that can be achieved with either open or closed techniques. The closed technique, as the standard treatment of nasal fracture, has long been used inpatiently or outpatiently. The closed technique under general anesthesia is performed within 2-10 days postoperatively. If this technique fails, the patient can be treated using septorhinoplasty in the following months (6). Because the nasal fracture occurs along with trauma to other areas, a large percentage of it is left undetected. Inappropriate treatment of the fracture of the nasal pyramid, due to diagnostic errors, affects the organ towards secondary deformity and chronic obstruction (5).

In nasal fractures, three factors should be taken into consideration in order to ensure the optimal method of treatment: the time of treatment, the type of anesthesia (local or general), and the surgical procedure (open or closed reduction) (7). Many prospective studies have regarded local anesthesia as equally effective in treating nasal fractures as general anesthesia. Overall, the complications of nasal fractures include sinus infection, shock (due to severe epistaxis), permanent nasal dysfunction, and nasal septum deviation (5). Nasal bleeding can be severe and lead to shock. However, it is upon controlled bleeding that definitive diagnosis and treatment follow. With some measures taken before nasal realignment, nasal bleeding can be minimized. One of these measures is the use of phenylephrine spray (8). This spray reduces the risk through direct effect on the alpha-adrenergic receptors in the arterioles of nasal mucosa and narrowing them. Other uses of this medicine include the temporary relief of nasal congestion in different conditions such as colds, sinusitis, hay fever, and allergies, which reduces swelling and congestion of the nose through the mechanism of vasoconstriction in the nose (8, 9). Phenylephrine is an alpha-adrenergic

drug with direct and indirect sympathomimetic effects that is attached to its receptors in the artery wall and increases blood pressure by vasoconstriction. Administration of this drug is associated with refractive bradycardia and a reduction in cardiac output and hence should not be prescribed for patients with hypertension (10).

The review of research indicates that although nasal fractures and treatments have been investigated in numerous studies, no studies have been conducted on the use of phenylephrine in the treatment of this condition. Therefore, this study aimed to investigate the effect of phenylephrine spray on closed reduction of nasal fractures in patients under general anesthesia.

Methods

In this single-blind clinical trial, 200 patients with nasal fractures who referred to the ENT clinic of Birjand Vali-e-Asr Hospital in 2015-2016 were selected by simple randomization method. They were randomly assigned into case and control groups. Inclusion criteria comprised of all patients with nasal fractures provided that they were ready to cooperate and complete written consent for participation in the study. The exclusion criteria were septum fracture, open fracture, nasal fracture together with fracture of other facial bones, coexistence of sinus infection, colds, and the infection of upper respiratory tract.

The goals of the study and the cons and pros of the treatment procedures were fully described to all the patients, and a written consent concerning the operation was taken from them. The patients were allocated into case group (receiving phenylephrine spray) and control group (not receiving phenylephrine spray) through systematic random method. The groups matched in terms of age and gender. The case group received phenylephrine spray twice at intervals of 30 minutes (before the operation at the time of admission, and before anesthesia on the operating bed) with two puffs at a time. Both groups underwent closed reduction of the nasal fracture similarly except that the controls did not receive the spray.

The efficiency of phenylephrine spray was measured with respect to the amount of bleeding during and after surgery (by measuring gauze weights before and after surgery) and the pain intensity (using Visual Analog Scale, which is a ruler with ten numbers from 0 to 10; the patient chooses the number that indicates the intensity of his/her pain). The blood pressure and the need for tampon were compared and recorded in the two

groups. All of these parameters were measured and recorded by a trained expert who was blind to study groups. SPSS software (version 18) was used to analyze the data. It should be noted that the data distribution of this study was normal according to Kolmogorov-Smirnov and Shapiro-Wilks tests. Thus, the data were analyzed using T-test and Chi-square test at a significance level less than 0.05.

Results

The mean age of the participants was 25.12 ± 13.73 years with a minimum age of 6 and a maximum age of 85 years. The 16-25 year-olds comprised the dominant age group (33.5%). The majority were men ($n=127$; 63.5%); 78.5% were residents of urban areas; and 37.4% were self-employed. The education level of 103 participants (51.5%) was primary or secondary. The demographic findings at a significance level of $P < 0.05$ showed that there was no significant difference in the parameters of place of residence (urban / rural), occupation (employee / self-employed / housewife / student), and education level between case and control groups.

The mean parameters of blood pressure, intraoperative bleeding and postoperative pain are

presented in Table 1. As shown in the table, the mean pre-operative systolic pressure in the case and control groups were 129.35 ± 10.44 and 117.35 ± 8.71 , respectively, and the mean postoperative systolic pressure of the participants in the case and control groups were 131.5 ± 9.44 and 117.7 ± 9.13 , respectively. This difference was statistically significant ($p=0.02$). Thus, the postoperative systolic pressure of the patients in case group who received phenylephrine was significantly higher than that of the patients in the control group, while there was no significant difference between the groups before the operation.

The amount of intraoperative bleeding was measured based on the difference in weight of the gauzes used before and after surgery. Results showed that those who received phenylephrine spray prior to the operation had significantly less bleeding during the operation than those who did not receive. In other words, the amount of intraoperative bleeding in the patients who received phenylephrine spray was significantly lower than that of the patients in the control group ($P=0.03$), whereas this difference did not show any significant difference in postoperative bleeding (Table 1).

Table 1: Comparison of blood pressure, intraoperative and postoperative bleeding, and the intensity of pain in case and control groups

Variable	Group	Mean \pm SD	P-value
Preoperative systolic blood pressure (mm/Hg)	Case	129.3 \pm 10.4	0.23
	Control	117.2 \pm 8.7	
Postoperative systolic blood pressure (mm/Hg)	Case	131.5 \pm 9.4	0.02 *
	Control	117.7 \pm 9.1	
Preoperative diastolic blood pressure (mm/Hg)	Case	73.0 \pm 7.9	0.08
	Control	71.1 \pm 6.8	
Postoperative diastolic blood pressure (mm/Hg)	Case	74.5 \pm 6.8	0.16
	Control	73.1 \pm 7.8	
Intraoperative bleeding (Difference in weight of gauze or bandage in grams)	Case	16.9 \pm 13.8	0.03 *
	Control	21.2 \pm 14.1	
Postoperative bleeding (Difference in weight of gauze or bandage in grams)	Case	17.9 \pm 14.0	0.12
	Control	21.2 \pm 14.7	
Postoperative pain intensity (benchmark score of pain)	Case	2.9 \pm 2.0	0.92
	Control	3.0 \pm 2.0	

The case group received phenylephrine spray; the control group did not. * Significant statistical difference

The comparison of the score of perceived pain intensity at the significance level of $P < 0.05$ showed no significant difference between the groups. Concerning the frequency of the need for tampon, none of the patients in the case group (0%) and 3 patients in the control group (3%) needed tampon during surgery. The comparison of this parameter with Chi-square test showed that this difference was not statistically significant ($P=0.123$).

Discussion

The nose is the most anterior part of the face and therefore is more prone to trauma than other facial organs. It is the most common site of the face for fractures. These fractures occur because of various reasons including accidents, quarrel and fighting, violent sports such as rugby, and martial arts such as boxing, karate, etc. (11). Nasal fractures are associated with complications such as bleeding and pain, and thus attempts are made to reduce these complications, especially bleeding.

Bleeding is a very important complication especially in children because of the low circulation of blood in them. Intense bleeding can lead to hypovolemic shock, which is very dangerous. Therefore, one of the most important parameters examined in surgical investigations – where different empirical techniques are compared and assessed – is intraoperative bleeding (12, 13). In this study, the amount of intraoperative bleeding in those who received phenylephrine spray preoperatively was lower than that of the patients in the controls ($P=0.03$). Thus, the use of phenylephrine spray could significantly reduce the complications of intraoperative bleeding. Nevertheless, postoperative bleeding showed no significant difference between the two groups. The findings of this study also showed that postoperative systolic blood pressure in the patients who received phenylephrine spray increased significantly compared to that of the controls ($P=0.02$), while preoperative systolic blood pressure was not significantly different between the two groups.

In this regard, the study of Afshari et al. (2005) showed that the infusion of phenylephrine immediately after spinal anesthesia increased blood pressure and prevented the hypotension due to spinal block, and that its effect was greater than intravenous ephedrine injection (14). Although no original research paper was found on the use of phenylephrine and the increase in blood pressure, numerous empirical reports are available on the use of this drug and its subsequent blood pressure and complications. Some of them are mentioned here. Tark et al. (2014) reported that oral intake of phenylephrine would increase blood pressure and stroke (15). Davila et al. (2008) showed that phenylephrine injection for the treatment of ischemia in a 23-year-old man in the United States led to subarachnoid bleeding due to increased blood pressure (16). In 2004, Son and Lee described a 13-year-old boy who had pulmonary edema and systemic hypertension following the use of phenylephrine spray. Also in a letter-to-editor published by Roberts in 1989 in the *New England Journal*, it was reported that the inadvertent dropping of phenylephrine in the eyes of a 28-year-old man who was unconscious due to overdose with alcohol and benzodiazepine led to the increase in blood pressure and hernia symptoms. These reports necessitate the accuracy of administration and use of phenylephrine spray in patients (18).

According to the findings of this study, those who preoperatively received phenylephrine spray did not differ significantly in their need for tampon

to control postoperative bleeding from those who did not receive. Of course, in both groups, tampons were rarely needed. Unfortunately, similar studies have not been performed in Iran or across the world concerning the effect of phenylephrine spray on the amount of bleeding, vital signs, and the need for tampon. Therefore, further studies are needed to assess the effects of phenylephrine spray.

Measuring the intensity of postoperative pain was another variable in this study. This variable is one of the most important parameters in the evaluation and comparison of different surgical techniques that is usually examined in this kind of research (19). According to the findings of this study, those who received phenylephrine spray before operation did not have a significant difference in postoperative pain from those who did not receive the spray. The results of the study by Rahimi et al. (2012), who examined the effect of adding 0.5 mg/kg ketamine to remifentanyl and midazolam to reduce postoperative pain, showed that adding ketamine would significantly decrease the pain of patients (20). The study by Makino et al. (2010) on rats showed that the administration of phenylephrine reduced pain modulation in mice (21). Zaczek (2000) also found that phenylephrine administration would reduce pain and increase brightness of the eyes (22). The results of these studies are not consistent with the results of the present study.

Conclusions

The findings of this study indicated a significant reduction in the amount of intraoperative bleeding in patients receiving phenylephrine spray. However, the amount of postoperative bleeding, the need for tampon to control postoperative bleeding, and the amount of postoperative pain were not significantly different in the two groups. Yet, since the mean postoperative systolic pressure increased significantly in those who received phenylephrine spray, it was necessary to have caution in selecting this procedure for different patients, especially those with heart failure and hypertension. Altogether, further research is required to find other risk factors, complications, and clinical and para-clinical outcomes of this treatment procedure.

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The present paper is the result of a doctoral dissertation. In the implementation of this project, all ethical codes were observed based on the University's Ethics Committee protocols. In addition, this research has been registered in the

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Conflict of Interest

The authors declare that there is no conflict of interest for this article.

References

- Balasubramanian T, Venkatesan U. Fracture nasal bones. *Online Journal of Otolaryngology*. 2013;3:1.
- Atighechi S, Baradaranfar MH, Akbari SA. Reduction of nasal bone fractures: a comparative study of general, local, and topical anesthesia techniques. *J Craniofac Surg*. 2009;20(2):382-4. doi: 10.1097/SCS.0b013e31819b945f.
- Plawewski A, Bobian M, Kandinov A, Svider PF, Folbe AJ, Eloy JA, et al. Recreational Activity and Facial Trauma Among Older Adults. *JAMA Facial Plast Surg*. 2017 Dec 1;19(6):453-458. doi: 10.1001/jamafacial.2017.0332.
- Hanba C, Svider PF, Chen FS, Carron MA, Folbe AJ, Eloy JA, et al. Race and sex differences in adult facial fracture risk. *JAMA Facial Plast Surg*. 2016 Dec 1;18(6):441-8. doi: 10.1001/jamafacial.2016.0714.
- Mondin V, Rinaldo A, Ferlito A. Management of nasal bone fractures. *Am J Otolaryngol*. 2005;26(3):181-5. DOI: <http://dx.doi.org/10.1016/j.amjoto.2004.11.006>.
- Ashoor AJ, Alkhars FA. Nasal bone fracture. *Saudi Med J*. 2000;21(5):471-4.
- Cook JA, McRae RDR, Irving RM, Dowie LN. A randomized comparison of manipulation of the fractured nose under local and general anaesthesia. *Clin Otolaryngol Allied Sci*. 1990;15(4):343-6.
- Mortuaire G, de Gabory L, François M, Massé G, Bloch F, Brion N, et al. Rebound congestion and rhinitis medicamentosa: nasal decongestants in clinical practice. Critical review of the literature by a medical panel. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2013 Jun;130(3):137-44. doi: 10.1016/j.anorl.2012.09.005.
- Gokdogan O, Kizil Y, Akyildiz I, Ahlat O, Kalkanci A, Uslu S, et al. Microbiological and Histopathological Effects of Nasal Packing Containing Probiotics on Nasal Mucosa. *J Craniofac Surg*. 2016 Nov;27(8):e730-e734. doi: 10.1097/SCS.00000000000003061.
- Santha E, Lendvai B, Gerevich Z. Low temperature prevents potentiation of norepinephrine release by phenylephrine. *Neurochem Int*. 2001;38(3):237-42.
- Yoon HY, Han DG. Delayed Reduction of Nasal Bone Fractures. *Arch Craniofac Surg*. 2016;17(2):51-5. doi:10.7181/acfs.2016.17.2.51.
- Mofatteh MR, Golbui SH, Hassanzadeh Taheri MM, Hossaini SM, Jannesar Borugherdi Y. Survey of the efficacy of antibiotic therapy on complications consequent of tonsillectomy and adenotonsillectomy. *J Birjand Univ Med Sci*. 2013;20(3):211-9. [Persian]
- Mofatteh MR, Meghdadi S, Sharifzadeh G, Salehi F, Taheri MMH. A study of the Complications of Bipolar Electrocautery Tonsillectomy in Patients Admitted to Vali-e-Asr Hospital of Birjand. *Journal of Surgery and Trauma*. 2015;3(3-4):33-8.
- Afshari A, Møller A, Hangaard N. [Comparison of prophylactic infusion of ephedrine and phenylephrine during Cesarean section under spinal anaesthesia]. *Ugeskr Laeger*. 2006 Apr 3;168(14):1428-31. [Danish]
- Tark BE, Messe SR, Balucani C, Levine SR. Intracerebral hemorrhage associated with oral phenylephrine use: a case report and review of the literature. *J Stroke Cerebrovasc Dis*. 2014;23(9):2296-300. doi: 10.1016/j.jstrokecerebrovasdis.2014.04.018.
- Davila HH, Parker J, Webster JC, Lockhart JL, Carrion RE. Subarachnoid hemorrhage as complication of phenylephrine injection for the treatment of ischemic priapism in a sickle cell disease patient. *J Sex Med*. 2008;5(4):1025-8. doi: 10.1111/j.1743-6109.2007.00715.x.
- Son JS, Lee SK. Pulmonary edema following phenylephrine intranasal spray administration during the induction of general anesthesia in a child. *Yonsei Med J*. 2005;46(2):305-8. doi: 10.3349/ymj.2005.46.2.305.18.
- Roberts JR. Pseudo cerebral herniation due to phenylephrine nasal spray. *N Engl J Med*. 1989;320(26):1757. DOI: 10.1056/NEJM198906293202618.
- Mofatteh MR, Salehi F, Hosseini M, Hassanzadeh-Taheri M, Meghdadi S, Hassanzadeh-Taheri M. Postoperative Outcomes in Cold Dissection Versus Bipolar Electrocautery Tonsillectomy: A Randomized Double-Blind Controlled Study. *Indian J Otolaryngol Head Neck Surg*. 2017;1-6. <https://doi.org/10.1007/s12070-017-1204-4>.
- Rahimi M, Honarmand A, Naderi F, Safavi R, Mohammad S, Morteza Heidari S. Effects of Adding Low-Dose Ketamine to Remifentanyl-Midazolam

- Infusion under Topical Anesthesia on Pain Relief after Nasal Bone Fracture. *Journal of Isfahan Medical School*. 2012;30(198):1-9.
21. Makino K, Kohase H, Sanada T, Umino M. Phenylephrine suppresses the pain modulation of diffuse noxious inhibitory control in rats. *Anesth Analg*. 2010;110(4):1215-21. doi: 10.1213/ANE.0b013e3181d2a768.
22. Zaczek A, Zetterström C. The effect of phenylephrine on pain and flare intensity in eyes with uveitis. *Acta Ophthalmol Scand*. 2000;78(5):516-8.