Randomized controlled trial showing the efficacy of prophylactic nasal drops of oxymetazoline versus ephedrine in reducing the incidence of bleeding following nasotracheal intubation

Yassin Eltahir Awad Gassim[1], Hadab. A. Mohamed[2], Sireesha Bala[3], Sateesh Arja[4], Tarig Fadlallah Altahir Ahmed[5*], Alaa Khedir Omer Altahir[6], Sahar M Elhadi[7]

[1-3,5-7]Professor, [4]Dean, [1]Omdurman Islamic University, Faculty of Medicine, Sudan, [2]University of Khartoum, Faculty of Medicine, Sudan, [3-6]Avalon University, School of Medicine, Ohio, [7]University of Khartoum, Faculty of Dentistry, Sudan

***Corresponding Author: Tarig Fadlallah Altahir Ahmed**
Email: tarig.ahmed@avalonu.org

Abstract

Introduction: Nasotracheal intubation (NTI) is the method of choice when orotracheal intubation is not feasible (Patients with limited mouth opening), where orotracheal intubation is predicted to be difficult and in patients having airway related mechanical issues (angioedema, Ludwig's angina, tongue haematomas, jaw fracture etc.).

A common problem facing anaesthetist while performing nasotracheal intubation is bleeding which might affect the course of intubation, surgery and recovery of the patient.

Oxymetazoline is a selective α1 and a partial α2 adrenergic receptors agonist. Since vascular beds widely express α1 receptors, the action of oxymetazoline results in vasoconstriction. The mechanism of action of ephedrine is shown to be increasing the effects of NE by mobilizing and releasing the NE from the mobile pool.

Aims: To evaluate and compare the effect of using prophylactic nasal drops of oxymetazoline versus ephedrine on the incidence of nasal bleeding when nasotracheal intubation is performed.

Materials and Methods: This interventional randomized single blinded controlled study was conducted in Khartoum Dental Hospital during the period from September to October 2017. Sixty patients undergoing dental surgery were selected and were randomly assigned into two groups to receive either 1 ml of oxymetazoline 0.05% nasal drops (30 patients) or 1 ml of Ephedrine 1% nasal drops (30 patients) 5 minutes before induction. The incidence and severity of epistaxis, the incidence of the commonest complications related to nasal bleeding and the mode of recovery were assessed following NTI.

Data was collected through predesigned data collection sheet then analyzed using a statistical package for the social sciences version and presented as tables and figures.

Results: Among 60 participants, 53.3% had no bleeding with oxymetazoline application compared to 30% with those who used ephedrine. Fair recovery was reported in 96.7% patients who received oxymetazoline compared to 63.3% from those who received ephedrine. Complicated recovery was significantly more in patients who received ephedrine (36.7%)) compared to a single patient 3.3% from oxymetazoline group.

Conclusion: the study concluded that patients undergoing NTI had no or minimal bleeding and lower rate of complications with the use of oxymetazoline 0.5% compared to ephedrine nasal drops.

Keywords: Ephedrine, Oxymetazoline, Nasotracheal intubation, Nasal bleeding.

Introduction

Airway management is a complex task in maxillofacial surgeries and patients with facial traumas. The choice of intubation technique requires good assessment by a multidisciplinary team that includes maxillofacial surgeons and the anaesthesiologists; as well as good communication between them.[1] Nasotracheal intubation (NTI) is commonly used in patients undergoing oral and maxillofacial surgery.[2] NTI is the method of choice when orotracheal intubation is not feasible (Patients with limited mouth opening), where orotracheal intubation is predicted to be difficult and in patients having airway related mechanical issues (angioedema, Ludwig's angina, tongue hematomas, jaw fracture, etc.). Although nasal intubation is ideally done using fiber-optic bronchoscope, blind nasal intubation remains to have a distinctly valuable role in emergency settings when fiber-optic bronchoscope is not available or inappropriate because of excessive bleeding that compromises visualization.

Although various complications resulting from NTI were reported, e.g. turbinectomy and retropharyngeal dissection, the most commonly encountered complication is epistaxis.

Epistaxis can cause difficulty in intubation due to obscured view during laryngoscopy, risk of blood aspiration and problems of airway management following induction.

Epistaxis may occur as a result of direct nasal tissue trauma, inexperienced intubator, poor quality rigid tubes or increased fragility of the nasal mucosa. Several methods have been postulated to reduce the incidence of epistaxis during nasotracheal intubation e.g. topical vasoconstrictors (epinephrine, phenylephrine, xylometazoline, oxymetazoline, and cocaine), thermo-softening of the nasotracheal tube, red rubber catheter etc.[3]

Oxymetazoline has been shown to induce pronounced decongestion and vasoconstriction of the nasal mucosa that lasts for 6-8 hours.[4] It is a sympathomimetic agent with marked alpha-adrenergic activity[5] which is intended for intranasal use. Oxymetazoline constricts the nasal blood vessels, thereby decongesting the mucosa of the nose and

neighboring regions of the pharynx.[5]

Ephedrine was first isolated in 1885.[4] It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system.[5] The wholesale cost in the developing countries is about 0.69 to 1.35 USD per dose.[6] In the United States it is described as being not expensive.[7] It can normally be found in plants of the *Ephedra* type.[1]

With the growing development of maxillofacial surgery, the influence of NTI on the current practice can be figured out by the fact that about 4112 operations, that require the use of NTI, are annually performed in Khartoum Dental Teaching Hospital.

Attempts to reduce the incidence of inadvertent bleeding when using nasal route for intubation, contributes greatly to the safety of anaesthetic practice and lessens the complications encountered. The efficacy and cost effectiveness of agents to be suitable for use as nasal decongestion in our setting were the main motivations to carry this study. For our knowledge, there were no previous studies done in Sudan assessing pre-emptive drug use for prevention of nasal bleeding following NTI.

Materials and Methods

This interventional randomized single blinded controlled study is designed to evaluate and compare the potential effects of Oxymetazoline versus Ephedrine in preventing nasal bleeding following NTI. In addition, the study compares the incidence of common complications related to nasal bleeding and the mode of patient's recovery following administration of either study drug.

This study took place at Khartoum Dental Teaching Hospital in the period from September 2017 to October 2017. Khartoum Dental Teaching Hospital, being the main dental hospital in the country, shoulders a huge bulk of surgical workload.

Patient's acceptance to be part of the study in addition to, ASA grade 1 and 2 and elective surgeries performed under general anaesthesia using NTI were the main criteria for inclusion in this study.

Patients who refuse to be part of the study, emergency surgeries, patients having hypertension or ischemic heart disease, patients receiving anticoagulants or having bleeding diathesis, patients having allergy from the study drugs, patients with American Society of Anaesthesiologist (ASA) physical status of >2 and patients with contraindications to NTI (e.g. patients with basal skull fracture) were excluded from the study.

Sixty patients, representing the total coverage of all patients fulfilling the inclusion criteria during the study period, were selected and were randomly by double blinded studies and are assigned to one of the two groups to receive either one ml of 0.05% Oxymetazoline nasal drops (Oxy group, 30 patients) or 1 ml of 1% Ephedrine nasal drops (Eph group, 30 patients) 5 minutes before induction of general anaesthesia.

Following a standard technique of anaesthesia to all candidates of the study, NTI was performed by an expert anaesthetists using Macintosh laryngoscope. The incidence and severity of epistaxis, the incidence of the commonest complications related to nasal bleeding (Laryngospasm, disturbed laryngeal view and surgical field) and the quality of recovery were assessed and reported by the researchers.

Data was collected using guided patient data form and were analyzed using a master sheet, excel computer programme and SPSS 16.0 version. Data was then presented in figures and tables as appropriate. Hypotheses were tested and 0.05 probability level was predetermined as the level of significance.

An ethical approval was granted from the ethical committee of Sudanese Medical Specialization Board (SMSB) together with verbal and written consent from patients enrolled in the study.

Results

The majority of patients in the study groups (43.3% of Oxy group and 23.3% of Eph group) were aged < 20 years while the rest were unequally distributed among all age ranges.

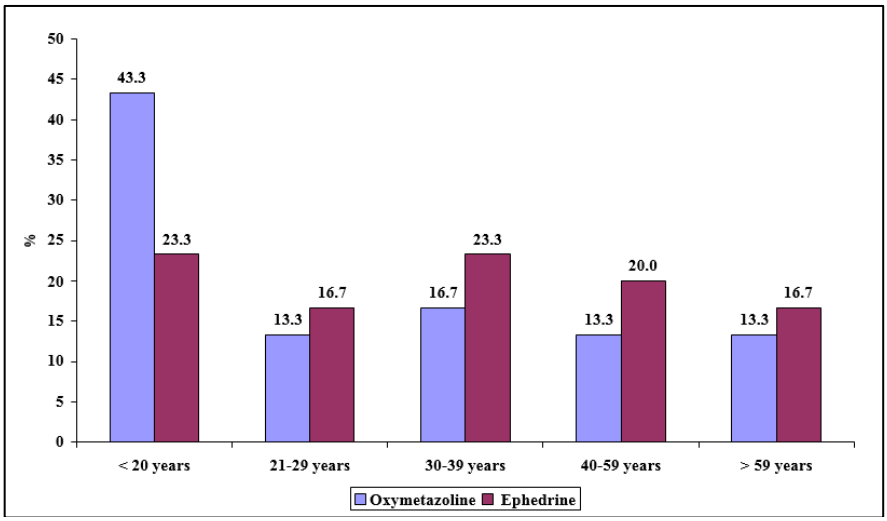

Fig. 1: Age distribution

As shown in fig. 2, the gender distribution was equal among the study groups. In either study group, the male gender represented 63.3% (38 patients) while the female gender represented the remaining 36.7% (22 patients).

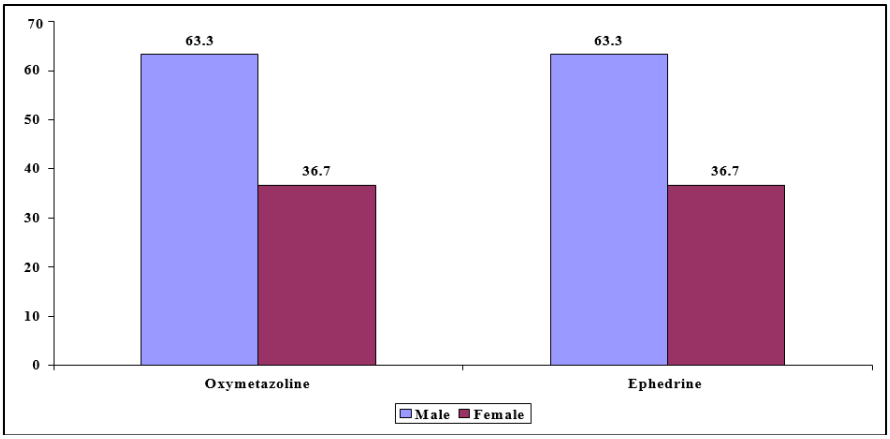

Fig. 2: Gender distribution

On attempting NTI, the magnitude of the resultant nasal bleeding was as follows (Table 1):

1. 16 patients (53.3%) had no bleeding when Oxymetazoline was applied, compared to 9 patients (30%) who received Ephedrine.
2. Eight patients (26.7%) had minimal bleeding when Oxymetazoline was applied compared to 11 patients (36.7%) when Ephedrine was use.
3. Patients who had moderate bleeding were 4 patients (13.3%) in Oxy group, compared to 6 patients (20%) in Eph group.
4. The incidence of severe bleeding was significantly low (P value <0.031) in both study groups (2 patients (6.7%) of those who received Oxymetazoline and 4 patients (13.3%) for the Eph group).

Table 1: Distribution of patients according to the amount of bleeding

	Vasoconstrictor			
	Oxymetazoline		**Ephedrine**	
Amount of bleeding	N	%	N	%
Minimal	8	26.7	11	36.7
Moderate	4	13.3	6	20.0
Severe	2	6.7	4	13.3
No bleeding	16	53.3	9	30.0
Total	30	100.0	30	100.0

P value = 0.031

Regarding the quality of recovery (Table 2), fair recovery was reported in 29 (96.7%) patients who received Oxymetazoline compared to 19 patients (63.3%) from those who received Ephedrine. Complicated recovery was significantly (P. value < 0.001) more in patients who received Ephedrine (11 patients (36.7%)) compared to a single patient (3.3%) from Oxy group).

Table 2: Distribution of the patients according to recovery

	Vasoconstrictor			
	Oxymetazoline		**Ephedrine**	
Recovery	N	%	N	%
Fair	29	96.7	19	63.3
Complicated	1	3.3	11	36.7
Total	30	100.0	30	100.0

P value = 0.001

Regarding the quality of recovery, the reported complications following NTI in patients receiving Ephedrine were either Laryngospasm, disturbed laryngeal view and surgical field seen in 5 (45.4%) patients), laryngospasm in 3 patients (27.3%) or both complications in 3 patients (27.3%). In comparison, the incidence of reported complication in the Oxy group were significantly fewer (P value <0.033). The only one reported complication in this group was a single patient who developed laryngospasm (Table 3).

Table 3: The incidence of postoperative complications

Complications	Vasoconstrictor			
	Oxymetazoline		Ephedrine	
	N	%	N	%
Laryngospasm	1	100.0	3	27.3
Disturbed surgical field	0	0.0	5	45.4
Laryngospasm + disturbed surgical field	0	0.0	3	27.3
Total	1	100.0	11	100.0

P value = 0.033

Discussion

Nasal bleeding following nasotracheal intubation is not an uncommon complication.

This study is designed to evaluate and compare the efficacy of prophylactic Oxymetazoline and Ephedrine nasal drops in reducing the incidence of nasal bleeding following nasotracheal route of intubation.

As derived from results of this study, the overall incidence of nasotracheal tube-related complications were noted to be less when Oxymetazoline nasal drops were used before intubation. Premedication with Oxymetazoline offered a significant reduction in the incidence of epistaxis. A majority of patients who received Oxymetazoline had no epistaxis following NTI compared to patients who received Ephedrine nasal drops. The latter group showed a variable degree of nasal bleed. Moreover, the pre-emptive Oxymetazoline administration has significantly reduced the possibility of complicated recovery. Our findings are compatible with the results of Katz et al who compared the alpha-adrenergic agonist oxymetazoline with cocaine and lidocaine with epinephrine regarding prevention of epistaxis following NTI. The nares of three groups of 14 patients each were topically pre-treated with 4% lidocaine with 1:100,000 epinephrine (group 1), 10% cocaine (group 2), or 0.05% oxymetazoline (group 3) prior to NTI. After intubation, epistaxis was estimated on a scale of 0 to 3, with 0 indicating no bleeding, 1 representing blood on the nasotracheal tube only, 2 indicating blood pooling in the pharynx, and 3 representing blood in the pharynx sufficient to impede intubation. Only 29% of the patients in group 1 displayed no bleeding, whereas 57% of those in group 2 and 86% of those in group 3 had no bleeding. Nonparametric analysis showed a statistically significant difference (p less than 0.013) between oxymetazoline and lidocaine with epinephrine.[8]

El-Seify et al tested the efficacy of prophylactic intranasal admixture of xylometazoline and local anaesthetic gel in reducing epistaxis after nasotracheal intubation in children. They found that the incidence and severity of bleeding were significantly reduced between the study group (7.5%) compared with the control group (27.5%; P<0.01). Navigability using fiber-optic bronchoscope was similar in both groups. Admixture of intranasal xylometazoline 0.1% drops and lidocaine 2% jelly reduced the incidence and severity of epistaxis after NTI in preschool children.[9]

In conclusion, the current study showed greater efficiency of Oxymetazoline in preventing or reducing the amount of epistaxis following nasotracheal intubation, compared to Ephedrine. In addition, Oxymetazoline significantly enhances the fairness of recovery associated with nasal intubation compared to Ephedrine.

Postoperative complications were significantly less noted with the preoperative use of Oxymetazoline compared to Ephedrine nasal drops.

Source of funding

None.

Conflict of interest

None.

References

1. Gray's anatomy. The anatomical basis of clinical practice; nose, nasal cavity and paranasal sinuses, 41st ed. Churchill Livingstone, London; 2015, pp 549–51.
2. Smith JE, Reid AP. Asymptomatic intranasal abnormalities influencing the choice of nostril for nasotracheal intubation. *B J Anaesth* 1999;83:882–6.
3. Ahmed Nusrath A, Tong JL, Smith JE. Pathways through the nose for nasal intubation: a comparison of three endotracheal tubes. *B J Anaesth* 2007;100:269-74.
4. Paul M, Dueck M, Kampe S, Petzke F, Ladra A. Intracranial placement of a nasotracheal tube after transnasal trans-sphenoidal surgery. *Br J Anaesth* 2003;91:601–4.
5. Hall CEJ, Shutt LE. Nasotracheal intubation for head and neck surgery. *Anaesth* 2003;58:249-56.
6. Guedel A, Waters R. A new intratracheal catheter. *Anesth Analg* 1928;7:238–9.
7. Guyton DC, Barlow MR, Besselievre TR. Influence of airway pressure on minimum occlusive endotracheal tube cuff pressure. *Crit Care Med* 1997;25:91–4.
8. Katz RI, Hovagim AR, Finkelstein HS, Grinberg Y, Boccio RV, Poppers PJ. A comparison of cocaine, lidocaine with epinephrine, and oxymetazoline for prevention of epistaxis on nasotracheal intubation. *J Clin Anesth* 1990;2(1):16-20.
9. El-Seify ZA, Khattab AM, Shaaban AA, Metwalli OS, Hassan HE, Ajjoub LF. Xylometazoline pretreatment reduces nasotracheal intubation-related epistaxis in paediatric dental surgery. *Br J Anaesth* 2010;105(4):501-5.

How to cite this article: Gassim YEAH, Mohamed A, Bala S, Arja S, Ahmed TFA, Altahir AKO, Elhadi SM. Randomized controlled trial showing the efficacy of prophylactic nasal drops of oxymetazoline versus ephedrine in reducing the incidence of bleeding following nasotracheal intubation. *Indian J Pharm Pharmacol* 2019;6(3):99-102.