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TOPICAL EPINEPHRINE VERSUS INFILTRATIVE EPINEPHRINE -WHAT IS SAFE FOR HEMOSTASIS IN ENDOSCOPIC SINUS SURGERY?

Otorhinolaryngology

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ABSTRACT

Aim: The study intents to compare the safety & efficacy of topical application versus intranasal injection of epinephrine during endoscopic sinus surgery(ESS) under general anaesthesia(GA) **Materials and Methods:** This is a tertiary hospital based ,1 year prospective study conducted in 200 patients randomly divided into 2 groups,with group I receiving topical application of 1:2000 epinephrine and group II receiving intranasal infiltration of 1:1,00,000 epinephrine,within age group of 10-60 years of both sexes who underwent ESS at GGH,Kurnool from January 2022 to December 2022.Intraoperative hemostatic and hemodynamic parameters following topical application and intranasal injection of epinephrine were analyzed **Results:** There were no significant hemodynamic changes or electrocardiographic abnormalities following topical application of 1:2000 epinephrine.There was increase in heart rate,Systolic and Diastolic blood pressure and mean arterial pressure following intranasal injection of epinephrine in study population($P<0.001$).12% of study population developed electrocardiogram variation in form of sinus tachycardia following local infiltration with 1:1,00,000 epinephrine.Using a standardised scale -Fromme-Boezaart grading to assess hemostasis,no statistical difference in the 2 groups was observed($P>0.05$) **Conclusion:** Topical application of 1:2000 dilution of epinephrine gives similar hemostatic effects compared to intranasal infiltration of 1: 1,00,000 dilution of adrenaline during ESS,and is safe due to no significant hemodynamic abnormalities and thus we can avoid the systemic adverse events such as tachycardia,arrhythmia and mean arterial pressure changes due to epinephrine infiltration

KEYWORDS

endoscopic sinus surgery, hemostasis, topical epinephrine, infiltrative epinephrine.

INTRODUCTION

Functional endoscopic sinus surgery (ESS) is a minimally invasive technique and provides magnified and angulated operating field.Intraoperative bleeding during ESS poses an additional dimension to an already technically challenging surgical approach because of narrow sinonasal surgical field.[1-3] It is necessary to attain adequate hemostasis to prevent complication and to improve the quality of surgical field. Vasoconstriction of nasal mucosa provides more or less bloodless field and is usually achieved by a combination of topical application and local infiltration of local anesthetic drugs containing epinephrine[4-6].Systemic absorption of epinephrine following local infiltration through the nasal mucosa is often accompanied by hemodynamic instability such as hypertension, tachycardia, and arrhythmias in patients with cardiovascular morbidity[7-9]. Evidence indicates that topical application of 1:2000 epinephrine with merocele pledgets alone achieves similar hemostatic effects compared with the use intranasal infiltration with 1;1,00,000 epinephrine, and thus, we can avoid the systemic adverse effects of epinephrine.[10]

METHODS

A total of 200 patients,within the age of 10-60, who underwent ESS under GA were evaluated prospectively for hemostatic and hemodynamic changes following topical application and intranasal infiltration of epinephrine. Informed consent was obtained from all patients.

Inclusion Criteria

Patients of both sexes in the age group of 10-60 years who underwent ESS under GA for recurrent acute sinusitis,chronic sinusitis,sinonasal polyposis

Exclusion Criteria

1. Patients with history of bleeding disorders
2. Patients who are on anti-platelet medications
3. Patients with history of allergy to lignocaine,epinephrine
4. Patients less than 10 yrs and more than 60 yrs
5. Nonconsenting patients

Randomization

All patients considered for the study were randomized and assigned to 1 of the 2 study groups. Assignment to groups was performed by computer-generated random numbers.

General Anaesthesia And Surgical Procedure

After receiving informed consent from patients who were posted for ESS under GA, detailed history, general physical and ENT examination, and routine preanesthetic evaluation were done. Baseline heart rate (HR), lead II electrocardiogram (ECG), systolic blood pressure (SBP),diastolic blood pressure(DBP) and mean arterial pressure (MAP) were noted from the multipara monitor.Premedication was done with glycopyrrolate, ondansetron, midazolam. Induction of GA was done with injection thiopentone sodium or propofol, and maintenance done with sevoflurane and vecuronium infusion. Throat pack was kept to prevent aspiration. In patients randomised to group I,after induction of anesthesia, merocele pledgets soaked in 1:2000 dilution of epinephrine were kept endoscopically in each nasal cavity at the floor of the nasal cavity, middle meatus, sphenoethmoidal recess, and at the uncinate process for about 30-60sec. In patients randomised to group II,2% lignocaine with 1 :1,00,000 epinephrine was infiltrated intranasally at the axilla of middle turbinate,posterior end of middle turbinate at the sphenopalatine area and at the uncinate process

.Changes in HR, systolic BP,diastolic BP and MAP were noted at 0 min,1 min, 3 min,5 min and 7 min respectively, after nasal packing in group I and after intranasal infiltration of epinephrine in group II.After completion of ESS hemostatic effect was analyzed using the Fromme–Boezaart Visual Analog Scale(table 1) and the volume of blood in the suction apparatus was also measured. All observations were entered by the principal investigator in the study proforma sheet. With all these information, the analysis was done to obtain the outcome of the study

Analysis Of Statistics

All data were entered into Microsoft Excel sheet and analyzed using the Statistical Software Package for the Social Sciences (SPSS) version 16.0 (IBM, USA). Descriptive statistics were summarized, using mean(SD) for continuous variables and frequency and percentages for discrete variables. Analysis of covariance by adjusting for baseline measurements was used to test for the difference between the groups in the HR and BP at 0, 1, 3, 5 and 7 minutes. Paired t test was used to test for the increase from baseline in the hemodynamic parameters for the 2 groups.P<0.05 was considered statistically significant.

RESULTS

In our study population,young age group(10-25)-16%;14 and 18,middle age group(26-50)-63%;64 and 62,old age group(51-60)-21%,22 and 20 from group 1 and 2 respectively(figure 1).46 patients (23%) were with comorbidities such as hypertension,diabetes(table 2).Among the study population 16% were having recurrent acute sinusitis,32% with chronic sinusitis,52% with sinonasal polyposis(table 4). It was found that Fromme– Boezaart grading(table 1) did not show any statistically significant difference (P > 0.05) between topical versus injection epinephrine among the study population(table 3) .Out of 200 patients, 152 (76%) showed <10ml difference in volume of blood loss and only 12 (6%) out of 200 study population showed more than 20ml difference in blood loss between topical and intranasal injections of epinephrine(figure 2). Tachycardia was observed in majority of the study population who received intranasal injection of epinephrine, whereas no variation in heart rate was observed in those who had topical application. In group II we noted an increase in HR at 1 and 3 minutes after injection, and levels plateaued down to the baseline level after 5 minutes. The increases from baseline at the1st and 3rd post injection marks were found to be statistically significant (P 0.001). This increase was not noted in group I patients,who received topical 1:2000 epinephrine(table 5) . 12 out of 100 (12%) study population developed ECG variation in the form of sinus tachycardia following local infiltration of epinephrine.No arrhythmias were noted in either group during the procedure.

Table1: Fromme-boezaart Grading Scale

grade	description
Grade 0	No bleeding
Grade 1	Slight bleeding;no suctioning required
Grade 2	Slight bleeding;occasional suctioning required;bleeding doesn't threaten surgical field
Grade 3	Slight bleeding;frequent suctioning required;bleeding threatens surgical field for a few seconds after removal of suction
Grade 4	Moderate bleeding;frequent suctioning equired;bleeding threatens surgical field immediately after removal of suction
Grade 5	severe bleeding;constant suctioning required;bleeding appears faster than it can be removed by suction; surgical field threatened and surgery not possible

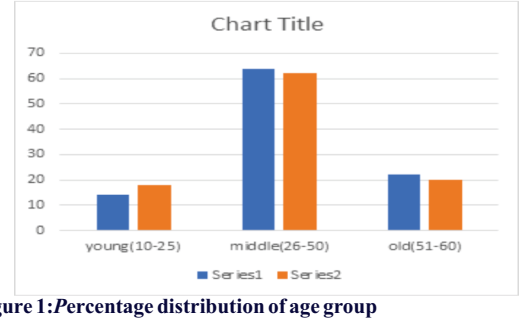

Figure 1:*P*ercentage distribution of age group

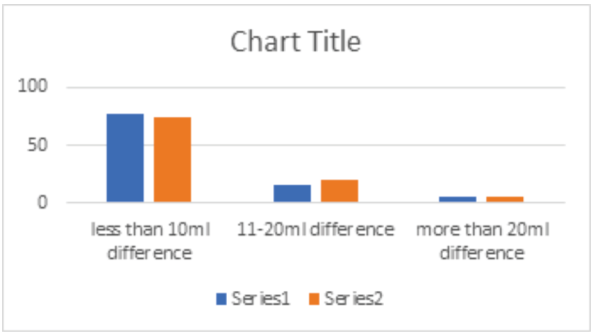

Figure 2:percentage distribution of difference in blood loss between 2 study groups

Table 2:patients with comorbidity status

COMORBIDITY STATUS	FREQUENCY (%)
With comorbidity	46 (23)
Without comorbidity	154 (77)
Total	200 (100)

Table 3:bleeding grades in 2 study groups

group	1	2	3	4
I	13(12.9)	50(50)	35(34.3)	2(1.9)
II	4(4.3)	52(51.4)	40(42.1)	4(5.4)

Table 4:distribution of patients with disease

Disease	Frequency(%)
Recurrent acute sinusitis	16
Chronic sinusitis	32
Sinonasal polyposis	52

A similar pattern was noted in SBP,DBP,and mean BP measurements in the 2 groups. Minimal fluctuations were noted again in group I patients receiving topical epinephrine. No statistical significance was noted in the hemodynamic parameters in group I patients. In groupII, an increase in SBP, DBP, and mean BP were noted in the 1st and 3rdminutes, and a gradual decrease to baseline was noted by the 5thand 7thminutes. These measurements were found to be statistically significant (P.001) [table 5]. The MAP was also found to be increased following intranasal injection of epinephrine, compared with topical application of epinephrine, and the P value of paired t-test for comparison of MAP with topical versus injection epinephrine was <0.001, which is also statistically significant

Following injection of the 1:1,00,000 epinephrine, increases in the HR of 10.2 and 7.4 bpm were noted after 1 and 3 minutes in group II compared with group I. Similarly, SBP had an estimated increase of 17.5 mm Hg more, on average, in group II compared with group I after 1 minute and increase of 18.8 mm Hg after 3 minutes.There were no differences in the mean change scores between the 2 groups by the 5 and 7 minutes postinjection mark. A statistical difference between the 2 groups was still present in SBP, DBP, and MAP at the 3-minute postinjection mark.[table 6]

Table 5: Mean (SD) hemodynamic parameters at base line and post injection of epinephrine

Group	0 min	1 min	3 min	5 min	7 min
I (topical 1:2000 epinephrine)					
HR,bpm	77.4 (14.7)	77.9 (14.5)	76.0 (14.0)	75.3 (13.4)	75.1 (13.5)
SBP,mm Hg	102.2 (15.4)	107.1 (15.8)	104.1 (15.8)	102.5 (16.9)	102.6 (17.3)
DBP,mm Hg	59.0 (12.8)	58.8 (10.7)	58.4 (10.7)	57.7 (9.8)	56.6 (10.7)
MAP,mm Hg	73.4 (12.1)	74.9 (11.3)	73.6 (11.5)	72.6 (11.1)	71.3 (11.9)
II (infiltration with 1:1,00,000 epinephrine)					

HR,bpm	75.4 (17.1)	86.8 (18.2)	82.3 (18.2)	76.7 (18.9)	75.0 (17.1)
SBP,mm Hg	107.3 (17.5)	127.5 (27.0)	128.0 (28.7)	110.2 (20.3)	104.8 (19.8)
DBP,mm Hg	61.1 (11.2)	72.7 (15.0)	70.6 (14.5)	61.3 (14.1)	57.2 (13.1)
MAP,mm Hg	76.5 (11.8)	91.0 (17.6)	89.7 (17.1)	77.6 (14.5)	73.1 (13.7)

Bpm: beats per minute; HR: heart rate, DBP: diastolic blood pressure, MAP: Mean arterial pressure, SBP: systolic blood pressure

Table 6: Difference in the Mean change hemodynamic parameters at 1,3 and 5 min between two groups.

Mean difference(95% CI)						
Variable	at 1 min	P Value	at 3 min	P Value	at 5 min	P Value
HR,bpm	10.18(6.22-14.13)	<0.001	7.40(2.96-11.86)	<0.001	1.06(0.85-4.97)	0.59
SBP,mm Hg	17.46(10.67-24.24)	<0.001	18.77(11.54-26.0)	<0.001	0.42(0.24-2.58)	0.88
DBP,mm Hg	12.64(9.01-16.27)	<0.001	9.52(6.06-12.98)	<0.001	0.66(0.58-3.22)	0.71
MAP,mm Hg	14.02(9.80-18.23)	<0.001	12.36(8.23-16.49)	<0.001	0.15(0.03.42)	0.94

CI: confidence interval, Bpm: beats per minute; HR: heart rate, DBP: diastolic blood pressure, MAP: Mean arterial pressure, SBP: systolic blood pressure

DISCUSSION

ESS uses high-definition nasal endoscopes to visualize the endonasal anatomy to eradicate diseases from nose and paranasal sinuses and restore the sinus drainage pathways and improve its ventilation.It is considered to be a moderate bleeding risk surgery. The presence of significant bleeding in the operating field is a drawback in the outcome of endoscopic sinus surgeries. This necessitates a bloodless field for the surgeon to operate upon easily and to minimize the complications. Various techniques have been used during ESS to achieve an optimal surgical field, such as local and topical anesthetics containing epinehrine, total intravenous or hypotensive anesthesia, preoperative administration of nasal and oral steroids, and beta-blockers. Local vasoconstriction is usually attained through a combination of topical and injectable decongestants containing epinephrine at various concentrations.[10-13]

The efficacy and the safety of epinephrine during ESS is a topic of considerable debate. To characterize the hemodynamic and hemostatic properties of topical and injected epinephrine during ESS and to provide a safer operative condition for both the surgeon and the patient, we compared topical and intranasal infiltration of epinephrine used with local anesthetic.In this study,we have shown that the hemodynamic fluctuations noted during the first few minutes after injection of lignocaine 2%, with 1:1,00,000 epinephrine can be prevented using topical 1:2000 epinephrine. This could prevent further cardiac complications in susceptible patients , therefore lead to safer operative conditions.

It was found that Fromme–Boezaart grading did not show any statistically significant difference (P > 0.05) between topical versus injection epinephrine among the study population. 76 % of the study population showed only <10ml difference in volume of blood loss between topical and injection epinephrine and only 6% of the study population showed more than 20ml difference in blood loss.

From the observations, it showed that there is no significant difference in blood loss between topical and infiltration of epinephrine and the topical application of 1:2000 epinephrine alone achieved a hemostatic effect similar to intranasal infiltration of 1:100,000epinephrine

Tangbumrungtham et al.[14] studied the effect of topical epinephrine 1:1000 with and without infiltration of 1% lidocaine with epinephrine 1:100,000 on endoscopic surgical field visualization and concluded that the addition of infiltration of 1% lignocaine with epinephrine 1:100,000 to topical application of adrenaline 1:1000 for ESS does not significantly improve the surgical field of view compared to topical epinephrine alone. In another study done by Lee et al.[6] to determine the feasibility of the use of a topical vasoconstrictor for hemostasis during FESS, the conclusion was that topical use of adrenaline achieved a hemostatic effect similar to intranasal injection and also that the latter may be avoided during surgery in consideration of its adverse effects. Sarmento Junior Krishnamurti Matos et al[10]studied the topical use of epinephrine in different concentrations for ESS and concluded in favoring the use of topical epinephrine 1:2000 dilution due to a clear superiority in hemostasis.

All these studies correlated with the findings from our study that the topical application of 1:2000 dilution of epinephrine alone achieves a hemostatic effect similar to intranasal injection of 1:1,00,000 dilution of epinephrine in ESS.

The choice of topical vs injected decongestants, the injection site, and the concentrations used are quite variable among otolaryngologists. Numerous reports have shown that injection of epinephrine, even in therapeutic doses, can lead to increased HR and stroke volume, resulting in arrhythmia in susceptible patients.The incidence of cardiovascular toxic adverse effects has been shown to increase in a dose-dependent manner.

Anderhuber et al[15]were the first group to analyze the systemic absorption of injected epinephrine during ESS. A significant increase in the plasma catecholamine level was noted after injection with associated hemodynamic fluctuations.In a more recent study, Cohen-Kerem et al[17]investigated the pharmacokinetic effect of topical and injected epinephrine during FESS. In this study, substantial hemodynamic fluctuations were noted following the use of injected epinephrine.Moshaver et al conducted an RCT and concluded that injection adrenaline with lignocaine during ESS,is associated with cardiac adverse effects apart from providing hemostasis.The hypotensive effects of epinephrine at subtherapeutic concentrations were recently evaluated in a series of reports by Yang et al[20].This mechanism was attributed to the preferential stimulation of the 2 receptors at lower concentrations.In our study, no hypotensive episodes were observed following injection of the study drugs.We attribute this to the use of a higher concentration of epinephrine preferentially stimulating the alphaand beta 1 receptors, thereby manifesting the vasoconstrictive effect.Another RCT done by Günel et al.[18] concluded that the use of adrenaline infiltration during septal surgery is associated with cardiogenic side effects due to systemic absorption.Rasheed M et al[19] conducted a prospective observational study to determine the hemodynamic and hemostatic effects of topical and intranasal infiltration of adrenaline and concluded that topical application of 1:2000 adrenaline has better hemostatic effect and avoids the hemodynamic instability due to systemic absorption of adrenaline.

Avoiding hemodynamic fluctuations is the key factor in preventing cardiac complications during FESS. All these studies correlate with the findings from our study that intranasal injection of local anesthetic containing epinephrine during ESS was associated with cardiac adverse effects such as tachycardia and hypertension due to systemic absorption of epinephrine.

CONCLUSION

From this study,we suggest that topical application of 1:2000 dilution of epinephrine can produce similar hemostatic effect compared to intranasal injection of 1:1,00,000 dilution of epinephrine in ESS under GA. Topical epinephrine does not cause clinically significant alterations in hemodynamic parameters or cardiovascular events,so intranasal infiltration of epinephrine can be avoided during ESS due to its systemic absorption causing hemodynamic instability.

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