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To Study the Oral Bisoprolol for Improving Surgical Field in FESS

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Abstract

Introduction: The success of Functional Endoscopic Sinus Surgery (FESS) depends on the visual clarity of the surgical field, through the endoscope. *Aims:* The objective of this double-blind, randomized, controlled study was to determine if a pre-operative dose of Bisoprolol (*2.5 mg*) would reduce the bleeding during FESS and improve the visualization of the operative field. *Methods:* Sixty ASA I or II patients, scheduled for FESS were randomized to receive either a Placebo (Group A) or *2.5 mg* of Bisoprolol (Group B) *90 min* prior to the surgery. All the patients received standard anesthesia and monitoring. The aim was to maintain the mean arterial pressure (MAP) of *60–70 mm Hg*, by titrating the dose of Sevoflurane and Fentanyl. *Results:* The blood loss in Control group was (97 ± 16.75 *ml*) and in Bisoprolol group was (58.3 ± 13.9 *ml*). The volume percent of Sevoflurane and the dose of Fentanyl used was significantly lower in those who received Bisoprolol. During the operative period, the MAPs were 92.87 ± 6.39 (Group A) and 78.25 ± 3.5 *mm Hg* (Group B) and the heart rate was 94.75 ± 3.14 *min* (Group A) and 67.97 ± 1.84 *min* (Group B). *Conclusion:* This clinical trial has demonstrated that administration of a single pre-operative dose of bisoprolol (*2.5 mg*) can significantly reduce the blood loss during FESS and improve the visualization of the operating field.

Keywords: Beta-blocker; Bisoprolol; Blood loss; Functional endoscopic sinus surgery; The surgical field.

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Introduction

One of the mainstays of surgical treatments of sinusitis and nasal polyps is Functional Endoscopic Sinus Surgery.[1] Advanced imaging techniques, better and increased understanding of the anatomy and the pathophysiology of the disease processes like chronic sinusitis, and image-guided surgery have allowed surgeons to perform more complex procedures with increased safety and reduced complications. FESS is a relatively recent and advanced surgical procedure which uses nasal endoscopes through the nostrils to visualize the inner aspect and to avoid cutting the skin. Its introduction associated with enhanced illumination and visualization has dramatically improved surgical dissection.[2] FESS came into existence through the pioneering work done by Dr Messerklinger and his assistants in 1960 to 1970s.[3] Remarkable short- and long-term results have been reported extensively in the literature. A report by Senior *et al*. says that symptoms improved in 66 of 72 (91.6%) patients following functional endoscopic sinus surgery, with a mean follow-up time of 7.8 years.[4] In addition to the relief of symptoms, endoscopic sinus surgery also

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significantly influences the quality of life. Damm *et al*. reported an improvement in the quality of life for 85% of the chronic sinusitis patient population, with a mean follow-up time of 31.7 months.[5] But the very success of the use of the endoscope for sinus surgeries depends on the visual clarity of the operating field. The sinonasal mucosa is very vascular and poor visualization due to excessive bleeding has been blamed for complications associated with this procedure. There is general agreement that bleeding can be reduced by maintaining low blood pressure during the surgery. This can be achieved using high concentrations of anesthetic agents or administration of vasodilators like sodium nitroprusside. Controlled hypotension is a technique used to limit intra-operative blood loss to provide the best possible field for surgery. Benefits of controlled hypotension for FESS include reduction in blood loss with improved quality of the surgical field. Various agents e.g., magnesium sulphate, vasodilators (sodium nitroprusside) nitroglycerine, high doses of potent inhaled anesthetics, and beta-adrenergic antagonist have been used to achieve controlled hypotension. Some disadvantages have been reported of these techniques including delayed recovery from inhaled anesthetics, resistance to vasodilators, tachyphylaxis, and cyanide toxicity for nitroprusside. However, these pharmacological techniques are associated with tachycardia which, apart from being an undesirable side effect, can increase the venous oozing and therefore, obscure the surgical field. β-adrenergic receptor antagonist such as labetalol, metoprolol and esmolol have been shown to be useful in lowering the blood pressure and provide a relatively bloodless field for surgery, but because of their short duration of action, this benefit does not last throughout the surgery.[6] The present work was designed to compare the efficacy of Bisoprolol as a hypotensive agent in FESS with attention on the amount of blood loss, quality of the surgical field and anesthetic requirements with Placebo.

Aims

1. To determine if a pre-operative dose of Bisoprolol *2.5 mg* orally would reduce the bleeding during Functional Endoscopic Sinus Surgery and improve the visualization of the operating field.
2. To compare the requirements of anesthetics like Sevoflurane and Fentanyl during the procedure with Bisoprolol and Placebo.

Materials and Methods

This was a randomized, prospective double-blinded clinical trial conducted over a period of *1 year* in the Department of Anesthesiology at Madurai Medical College, Madurai.

Inclusion criteria

1. Functional Endoscopic Sinus Surgeries;
2. Both sexes;
3. Age between *15–65 years*;
4. ASA Grade I & II

Exclusion criteria

1. Patients with history of Hypertension;
2. Patients with history of Asthma;
3. Patients with history of Heart blocks;
4. Patients with history of Bleeding disorders;
5. Patients taking Antiplatelet drugs or Antihypertensive drugs;
6. Patients with known Allergy or Hypertensive reactions to medications.

Sixty patients of age between *15* and *65 years* belonging to ASA Grade I & II who are posted for Functional Endoscopic Sinus Surgery were randomized into one of the two groups. Group A (receiving placebo) and Group B (receiving bisoprolol) of 30 each for induction and maintenance of anesthesia (sample size was taken in accordance with the similar type of studies done in the past).

All patients underwent a thorough pre-anesthetic assessment on the evening before the day of surgery. A thorough medical and surgical history was taken and all the required investigations were reviewed. detailed and valid informed consent was obtained from each patient after explaining the procedure.

In the morning of surgery, all patients received Inj Glycopyrrolate *0.2 mg* and Inj Midazolam *1 mg* as pre-medication. All patients were fasting for at least *8 hours* before the start of the surgery. Group B patients were given Bisoprolol *2.5 mg* orally with a sip of water *90 mins* before the surgery by an assistant as the anesthesiologist was blinded to the randomization.

After the patients were wheeled inside the operating room, a large-bore intravenous cannula (18 G) was inserted on the left upper limb. All patients received crystalloid infusion as standard. Monitoring includes ECG, Pulse oximetry, $ETCO_2$ and non-invasive blood pressure.

Anesthetic management of all patients was similar. Before induction patients were pre-oxygenated with 100% oxygen for a *period of 3 mins* followed by induction with Inj. Thiopentone in a dose of *5 mg/kg*, Inj Fentanyl in a dose of *2 µg/kg* and Inj Atracurium *0.5 mg/kg*. Patients were intubated with a suitable sized cuffed endotracheal tubes. The throat was packed with tape gauze to prevent microaspirations. All patients received crystalloid infusion at a rate of *4 ml/kg/hr*. Patients were positioned supine with about *30-degree* head elevation.

The surgeons used 2% Lignocaine with Adrenaline (1:2,00,000) for the nasal mucosa infiltration. Maintenance was with O_2:N_2O (40:60) and Sevoflurane.

The target MAP was around 60–70 *mm Hg* during the surgery and was left to the anesthesiologist who is conducting anesthesia to judge the clinical situation and to adjust the concentration of Sevoflurane and the additional doses of Fentanyl. All patients received Inj Dexamethasone *4 mg* and Inj Ondansetron *4 mg* after the start of the procedure.

After the surgery is over, patients were reversed with Inj Neostigmine *0.05 mg/kg* dose and Inj Atropine *0.02 mg/kg* dose. Patients were shifted to the PACU and were observed for an *hour* and then shifted to the respective wards. Post-operative hemoglobin estimation was done on the evening of the day of surgery.

During the surgery, Sevoflurane volume percentage, MAP and HR were recorded every *10 mins*. The blood loss was estimated from the number of soaked cotton strips and the volume of blood loss in the suctioning apparatus which was kept empty before the start of the surgery.

A fully soaked cotton strip was estimated to contain *5 ml* of blood and a partially soaked cotton strip was estimated to contain *2.5 ml* of blood.

After the procedure was over, surgeons who performed the surgery were asked about the condition of the operating field and to grade it using the Fromme Boezaart Scale.

Results

In Group A the mean age was 34.96 ± 12.69 and in Group B the mean age was 32.73 ± 1.87. The *p*-value was 0.35 which was not statistically significant. Nearly 56.66% of the study was males and 43.33% was females among the study population. In Group A the mean pre-operative hemoglobin was 10.86 ± 0.563 and in Group B it was 11.05 ± 0.635. The *p*-value is 0.12 which is not significant. The mean duration of surgery in Group A was 75.66 ± 10.48 and in Group B it was 67.0 ± 5.81. The *p*-value is < 0.0001 which is statistically significant. In Group A the mean blood loss during the surgery was 97 ± 16.75 and in Group B the mean blood loss was 58.3 ± 13.9. The *p*-value is < 0.0001 which is statistically significant. The mean post-operative hemoglobin in Group A was 9.5 ± 0.65 and in Group B it was 10.63 ± 0.65. The *p*-value is < 0.0001 which is statistically significant. The mean difference in hemoglobin in Group A was 1.04 ± 0.22 and in Group B was 0.5 ± 0.21. The *p*-value is < 0.0001 and is statistically

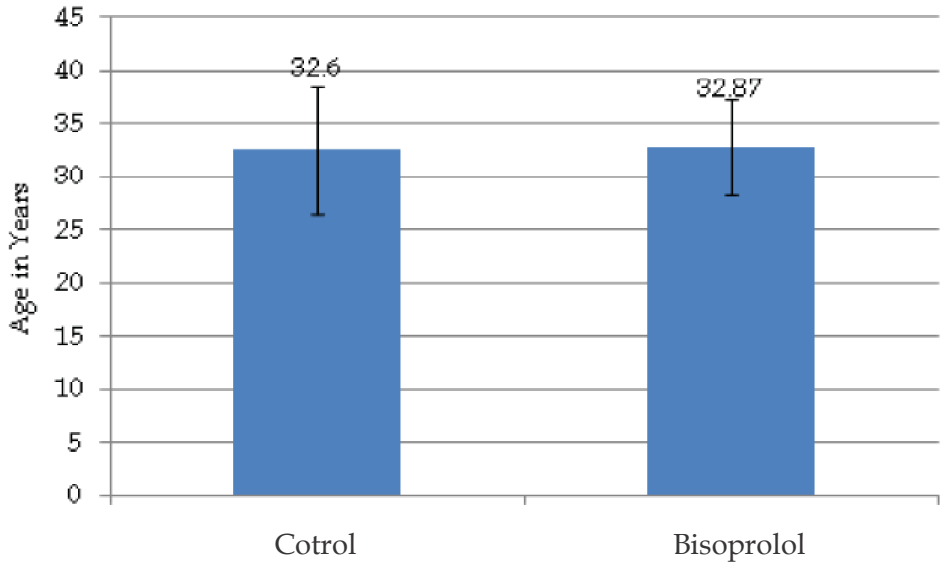

Fig. 1: Age distribution

significant. In Group A the mean MAP value was 92.87 ± 6.39 and in Group B it was 78.25 ± 3.5. The *p*-value is < 0.0001 which is statistically significant. In Group A the mean HR was 94.75 ± 3.14 and in Group B the mean HR was 67.97 ± 1.84. The *p*-value is < 0.0001 and it is statistically significant. In Group A the mean sevoflurane volume percentage used was 2.03 ± 0.25 and in Group B the mean value was 1.11 ± 0.11. The *p*-value is < 0.02 and it is statistically significant. The mean volume of liquid sevoflurane used in Group A is *37.3* ± *2.2 ml* and in group B it is 18.58 ± 3.1. The *p*-value is < 0.0001 which is statistically significant.

In Group A the mean value of Fentanyl used was 133.33 ± 22.5 and in Group B it was 122 ± 11.87. The *p*-value is < 0.02 which is statistically significant. In Bisoprolol Group 5 patients had slight bleeding with no need for suctioning, 20 patients had slight bleeding which required occasional suctioning, 5 patients had slight bleeding which required frequent suctioning and none had moderate to severe bleeding. In Group A 10 and 3 patients had moderate and severe bleeding respectively. The *p*-value is < 0.0001 and is statistically significant, (**Figs. 1–3**) & (**Tables 1–3**).

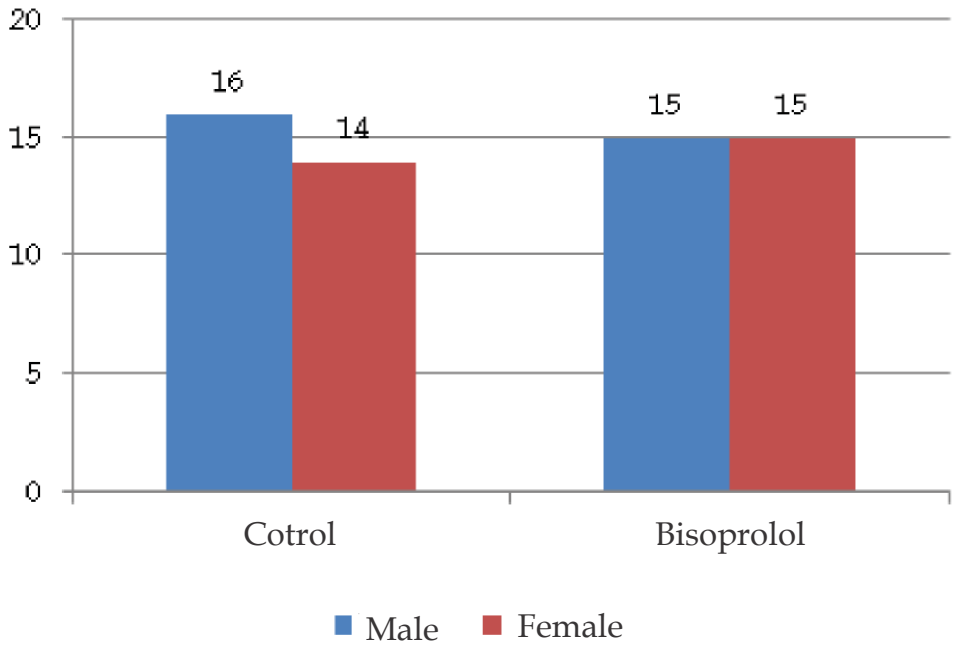

Fig. 2: Sex distribution

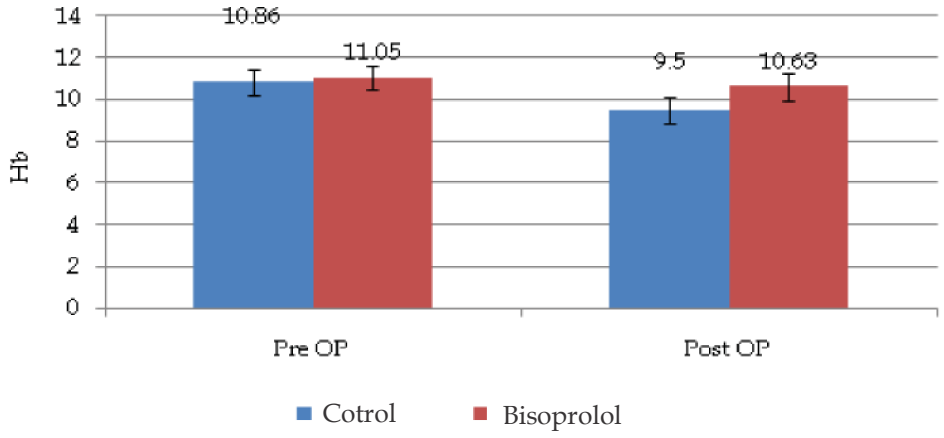

Fig. 3: Distribution of Hemoglobin

Table 1: Distribution of Study Variables

Variables	Control		Bisoprolol	
	Mean	SD	Mean	SD
Duration of Surgery	75.66	10.48	67	5.81
Blood loss during the Surgery	97	16.75	58.3	13.9
Map	92.87	6.39	78.25	3.5
HR	94.75	3.14	67.97	1.84

Table 2: Distribution of Study Variables

Variables	Control		Bisoprolol	
	Mean	SD	Mean	SD
Sevoflurane volume used (%)	2.03	0.25	1.11	0.11
Liquid Sevoflurane used (*ml*)	37.3	2.2	18.58	3.1
Fentanyl requirement	133.33	22.5	122	11.87

Table 3: Comparison of Fromme–Boezaart Scale

FB scale	Control	Bisoprolol	Total
Slight bleeding no suctioning	0	5	5
Slight bleeding, suctioning, no obliteration of field	3	20	23
Slight bleeding, frequent suctioning	14	5	19
Moderate bleeding	10	0	10
Heavy bleeding	3	0	3
Total	30	30	60

Discussion

FESS is one of the well-accepted treatment modalities (rhinosurgeries) for the chronic inflammatory sinus diseases.[1,7] FESS is done by introducing a high definition telescope into the nasal cavity through the anterior nares. As the nasal cavity is a very sensitive one, any surgical manipulation of the area can result in severe sympathetic stimulation which would cause tachycardia and hypertension. In addition to that the nasal mucosa has got a very rich network of blood supply and very delicate to touch in nature it would bleed easily which severely compromises the visualization of the operating field. This becomes even more difficult with the use of endoscopes. As a result of this there could be an inadvertent tissue injury which leads to post-operative adhesions and even scarring. At the worst it can lead to severe complications such as orbital or brain injury.[1,7–9]

During FESS the major issue from surgeon's perspective is the bleeding surgical field. In order to minimize the bleeding we use many techniques intra-operatively. One common thing is using Volatiles. The reason behind this is while using Vasodilators like Nitroglycerin and Sodium Nitroprusside reflex tachycardia becomes inevitable which is again going to be a problem in the surgical field. So, using Volatiles reduces this complication. But the consumption of this volatile is more and the cost of the surgery becomes high. So, in order to reduce the cost we need to add some drugs or technique to reduce the quantity of volatile used during surgery. In this study, Bosoprolol is used for this purpose. while using BisoprololL at a dose of *2.5 mg* orally we found that the amount of Sevoflurane (Volatile used in this study) was reduced to a significant amount when compared to the control group.

This necessitates a bloodless field for the surgeon to operate upon easily so as to minimize the complications. Various techniques have been used during FESS to achieve a bloodless field and an acceptable operating condition, including local anesthesia, TIVA and inhalational anesthesia. Many of these techniques are not without complications. Adrenaline used along with local anesthesia for the infiltration of the nasal mucosa causes local vasoconstriction and reduces bleeding for a short period of time but at the cost of transient hypertension and tachycardia.[8]

Reducing the inflammatory process of the disease by using steroids for several pre-operative days can also reduce the bleeding during surgery.[7,10] Other drugs like Propofol, Dexmedetomidine and Remifentanil have also been used to reduce the bleeding which provides an optimal surgical field. However, the expenditure and the availability of these drugs could be a factor to be considered.[11]

To minimize the intra-operative bleeding at the surgical field reduction of the arterial blood pressure is required. This is achieved by either increasing the concentration of the volatile anesthetic agent or with the use of vasodilator drugs like Sodium nitroprusside. But with these techniques reflex tachycardia is a common side effect which increases the venous oozing in the surgical field. This is because the extent of bleeding in the operative field not only depends on the MAP but also on the venous pressure and capillary blood flow. Studies have suggested that if the heart rate is decreased it increases the diastolic filling time and lowers the venous pressure and causes reduced venous oozing at the surgical field.[12,13]

The usage of beta-blocker to lower the heart rate and blood pressure reduces the bleeding and improves the visualization of the surgical field. Metoprolol and Esmolol have been used for this purpose and did reduce the bleeding. However, the effect lasted for a short period of time as these drugs belong to the short-acting beta-blockers.

Also these drugs caused rebound bleeding due to increased heart rate and venous pressure after the effect wore off. Continuous infusion of Esmolol can also be used to produce the same effect throughout the surgery but a simpler, easier and single-dose orally would be considered both prudent and cost-effective. This clinical trial was done to study the effect of Bisoprolol a long-acting beta-blocker, orally in reducing the bleeding and improvement in the surgical field during FESS.[7,14,15]

Conclusion

In conclusion, the data obtained and statistical analysis suggests that the bleeding is significantly less with Bisoprolol when compared with placebo. Improvement in the surgical field is significantly better with Bisoprolol. The hemodynamic variables like MAP and heart rate were significantly low when compared with placebo. There is a significant reduction in the anesthetic requirement of Sevoflurane and Fentanyl with Bisoprolol. Bisoprolol can be used as an alternative drug in controlled hypotension by which the patients are benefitted clinically and financially.

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