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**Original Research Article**

# Effect of preoperative oral bisoprolol on intraoperative outcomes in endoscopic sinus surgery

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## ABSTRACT

**Background:** Endoscopic sinus surgery (ESS) presents challenges in managing intraoperative bleeding and hemodynamic stability. This study evaluates the efficacy of pre-operative oral bisoprolol in improving surgical conditions and outcomes in ESS.
**Methods:** This study was conducted between March 2021 and June 2022 at the department of anaesthesia, Bangabandhu Sheikh Mujib medical University, Dhaka, Bangladesh. This randomized controlled trial was conducted with 50 participants undergoing elective ESS, divided into bisoprolol and placebo groups.
**Result:** The study involved 50 participants undergoing elective ESS, with 25 in the bisoprolol group and 25 in the placebo group. While demographic characteristics, such as age, weight, height, and gender distribution, showed no statistically significant differences between the groups. The placebo group experienced significantly higher estimated blood loss (421.72 ml vs. 156.24 ml, $p<0.001$) and postoperative hemoglobin levels (12.88 g/dl vs. 11.07 g/dl, $p<0.001$) compared to the bisoprolol group. Hemodynamic parameters, particularly heart rate, exhibited significant differences at various time points, with the bisoprolol group maintaining a higher heart rate post-premedication, intra-operatively, and post-operatively ($p<0.05$ for all). In the assessment of intraoperative bleeding using the Fromme-Boezaart scale, the placebo group demonstrated higher incidences of severe bleeding grades (3 and 4) compared to the bisoprolol group, with these differences being statistically significant ($p<0.001$).
**Conclusions:** Pre-operative oral bisoprolol in ESS patients significantly reduces intraoperative bleeding and anesthetic requirements while maintaining hemodynamic stability. These findings suggest bisoprolol as a beneficial pre-operative medication in ESS, warranting further research to optimize surgical outcomes.

**Keywords:** Bisoprolol, Sinus surgery, Beta blocker, Surgical field visibility

## INTRODUCTION

Endoscopic sinus surgery (ESS) is a common procedure performed to treat chronic rhinosinusitis that fails to respond to medical management.[1] While generally safe and effective, ESS can be technically challenging for surgeons due to intraoperative bleeding from sinus mucosa and changes in blood pressure that obscure visualization of the surgical field. Maintaining optimal

surgical conditions is important for maximizing surgical outcomes and minimizing complications.[2] Several factors contribute to poor visualization during ESS. Hypertension is common in up to 30% of ESS cases and increases the risk of bleeding from sinus mucosa.[3] Hypotension may also occur due to vasovagal responses or fluid shifts and negatively impacts surgical field visibility.[4] Prior studies have found associations between intraoperative hypertension and increased operative time, blood loss, and postoperative complications such as synechiae formation.[5-7] Strategies to control blood pressure during ESS, such as controlled hypotensive anesthesia, have demonstrated benefits for surgical exposure but require invasive monitoring and intravenous drug administration.[8] Oral beta-blockers represent a non-invasive alternative for modulating hemodynamics before surgery. Bisoprolol is a cardio-selective beta-1 receptor antagonist commonly used for hypertension that has a long duration of action and favorable side effect profile.[9] In other procedures, pre-operative bisoprolol has been shown to reduce intraoperative blood pressure and heart rate without compromising patient safety.[10,11] Its pre-treatment effects last throughout the intraoperative period, avoiding risks of intravenous antihypertensives. The potential application of pre-operative bisoprolol for ESS has been investigated in a few preliminary studies. A randomized trial of 30 patients found bisoprolol 2.5 mg given 1 hour before ESS significantly lowered mean arterial pressure during surgery compared to placebo and improved surgical grading scores.[10] Another study of 60 patients similarly reported bisoprolol was associated with better surgical exposure and fewer complications.[7] However, larger trials are still needed to validate these findings. The aim of the current study is to determine whether pre-operative oral bisoprolol 2.5 mg is effective at reducing intraoperative blood pressure and improving surgical field visibility during ESS when compared to placebo. The primary outcome is mean arterial pressure during key steps of ESS. It is hypothesized that bisoprolol administration before ESS will lead to more favorable hemodynamic control and surgical exposure compared to placebo. The results of this study may help establish an easy-to-administer preoperative regimen to optimize ESS.

## METHODS

This prospective, randomized controlled trial was conducted between March 2021 and June 2022 at the department of anaesthesia, Bangabandhu Sheikh Mujib medical university, Dhaka, Bangladesh. Adult patients scheduled for elective ESS under general anesthesia were recruited. Patients with severe cardiovascular disease, pregnancy, allergy to bisoprolol, or inability to take oral medications were excluded. Eligible patients were randomly allocated to receive either oral bisoprolol 2.5 mg or placebo 90 minutes prior to surgery. A total of 25 patients receiving bisoprolol 2.5 mg were placed in group A, while another 25 patients receiving placebo were placed into group B. The primary outcome was mean arterial pressure during key surgical steps including ethmoidectomy and sphenoidotomy. Intra-operative bleeding was assessed into different grades following the Fromme-Boezaart grading scale.[12] Anesthesia was standardized across all patients. Induction was achieved using Inhalation Isoflurane, maintained at a concentration necessary to achieve adequate anesthesia depth throughout the surgery. According to Avogadro's law, 1 gram-molecular weight (gmw) of any gas occupies 22.4 liters at standard temperature and pressure (STP). Applying this to isoflurane, with a molecular weight of 184 g/gmw, we find that 184 g of isoflurane vapor occupies 22.4 liters. Therefore, 1 g of isoflurane vapor occupies 22,400/184 ml, which equals 121.73 ml. Given the density of isoflurane is 1.495 g/ml, 1 ml of liquid isoflurane yields 182 ml of vapor (121.73 ml/g×1.495 g/ml). During surgery, the concentration of isoflurane delivered was monitored every 15 minutes and averaged. If the average concentration delivered is X% and the fresh gas flow rate is Y ml/min, the volume of isoflurane vapor delivered is (Y×X)/100 ml/min. To calculate the total volume of isoflurane vapor delivered, we use the formula (Y×X)/100 ml /min × time. Since 182 ml of vapor is derived from 1 ml of liquid isoflurane, (Y×X)/100 ml of vapor corresponds to (Y×X)/18,200 ml of liquid isoflurane. Therefore, the total volume of liquid isoflurane used over the duration of surgery is calculated as (Y×X)/18,200×time (ml). All patients received monitoring of vital signs including heart rate, noninvasive blood pressure, respiratory rate and oxygen saturation continuously intraoperatively. Surgery time was defined from general anesthesia administration to completion of the procedure. Blood loss was calculated from fluid volume suctioned minus irrigate volume used. Data was analyzed using SPSS version 25. Demographic characteristics were compared using Fischer's exact test. Continuous variables were analyzed using the student's t test. Results are reported as mean, standard deviation and percentages. Statistical significance was set at $p<0.05$.

## RESULTS

The mean age of participants in the bisoprolol group was 27.29 years (SD±6.51), while it was slightly higher in the placebo group at 29.82 years (SD±8.14), but this difference was not statistically significant ($p>0.05$). Similarly, there were no significant differences between the two groups in terms of weight (bisoprolol group: 58.17 kg±2.82 vs. placebo group: 60.07 kg±3.14, $p>0.05$) and height (bisoprolol group: 163.28 cm±4.18 vs. placebo group: 161.72 cm±7.07, $p>0.05$). Pre-operative hemoglobin levels were also comparable between the groups (Bisoprolol group: 13.10 g/dl±1.07 vs. placebo group: 13.18 g/dl±1.24, $p>0.05$). Gender distribution showed a slightly higher percentage of males in the placebo group (64%) compared to the bisoprolol group (52%), and females constituted 48% of the bisoprolol group and 36% of the placebo group. However, these differences were not statistically significant ($p>0.05$). In terms of ASA status, 60% of the bisoprolol group and 56% of the placebo group were classified as ASA I, while

40% of the bisoprolol group and 44% of the placebo group were classified as ASA II, with no significant difference between the groups (p>0.05).

The duration of surgery was slightly longer in the bisoprolol group, averaging 142.18 minutes (SD±17.19), compared to 130.72 minutes (SD±15.42) in the placebo group, although this difference was not statistically significant (p>0.05). However, significant differences were noted in other post-operative parameters. The estimated blood loss was markedly higher in the placebo group, with an average of 421.72 ml (SD±28.24), compared to just 156.24 ml (SD±41.72) in the bisopropol group, and this difference was statistically significant (p<0.001). Postoperative hemoglobin levels were lower in the bisoprolol group (11.07 g/dl, SD±1.47) compared to the placebo group (12.88 g/dl, SD±0.75), with this difference also being statistically significant (p<0.001). Furthermore, the difference in pre and post-operative hemoglobin levels was significantly greater in bisoprolol group (2.03 g/dl, SD±0.4) than in the placebo group (0.3 g/dl, SD±0.49), with a p value of less than 0.001.

In the evaluation of hemodynamic parameters among the 50 participants undergoing elective ESS, differences were observed between the bisoprolol and placebo groups at various time points. For mean arterial pressure, both groups showed similar baseline values (bisoprolol group: 75.04 mmHg±4.5 vs. placebo group: 74.71 mmHg±6.7, p>0.05). This similarity persisted pre-operatively (90 minutes after premedication), intra-operatively, and post-operatively, with no statistically significant differences noted at any of these time points (p>0.05 for all). However, heart rate measurements revealed significant differences. At baseline, both groups had comparable heart rates (bisoprolol group: 98.02 bpm±4.5 vs. placebo group: 98.11 bpm±5.2, p>0.05). Notably, 90 minutes after premedication, the bisoprolol group maintained a higher heart rate (92.47 bpm±5.8) compared to the placebo group (63.41 bpm±4.8), with this difference being statistically significant (p<0.05). This trend continued intra-operatively (bisoprolol group: 93.77 bpm±5.8 vs. placebo group: 62.16 bpm±4.3, p<0.005) and post-operatively (bisoprolol group: 92.04 bpm±4.7 vs. placebo group: 61.82 bpm±3.5, p<0.005).

**Table 1: Distribution of baseline demographic characteristics among participants of both groups, (n=50).**

| Demographic information | Bisoprolol group, (n=25) (%) | Placebo group, (n=25) (%) | P value |
|---|---|---|---|
| **Age (In years)** | 27.29±6.51 | 29.82±8.14 | >0.05 |
| **Weight (kg)** | 58.17±2.82 | 60.07±3.14 | >0.05 |
| **Height (cm)** | 163.28±4.18 | 161.72±7.07 | >0.05 |
| **Pre-operative hemoglobin (g/dl)** | 13.10±1.07 | 13.18±1.24 | >0.05 |
| **Gender** | | | |
| Male | 13 (52) | 16 (64) | >0.05 |
| Female | 12 (48) | 9 (36) | |
| **ASA status** | | | |
| ASA I | 15 (60) | 14 (56) | >0.05 |
| ASA II | 10 (40) | 11 (43) | |

**Table 2: Post-operative findings among participants of both groups, (n=50).**

| Post-operative findings | Bisoprolol group, (n=25) | Placebo group, (n=25) | P value |
|---|---|---|---|
| **Duration of surgery (min)** | 142.18±17.19 | 130.72±15.42 | >0.05 |
| **Estimated blood loss (ml)** | 156.24±41.72 | 421.72±28.24 | <0.001 |
| **Postoperative hemoglobin (g/dl** | 11.07±1.47 | 12.88±0.75 | <0.001 |
| **Difference of pre and post-op Hb (g/dl)** | 2.03±0.4 | 0.3±0.49 | <0.001 |

**Table 3: Distribution of hemodynamic parameters at different time points among participants of both groups, (n=50).**

| Hemodynamic parameters | Bisoprolol group, (n=25) | Placebo group, (n=25) | P value |
|---|---|---|---|
| **Mean arterial pressure** | | | |
| Baseline | 75.04±4.5 | 74.71±6.7 | >0.05 |
| Pre-operative (90 min after premedication) | 74.82±3.4 | 68.24±5.9 | >0.05 |
| Intra-operative | 73.14±3.4 | 61.44±2.7 | >0.05 |
| Post-operative | 74.97±3.7 | 63.82±2.3 | >0.05 |
| **Heart rate** | | | |
| Baseline | 98.02±4.5 | 98.11±5.2 | >0.05 |
| Pre-operative (90 min after premedication) | 92.47±5.8 | 63.41±4.8 | <0.05 |
| Intra-operative | 93.77±5.8 | 62.16±4.3 | <0.005 |
| Post-operative | 92.04±4.7 | 61.82±3.5 | <0.005 |

**Table 4: Distribution of participants of both groups by Fromme-Boezaart bleeding scale, (n=50).**

| Gradings | Interpretation | Bisoprolol group, (n=25) (%) | Placebo group, (n=25) (%) | P value |
|---|---|---|---|---|
| **Grade 0** | No bleeding | 0 (0) | 0 (0) | <0.001 |
| **Grade 1** | Slight bleeding, no suctioning of blood required | 14 (56) | 0 (0) | |
| **Grade 2** | Slight bleeding, occasional suctioning required, bleeding does not threaten surgical field | 11 (44) | 10 (40) | |
| **Grade 3** | Slight bleeding, frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed | 0 (0) | 10 (40) | |
| **Grade 4** | Moderate bleeding frequent suctioning required. Bleeding threatens surgical field immediately after suction is removed | 0 (0) | 5 (20) | |
| **Grade 5** | Severe bleeding constant suctioning required. Bleeding appears faster than can be removed by suction. Surgical field threatened and surgery not possible | 0 (0) | 0 (0) | |

In assessing intraoperative bleeding using the Fromme-Boezaart scale among the 50 participants of the study, significant differences were observed between the bisoprolol and placebo groups. Notably, no participants in either group experienced grade 0 (no bleeding) or grade 5 (severe bleeding) conditions. However, in the bisoprolol group, a majority of participants (56%) were classified as grade 1, indicating slight bleeding without the need for suctioning, while none in the placebo group fell into this category. Additionally, 44% of the bisoprolol group experienced grade 2 bleeding, characterized by slight bleeding with occasional suctioning required but not threatening the surgical field, compared to 40% in the placebo group. In contrast, the placebo group had a higher incidence of more severe bleeding: 40% of participants in the placebo group were classified as grade 3, where slight bleeding required frequent suctioning and threatened the surgical field a few seconds after suction removal, and 20% were classified as grade 4, with moderate bleeding that threatened the surgical field immediately after suction removal. None of the participants in the bisoprolol group fell into these higher-grade categories. The differences in bleeding grades between the groups were statistically significant ($p<0.001$).

**Table 5: Distribution of participants of both groups by requirement of isoflurane, (n=50).**

| Variables | Bisoprolol group, (n=25) | Placebo group, (n=25) | P value |
|---|---|---|---|
| **Isoflurane (vol%)** | 0.7±0.32 | 1.5±0.55 | <0.001 |

In the evaluation of anesthetic requirements among the 50 participants undergoing elective ESS, significant differences were observed between the bisoprolol and placebo groups in terms of isoflurane usage. In the Bisoprolol group (n=25), the mean requirement for isoflurane was 0.7±0.32 vol%, while the placebo group (n=25) had a higher mean of 1.5±0.55 vol%, with a significant $p<0.001$ indicating a statistical difference.

## DISCUSSION

In our study investigating the effects of pre-operative oral bisoprolol on ESS, we observed several intriguing outcomes, which, when juxtaposed with existing literature, offer a multifaceted view of bisoprolol's role in surgical settings. Starting with demographic and baseline characteristics, our findings showed no significant differences between the bisoprolol and placebo groups across various parameters such as age, weight, height, pre-operative hemoglobin levels, gender distribution, and ASA status. This lack of disparity is crucial, as it establishes a level playing field, allowing us to attribute observed differences in surgical outcomes directly to the intervention rather than to underlying demographic variances. This approach echoes the principles outlined in studies emphasizing the importance of participant homogeneity in clinical trials.[13,14] The duration of surgery in our study showed no significant difference between the bisoprolol and placebo groups, indicating that pre-operative bisoprolol administration does not affect length of ESS, as was observed in other studies as well.[10,15] Interestingly, estimated blood loss was significantly lower in the bisoprolol group compared to the placebo group. This finding supports the hypothesis that beta-blockers like bisoprolol can effectively reduce intraoperative bleeding, likely due to their stabilizing effects on blood pressure. The reduced blood loss in the bisoprolol group is a critical observation supported by multiple other studies, as it suggests that pre-operative administration of bisoprolol may improve surgical conditions by minimizing bleeding.[10,16,17] This outcome is particularly relevant in ESS, where clear visibility of the surgical field is essential for the success of the procedure and reduction of postoperative complications. Significant decrease in blood loss in the bisoprolol group highlights the potential of bisoprolol as a valuable pre-operative intervention to enhance surgical outcomes in ESS. In

assessing hemodynamic parameters, our study observed that mean arterial pressure (MAP) remained stable throughout the surgery in the bisoprolol group. Specifically, the MAP was 75.04 mmHg±4.5 at baseline and 73.14 mmHg±3.4 intra-operatively in the bisoprolol group, demonstrating minimal fluctuation. This stability in MAP is consistent with existing literature highlighting effectiveness of beta blockers in maintaining intra-op hemodynamic stability.[18] Notably, heart rate differences were significant, especially post-medication and intraoperatively. The bisoprolol group exhibited a higher heart rate, averaging 92.47 bpm±5.8 post-medication and 93.77 bpm±5.8 intra-operatively, compared to the placebo group's 63.41 bpm±4.8 and 62.16 bpm±4.3, respectively. These findings indicate that while bisoprolol effectively stabilizes blood pressure, it does not lead to excessive suppression of heart rate.[15,19] This aspect is crucial, as it suggests bisoprolol's capability to achieve hemodynamic stability without adversely impacting cardiac output, a critical balance in surgical settings. In our study, the application of the Fromme-Boezaart scale for intraoperative bleeding assessment showed marked reduction in bleeding severity in the bisoprolol group. Specifically, 56% of participants in the bisoprolol group experienced grade 1 bleeding, characterized as slight bleeding without the need for suctioning. In contrast, none in the placebo group were in this category. Furthermore, 44% of the bisoprolol group had grade 2 bleeding, which involves slight bleeding with occasional suctioning required, but not threatening the surgical field. This is compared to 40% in the placebo group. Notably, none of the participants in the bisoprolol group experienced the more severe grade 3 or grade 4 bleeding, which were observed in 40% and 20% of placebo group, respectively. These findings align with other research indicating that preoperative beta-blocker administration can lead to reduced intraoperative bleeding.[20-22] Significantly lower incidence of higher-grade bleeding in the bisoprolol group highlights its effectiveness in enhancing surgical field visibility by minimizing bleeding, a key factor in success of ESS. Evaluation of anesthetic requirements revealed significant differences between bisoprolol and placebo groups, particularly in usage of isoflurane. Bisoprolol group (n=25) required a notably lower mean volume of isoflurane, averaging 0.7±0.32 vol%, compared to the placebo group (n=25), which required a higher mean volume of 1.5±0.55 vol%. This difference was statistically significant, with $p<0.001$. These findings suggest that bisoprolol may contribute to reduced anesthetic requirements, possibly due to its effects on stabilizing hemodynamics.[19] This aspect of bisoprolol's interaction with anesthetic agents, particularly in context of elective ESS, presents an intriguing area for further research and understanding.

### *Limitations*

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

## CONCLUSION

The present study underscores the efficacy of pre-operative oral bisoprolol in ESS. We found no significant differences in demographic and baseline characteristics between the bisoprolol and placebo groups, ensuring a reliable comparison. Notably, bisoprolol did not prolong the duration of surgery, aligning with existing literature. A key finding was the significantly lower estimated blood loss in the bisoprolol group, suggesting that bisoprolol effectively reduces intraoperative bleeding, likely due to its blood pressure stabilizing effects. This is particularly beneficial in ESS, where clear visibility is crucial. Hemodynamically, bisoprolol maintained stable mean arterial pressure throughout the surgery without significantly suppressing heart rate. This indicates its potential to ensure hemodynamic stability while preserving cardiac output. The Fromme-Boezaart scale assessment showed lower-grade bleeding in the bisoprolol group, aligning with studies that report reduced bleeding with preoperative beta-blocker use. This enhances surgical field visibility, crucial for ESS success. Additionally, our study observed lower anesthetic requirements (inhalation-isoflurane) in the bisoprolol group, hinting at bisoprolol's role in reducing anesthetic needs, possibly due to hemodynamic stabilization.

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