



Metoprolol significantly improves visual clarity and hemodynamic parameters during functional endoscopic sinus surgery

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Abstract

Keywords: Metoprolol; endoscopic sinus surgery; hemodynamic.

Background and objectives: The success of functional endoscopic sinus surgery (FESS) depends on visual clarity of the surgical field, which is under studied. Controlled hypotension has many advantages for FESS including reduction in blood loss and improved quality of the surgical field. This study determined whether the use of β -blockers as a premedication could improve the operative field in FESS. **Methods:** 60 patients aged from 18-50 years, undergoing septoplasty, and FESS were included in this prospective, randomized, double-blinded, placebo-controlled study. Patients were randomly assigned to receive either metoprolol (100mg, group 1) or a placebo (a vitamin tablet, group 2) 60 minutes before surgery.

Results: The average blood loss and surgery duration were not significantly higher in the placebo group. The surgical field was graded using Fromme-Boezaart scale and it was significantly clearer ($p < 0.001$) in metoprolol group. The mean arterial blood pressure was significantly lower in the metoprolol group after 30 minutes of induction till the end of surgery ($p < 0.001$). The heart rate was also significantly lower ($p < 0.001$) in those who received metoprolol from before induction of anesthesia up to the end of surgery.

Conclusion: metoprolol significantly improves visual clarity and hemodynamics during FESS. Conclusion: metoprolol significantly improves visual clarity and hemodynamics during FESS.

INTRODUCTION:

Functional endoscopic sinus surgery (FESS) is the most exciting recent surgical treatment of sinusitis and nasal polyps. However, the success of this procedure depends on visual clarity of the surgical field through the endoscope^{1,2}. The sinonasal mucosa is very vascular and poor visualization is due to excessive bleeding that leads to

complications associated with this procedure³.

Controlled hypotension is defined as a reduction in the mean arterial blood pressure to 50–60 mmHg in normotensive subject⁴. Controlled hypotension has many advantages for FESS including reduction in blood loss and improved quality of the surgical field. Multiple agents have been used to achieve controlled hypotension e.g.,

magnesium sulfate, vasodilators (e.g. sodium nitroprusside), nitroglycerine, high doses of potent inhaled anesthetics, and beta (β) adrenergic antagonist⁵⁻⁷. Studies show that using β -blockers before surgery reduces long term cardiovascular complications and intraoperative bleeding⁸⁻⁹. It is believed that β -blockers are responsible for improvement of the cardiovascular condition and patients' hemodynamic stability via changes in stress related physiological response¹⁰. Data regarding this issue are limited in the literature with few studies¹¹⁻¹⁴ that examined the usage of β -blockers to control blood pressure and improve hemodynamic parameters and visual clarity during endoscopic sinus surgery. The aim of this study was to determine whether the routine use of β -blockers as a premedication could improve the operative field in ESS. We show that metoprolol significantly improves visual clarity and hemodynamic parameters during FESS.

Material and Methods

Inclusion and Exclusion Criteria

60 patients including both male and female patients (physical status I and II as described by the American Association of Anesthesiologists; ASA), aged from 18-50 years, undergoing septoplasty, and functional endoscopic sinus surgery were included in this prospective, randomized, double-blinded, placebo-controlled study. All surgical procedures were done by the same surgeon. The study did not include patients with pregnancy, cardiac failure, chronic hypotension, patients with asthma, chronic obstructive airway disease, and emphysema, patients with blood pathology, coagulation disorder, anemia (Hb < 10 g/dL), those on medications affecting their coagulation

system, and patients with kidney or liver dysfunctions.

Study Design

The study was conducted at Minia University Hospital, during the period from July 2017 to December 2017 after obtaining an informed consent from patients and approval of the local ethical committee. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Sample size calculation was based on keeping the mean arterial pressure (MAP) between 50 and 60 mmHg. The calculation determined that 60 patients (30 in each group) would be required for a study with a power of 1 and an alpha of 0.05 set for significance. Before surgery, the patients' blood cell count, urea, serum creatinine, and prothrombin time (PT) were examined.

Patients were randomly assigned through computer-generated numbers to receive either metoprolol (Betaloc tablets 100mg, AstraZeneca, EGYPT) (group 1) or a placebo tablet (a vitamin tablet that was identical to metoprolol in appearance) (group 2) 60 minutes before surgery.

Anesthesia Regimen

All patients were kept nil per oral the night before surgery and received oral alprazolam (0.25–0.5 mg) in the night before surgery and 2 h prior to surgery. Standard monitors including pulse oximeter, noninvasive blood pressure, 5 lead electrocardiogram (ECG), end tidal CO₂ (EtCO₂) and temperature probes were attached, and baseline values recorded (Philips monitors, Germany). All patients received 10 to 15 mL/kg normal saline (0.9%) infusion. Patients were first pre-medicated with an infusion of midazolam 0.05 mg/kg, fentanyl 1 μ g/kg and lidocaine 1 mg/kg. All the

patients were pre-oxygenated with 100% oxygen for 3 minutes. Induction of anesthesia was achieved with an infusion of propofol 2 mg/kg, atracurium 0.5 mg/kg and after 3 to 5 minutes, patients were intubated with the appropriate tube size. Anesthesia was maintained with isoflurane 1.5%, atracurium with incremental dose 0.15 mg/kg every 30 minutes and 50 µg of fentanyl per hour. Ventilation was maintained to end-expiratory CO₂ tension at 35 ± 2 mm Hg (Dräger medical AG/COKGaA; model 23542, Germany).

The hemodynamic endpoint of anesthetic management was the maintenance of mean blood pressure (MBP) at 50-60 mmHg for producing bloodless surgical field. To eliminate observer bias, the operating surgeon and the anesthetist were blinded to whether the patient had been given a beta blocker. Patients were placed in a 10° reverse Trendelenburg position to improve venous drainage. Patients in both groups received topical application of mixture of 4 ml lignocaine 2% and 1 ml of epinephrine 1 in 1,000 on a well wrung out cotton pledges to the nasal mucous membrane, which was kept in situ for 10–15 min.

After removal of pledges, lateral nasal wall was infiltrated with 0.5–1 ml of 1% lignocaine with epinephrine 1 in 100,000–200,000 dilution before commencement of surgery.

At the end of surgery, administration of anaesthetic agent was discontinued and reversal of neuromuscular blockage was done using atropine sulfate in a dose of 0.02 mg/kg IV injection plus neostigmine (0.05mg/kg) IV injection. Endotracheal extubation was done after the return of adequate muscle tone, power, protective reflex (cough) and

when the breathing pattern of patient was smooth. Patients were observed every 15 minutes for two hours for SPO₂, pulse rate, blood pressure, sedation score, visual analogue scale (pain), nausea and vomiting, complications and adverse effects; if any; were recorded.

Measured parameters:

(1) Hemodynamics (Heart rate and mean arterial pressures were recorded immediately prior to induction of anesthesia and subsequently every 3 min for 15 min and then every 15 min till the termination of anesthesia).

(2) amount of blood loss. Total blood loss during surgery was calculated from the fluid volume of the suction canister. The volume of irrigating fluid was subtracted from the total volume of fluid collected in the suction bottle. A fully soaked cotton strip was estimated to contain 5 ml of blood and partially soaked one to contain 2-3 ml of blood.

(3) Surgical time was recorded from the first injection of regional anesthetic to the end of surgery.

(4) Surgeon's assessment of operative field condition, the quality scale proposed by Fromme-Boezaart surgical field grading¹⁵⁻¹⁶ as follows:

Grade 0: No bleeding.

Grade 1: Slight bleeding - no blood suctioning required.

Grade 2: Slight bleeding - occasional suctioning required.

Grade 3: Slight bleeding - frequent suctioning required. Operative field is visible for some seconds after evacuation.

Grade 4: Moderate bleeding - frequent suctioning required. Operative field is only visible immediately after evacuation.

Grade 5: Severe bleeding - constant suctioning required. Bleeding appears faster than can be removed by suction. Surgery is hardly possible, and sometimes impossible.

Statistical analysis:

Analyses were done for parametric quantitative data between the two groups using independent sample student -t- test and for non- parametric quantitative data using Mann Whitney test. Analyses were done for qualitative data between the two groups using Fisher's exact test.

minutes of induction up to end of surgery [Table 4]. The heart rate was significantly lower in those who received metoprolol before the operative procedures [Table 5].

Results

Sixty, ASA physical status I or II patients, scheduled for FESS were consented for the study and randomly allocated into either metoprolol group (group 1) or placebo group (group 2). The age, gender, body weight and ASA physical status were comparable between the two groups [Table 1].

Blood loss and surgical field: The average blood loss was significantly more in the placebo group as compared to that in the metoprolol group. The duration of surgery was slightly shorter in the metoprolol group. However, the difference was not statistically significant Table (2): The duration of surgery and amount of blood loss.

The surgical field was graded by the surgeon using Fromme-Boezaart grading scale and there was a statistically significant difference between those who received metoprolol as compared with those in the placebo group [Table 3].

Hemodynamic parameters: Regarding mean arterial blood pressure (MAP), metoprolol group showed no statistically significant difference when compared to control group at basal measurement up to 30 min after induction of anesthesia. MAP was significantly lower in group 1 as compared to group 2 from after 30

Table (1): Demographic and clinical data of the study groups.

Variables	Metoprolol group n=30 (%)	Placebo group n=30 (%)	P value
Age (years): Range. Mean \pm SD	(18-50) 31.6 \pm 6.91	(18-50) 33.8 \pm 7.2	0.722
Sex: Male. Female.	16(53.3) 14 (46.7)	14 (46.7) 16 (53.3)	0.416
ASA (I/II):	13(43.3) 17 (56.7)	14(46.7) 16 (53.3)	0.174
Weight (kg): Range. Mean \pm SD	(31-99) 70 \pm 15.7	(52-103) 73.9 \pm 11.8	0.27

Data are expressed as median (range) and mean \pm standard deviation

Table (2): The duration of surgery and amount of blood loss

Variables	Metoprolol group (n=30)	Placebo group (n=30)	P value
Duration of surgery (min) Range. Mean \pm SD	70-124 88 \pm 15.3	68-118 90 \pm 12.9	0.622
Amount of blood loss (ml) Range. Mean \pm SD	90-200 100 \pm 20	100-190 125.6 \pm 25.9	0.74

Data are expressed as median (range) and mean \pm standard deviation

Table (3): The surgical field grading by the surgeon, according to Fromme-Boezaart grading scale

Fromme-Boezaart grades	Metoprolol group n=30 (%)	Placebo group n=30 (%)	P value
0	0 (0)	0 (0)	0.0001
1	17(56.7)	0 (0)	
2	13 (43.3)	12 (40)	
3	0 (0)	10 (33.3)	
4	0 (0)	8 (26.7)	
5	0 (0)	0 (0)	

Data are expressed as numbers

Table (4): MAP changes in the study groups (mmHg).

Time	Metoprolol group n=30; Mean ± SD	Placebo group n=30; Mean ± SD	P value
Basal measurement	70.65±6.67	72±6.49	0.867
3 min post-induction	69.85±6.69	73.8±8.06	0.657
6 min	67.45±8.31	65.85±6.17	0.494
9 min	67.1±8.77	67.45±9.17	0.903
12 min	66.35±8.22	64.15±6.76	0.187
15 min	64.65±6.61	68.75±9.38	0.120
30 min	65±8.22	66.95±5.55	0.639
45min	57.3±5.97	67.25±7.27	0.0001
60 min	55.3±7.26	68.25±6.98	0.0001
75min	55.45±9.08	65.5±6.26	0.0001
90 min	57.4±7.26	67.25±7.27	0.0001
105 min	55.15±4.08	68.25±6.98	0.0001
120min	58.15±1.18	67.45±9.17	0.0001

Data are expressed as mean ± standard deviation

Table (5): Heart rate changes in the study groups (beat/min).

Time	Metoprolol group n=30; Mean ± SD	Placebo group n=30; Mean ± SD	P value
Basal measurement	60.65±6.67	72±6.49	0.0001
3 min post-induction	62.85±6.69	73.8±8.06	0.0001
6 min:	65.45±8.31	70.85±6.17	0.0001
9 min:	67.1±8.77	77.45±9.17	0.0001
12 min:	66.35±8.22	79.15±6.76	0.0001
15 min:	64.65±6.61	78.75±9.38	0.0001
30 min:	65±8.22	76.95±5.55	0.0001
45min:	63.3±5.97	77.25±7.27	0.0001
60 min:	62.3±7.26	78.25±6.98	0.0001
75 min:	61.45±9.08	75.5±6.26	0.0001
90 min	62.4±7.26	77.25±7.27	0.0001
105 min	63.15±4.08	78.25±6.98	0.0001
120min	66.15±1.18	77.45±9.17	0.0001

Data are expressed as mean ± standard deviation

Discussion

In this study, using a pre- and intra-operative medication regimen, we show that metoprolol significantly improves visual clarity and hemodynamic parameters during FESS. Induced hypotension can be achieved by multiple pharmacological agents. Among these agents, we choose to add metoprolol 100 mg tablet to 30 patients included in the study (group 1) compared to the other half of patients receiving a placebo (group 2).

During FESS, minor bleeding can markedly compromise an already restricted surgical field, which could lead to complications as injury to the brain and eye globe and interfere with the completion of successful surgical procedure¹⁴. Induced hypotension decreases intraoperative bleeding and improves visibility of the operative field. Multiple factors can influence the surgical field, including physical status of the patient, concomitant disease such as bleeding disorders, obesity and systolic hypertension¹⁷. Injected vasoconstrictors can lead serious side effects. After injection of lignocaine with adrenaline, plasma levels of adrenaline reach a peak value that is highly variable and not related to the amount injected into the nasal mucosa¹⁸. Also, with topical anesthesia with cocaine, idiosyncratic absorption can occur. Toxicity may result in central nervous system stimulation or depression and respiratory failure¹⁹.

Induced hypotension achieved by using only inhalation or intravenous anesthetic agents requires the application of higher doses, which causes recovery time to be prolonged. So, in order to achieve the desired level of hypotension in addition to an anesthetic agent, additional hypotensive drugs are the

preferred method²⁰. Our data show that there was no statistical significance between the metoprolol group and placebo group as regard to the surgical operating time and the amount of surgical bleeding. These findings are in accordance with a previous study¹⁴ which investigated eighty patients undergoing endoscopic sinus surgery to receive either 30 mg metoprolol (group 1), or a placebo tablet (group 2) 30 minutes before surgery.

Quality of surgical field was compared in both groups using Fromme-Boezaart grades. In group 1, 17 patients had grade 1 surgical field and 13 patients had grade 2 surgical field. In group 2, 12 patients had grade 2 surgical field, 10 patients had grade 3 and 8 patients had grade 4 surgical field. So, group 1 (metoprolol) patients had better quality of surgical field with statistical significance as compared to group 2 (placebo). Our data agree with the findings of a randomized controlled trial performed by Rahimzadeh and colleagues²¹. Patients entering their study were divided into four groups: 50 mg metoprolol at night before the operation, 50 mg metoprolol on the day of operation, 50 mg metoprolol at night and on the day of the operation, or a placebo. Their results showed that there is a statistical significance between the amount of surgical bleeding and receiving metoprolol ($P = 0.029$).

HR and MAP were significantly lower in the metoprolol group. These data alone would suggest that the surgical field was likely to be better in the metoprolol group. Another prospective, randomized, double-blinded, placebo-controlled trial performed by others¹⁴ is in agreement with our results. Patients were randomly assigned to receive either 100 mg Metoprolol (group 1) or a placebo tablet (group 2) 30 minutes

before surgery. Their 2-h data showed statistical significance difference between metoprolol group and the placebo group as regard HR and MAP. In conclusion, our data show that metoprolol significantly improves visual clarity and hemodynamics during FESS.

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