

## Comparative Study of Oral Clonidine Vs Oral Metoprolol for Induced Hypotensive Anaesthesia in Functional Endoscopic Sinus Surgery

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### Abstract

**Background:** Over the last few years, considerable interest in endoscopic surgery of the paranasal sinuses has been expressed, which is a minimally invasive technique. Complications related to this technique often arises due to excessive bleeding during surgery. This study compares oral Clonidine (centrally acting  $\alpha_2$  agonist) and oral Metoprolol (cardioselective beta blocker) used as premedication in functional endoscopic sinus surgery to evaluate improvement in operative field.

**Method:** This prospective, randomized, double blind study included 50 ASA Grade I and II patients, aged between 18-60 years, who were equally divided into two groups as Group I (received oral Metoprolol 50 mg) and Group II (received oral Clonidine 3mcg/kg ) 90 min prior to surgery. Pulse Rate and blood pressure were recorded at different time intervals including before starting the drug, before pre medication, after intubation, every 5 minutes thereafter for 30 minutes, every 10 minutes thereafter till the end of surgery and after extubation. Assessment of surgical field was done by using Fromme et al scale adapted by Boezaart et al.

**Results:** Metoprolol was more effective in controlling heart rate intra operatively than Clonidine, whereas Clonidine was more effective than Metoprolol in maintaining better surgical field that too in lower doses as compared to the one used in previous studies. Both the drugs were effective in preventing the haemodynamic response associated laryngoscopy, intubation and surgical stimulus.

**Conclusion:** Clonidine is more effective than Metoprolol in reducing intra operative bleeding and maintaining better surgical field even in low doses of 3 mcg/ kg.

**Keywords:** Clonidine, Metoprolol, Paranasal Sinus, Endoscopic Surgery.

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### Introduction

Functional Endoscopic Sinus Surgery (FESS) is gaining popularity over past few decades as it is helpful in restoring the drainage and aeration of the paranasal

sinuses, while maintaining the natural mucociliary clearance mechanism and seeking to preserve the normal anatomical structures. However, there are some

limiting factors in this surgery and mostly they are due to excessive blood loss because of mucosa which is rich in blood vessels. [1] Serious complications such as bleeding, blindness, cerebrospinal fluid leak [2], orbit cellulitis, rhinoliquoral fistula, lesions of optic nerve of dura mater and meningitis which occur due to impaired visibility due to excessive bleeding and can be avoided by using either local anaesthesia with vasoconstrictors or general anaesthesia associated with controlled hypotension.

General anaesthesia with controlled hypotension is relatively safe and viable option for endoscopic sinus surgery as compared to local anaesthesia, due to less complications. [3] Many agents have been tried in the past for hypotensive anaesthesia such as beta blockers, magnesium sulphate, centrally acting antihypertensive and various inhalational agents. Clonidine, a centrally acting  $\alpha$ -2 agonist, has antihypertensive property by decreasing sympathetic outflow. It also decreases post operative analgesic consumption [4], postoperative nausea, vomiting and shivering [5]. Metoprolol, on the other hand, is a cardio selective beta blocker having antihypertensive property and it also decreases heart rate. This study compared the effects of oral Clonidine and oral Metoprolol used as premedication in FESS in order to see improvement in operative field by creating induced hypotension so as to minimize the complications of endoscopic sinus surgery due to excessive bleeding.

### Material and Method

This prospective, randomized double blind study was carried out in the Department of Anaesthesia, TNMC & B.Y.L. Nair Ch Hospital for a period of 1 year after obtaining approval from the institutional ethics committee. The study included total 50 patients (25 patients in each group) based on following inclusion and exclusion criteria:

### Inclusion criteria:

- Age Group 18-60 yrs
- ASA Grade I & II

### Exclusion criteria:

- ASA Grade III & IV
- Hypertensive patients on/off medications
- Patients on Cardiac drugs
- Heart Blocks/other ECG Changes
- Asthmatics
- Baseline pulse <55/systolic BP <100mmHg
- H/o Bleeding disorder
- Consent not given

All the study patients were equally distributed into one of the following two study groups:

**Group I:** Patients receiving Oral Metoprolol

**Group II:** Patients receiving Oral Clonidine

On the day of surgery, preoperative fasting was confirmed. 90 minutes before surgery, 50mg Oral Metoprolol (Group I) or 3 $\mu$ g/kg Oral Clonidine (rounded to 100 $\mu$ g/150 $\mu$ g) (Group II) was given if Baseline pulse was more than 55/min and systolic BP was greater than 100 mmHg. After taking the patient into the operation theatre (OT), BP (NIBP), Cardioscope, and Pulse oximeter were attached. Peripheral line was taken and IV fluid (Ringer lactate) was started. Pre medications included IV Glycopyrrolate (0.004mg/kg), IV Ranitidine (not > 50 mg), IV metoclopramide (10 mg), IV Midazolam (0.03mg/kg) and IV fentanyl (2 $\mu$ g/kg). Preoxygenation with 100% O<sub>2</sub> for 5 min was done. 5 min after premedication, the patients were induced with intravenous (i.v.) Propofol 2mg/kg (increments of 10mg if required). i.v. succinylcholine 2mg/kg was given to facilitate intubation. After ventilating the patient with O<sub>2</sub> under mask, tracheal intubation with cuffed tube of adequate size was done followed by auscultation for confirming tracheal placement by bilateral equal air entry and cuff inflation. Patients were maintained on

O<sub>2</sub> (50%)+ N<sub>2</sub>O (50%)+ i.v. Propofol 6mg/kg/hr infusion + i.v. Vecuronium (0.1mg/kg loading dose, 1mg top ups thereafter) with controlled ventilation with Modified Magills Circuit and NRV. Heart Rate and blood pressure (systolic blood pressure, diastolic blood pressure and mean arterial pressure) were recorded at different time intervals including before giving study drug (Metoprolol or Clonidine), before premedication, after intubation, every 5 minutes thereafter for 30 minutes, every 10 minutes thereafter till end of surgery and after extubation. Assessment of surgical field was done by using Fromme et al scale adapted by Boezaart et al as follows:

- 0- No bleeding
- 1. Slight bleeding; no suctioning of blood required
- 2. Slight bleeding; occasional suctioning required. Surgical field not threatened.
- 3. Slight bleeding; frequent suctioning required. Bleeding threatened surgical field a few seconds after suction was removed.

- 4. Moderate bleeding; frequent suctioning required. Bleeding threatened surgical field directly after suction was removed.
- 5. Severe bleeding; constant suctioning required

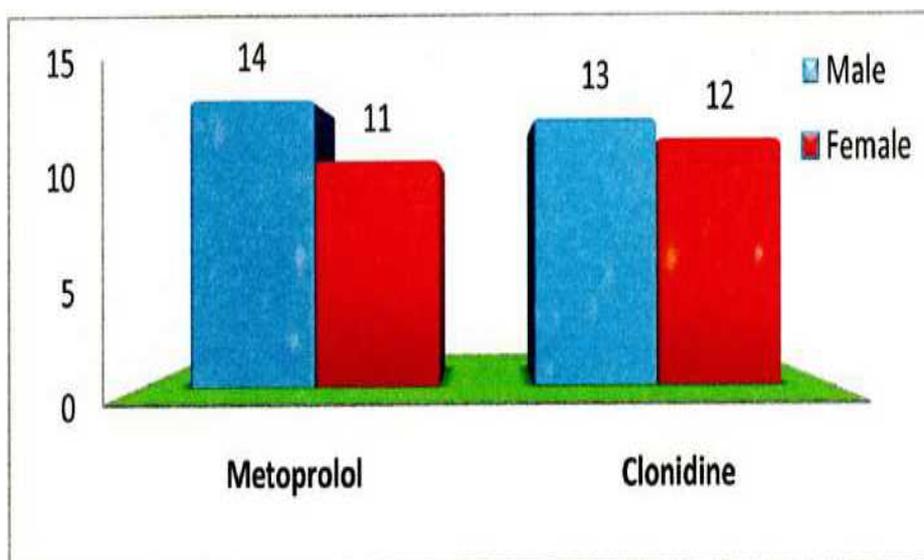
Patients were reversed with i.v. atropine 0.02mg/kg + i.v. neostigmine 0.05mg/kg and extubated after commands, adequate tone, power, respiration, SpO<sub>2</sub>. Patients were shifted to post-operative recovery room for observation. Postoperative analgesia if required was given with intramuscular Diclofenac 75 mg.

**Results**

The mean age of the study patients in Metoprolol group was 25.84±5.01 years and in Clonidine group was 26.20±5.40 years. Unpaired t-test showed no significant difference between the groups in terms of age and weight of the patients.(Table 1) Fischer's test showed no significant difference in gender distribution between the two groups. (Figure 1)

**Table 1: Age and weight distribution of the patients in both groups**

	Metoprolol		Clonidine		p value	Significance
	Mean	SD	Mean	SD		
<b>Age</b>	25.84	5.014	26.20	5.401	0.5259	NS
<b>Weight</b>	57.60	6.144	57.96	7.845	0.8574	NS



**Figure 1: Graph showing gender distribution between the two study groups**

Pre-operative haemodynamic parameters between both the groups were noted and compared by unpaired t test. No significant difference was found between both the groups. At premedication all parameters were tabulated and compared with unpaired

t test. There was significant difference found in heart rate between both the groups with p value of 0.01. There was also statistical difference found in DBP between the groups but it was not clinically significant. (Table 2)

**Table 2: Mean Premedication Haemodynamic Variables between the Groups**

Mean	Group	Mean	SD	Unpaired t test	
				P value	Significance
Pulse	Metoprolol	72.12	9.993	0.010	SIG
	Clonidine	80.68	12.442		
SBP	Metoprolol	112.40	10.665	0.481	NS
	Clonidine	110.40	9.179		
DBP	Metoprolol	72.40	5.568	0.038	SIG
	Clonidine	75.48	4.602		
MAP	Metoprolol	85.73	6.424	0.415	NS
	Clonidine	87.12	5.455		

Post induction parameters comparison was done using unpaired t test. Only heart rate showed significant difference in Metoprolol group having lower heart rate than Clonidine group with p value of 0.005.(Table 3)

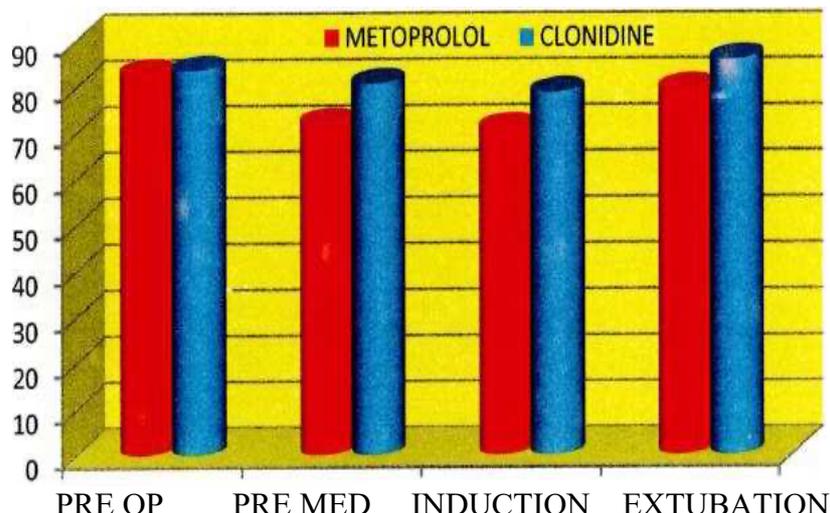
**Table 3: Mean Post Induction Haemodynamic Variables between the Groups**

Mean	Group	Mean	SD	Unpaired t test	
				P value	Significance
Pulse	1 Metoprolol	70.88	9.315	0.005	SIG
	2 Clonidine	78.72	9.515		
SBP	1 Metoprolol	113.40	10.316	0.324	NS
	2 Clonidine	110.60	9.535		
DBP	1 Metoprolol	73.88	3.993	0.294	NS
	2 Clonidine	75.08	4.010		
MAP	1 Metoprolol	85.73	4.903	0.924	NS
	2 Clonidine	86.92	4.941		

Unpaired t test showed no significant difference between the two groups in terms of post extubation haemodynamic parameters.

Unpaired t-test showed a significant decrease in premedication and post

induction values of pulse rate in Metoprolol group, while Clonidine group showed lower values but they were not statistically significant. Post extubation values showed no significant difference in both group. (Figure 2).



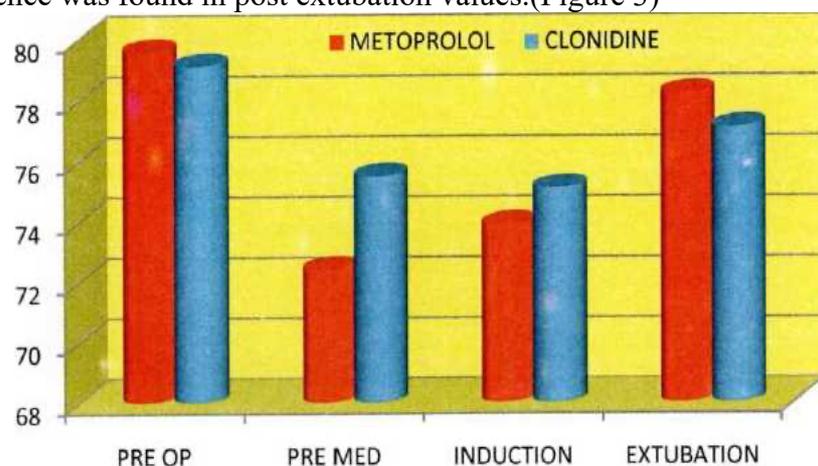
**Figure 2: Comparison of Pulse rate between study group**

There was significant decrease in premedication and post induction values of systolic blood pressure (SBP) in Metoprolol group but no such difference was found in post extubation values. In Clonidine group, significant decrease in premedication, post induction and post extubation values were found.(Table 4)

**Table 4: Comparison of SBP between study group**

Group	Duration			
	Basal	Premed	Ind	Ext
<b>Metoprolol</b>	122.3±	112.4±	113.4±	119.3±
	8.994	10.665 <b>SIG</b>	10.316 <b>SIG</b>	12.02 <b>NS</b>
<b>Clonidine</b>	119.16±	110.4±	110.6±	114.2±
	8.285	9.179 <b>SIG</b>	9.535 <b>SIG</b>	8.607 <b>SIG</b>

There was significant decrease in premedication and post induction values of mean perioperative diastolic blood pressure (DBP) in both Metoprolol and Clonidine group, while no such difference was found in post extubation values.(Figure 3)



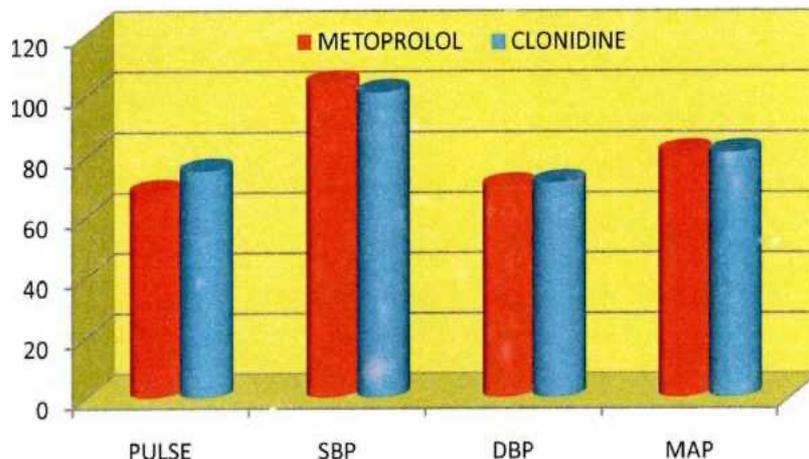
**Figure 3: Comparison of DBP between study group**

There was a significant decrease in premedication and post induction values of mean perioperative MAP in both Metoprolol and Clonidine group, while no such difference was found in post extubation values. (Table 5)

**Table 5: MAP Comparison of MAP between the groups**

Group	Duration			
	Basal	Premed	Ind	Ext
<b>Metoprolol</b>	93.84±5.242	85.73±6.424 SIG	87.05±4.903 SIG	91.84±6.872 NS
<b>Clonidine</b>	92.44±6.266	87.12±5.455 SIG	86.92±4.941 SIG	89.44±4.976 NS

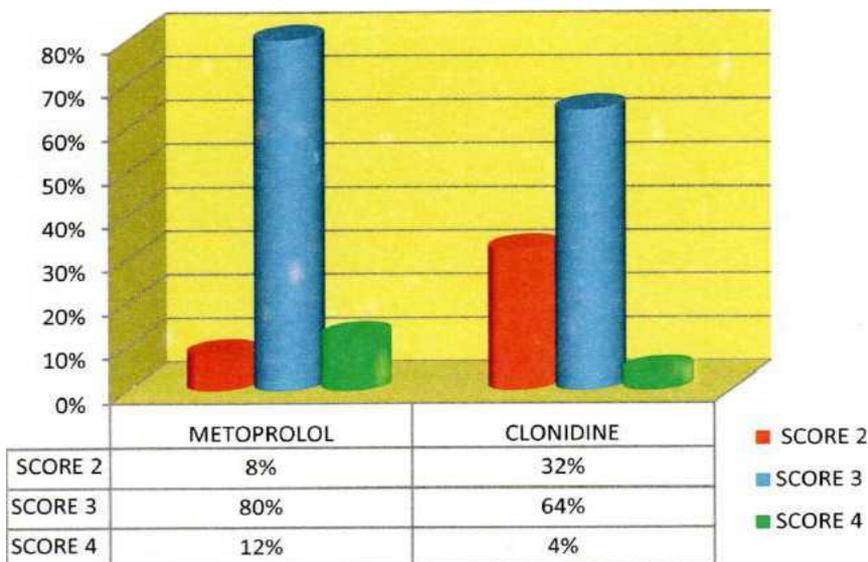
Mean haemodynamic variables during surgery were compared and it was observed that there was a statistically significant difference in the mean pulse and SBP between the groups. (Figure 4)



**Figure 4: Mean Haemodynamic Variables during surgery**

Surgical field score was noted intra operatively and compared with unpaired t test with p value of 0.0282 and found that Clonidine group pre-luce better surgical field as compared to Metoprolol. Clonidine

group had surgical score of 2 in 8 patients as compared to just 2 patients in Metoprolol group, while Clonidine group had score of 4 in only one patient as compared to 3 in Metoprolol group. (Figure 5)



**Figure 5: Percentagewise Distribution of Surgical Field**

**Discussion**

Functional endoscopic sinus surgery (FESS) is minimally invasive technique in which sinus air cells and sinus ostia are

opened under direct visualization. The term “functional” was introduced to distinguish this type of endoscopic surgery from non-endoscopic “conventional” procedures. [6,7] Goal of FESS is to return the mucociliary drainage of the sinuses to

normal function. [6,8] FESS, like all minimally invasive surgery, is designed to combine an excellent outcome with minimal patient discomfort. The main advantage of FESS compared with traditional techniques is that it is less invasive, resulting in minimal postoperative discomfort. Scars and damage to the nerve supply of the teeth are also avoided. The use of the endoscope permits a better view of the surgical field, and this is probably responsible for the lower rate of complications. However, complications often arise on account of excessive bleeding during surgery. [9] This study compared 25 ASA Grade I and II patients, aged between 18-60 years in each group, wherein Group I received oral Metoprolol 50 mg and Group II received oral Clonidine 3mcg/kg, 90 min prior to surgery.

The results of this study showed that the groups were similar in terms of demographic variables like age, gender and weight. The heart rate and blood pressure at the time of study drug administration were comparable between both the study groups.

#### **Pulse Rate:**

In Metoprolol group, lowest heart rate was 60/min and highest heart rate was 110/min, while in Clonidine group it was 70/min and 110/min respectively. There was no significant difference in heart rate between the two groups pre-operatively. There was significant decrease ( $p=0.009$ ) in heart rate after premedication as compared to pre operative values in the Metoprolol group. In Clonidine group, the mean heart rate was  $80.68 \pm 12.442$  which was lower than pre operative value but was not statistically significant. Comparison of pulse rate between both the groups by unpaired t test showed that there was significant ( $p=0.01$ ) decrease in heart rate at pre medication in Metoprolol group as compared to pre operative value and Clonidine group after premedication.

Intra group comparison showed that there

was statistically significant decrease in heart rate after induction in Metoprolol group as compared to pre operative value, but in Clonidine group there was no significant decrease as compared to pre operative values ( $p=0.0891$ ). Intergroup comparison revealed that Metoprolol showed significant decrease in heart rate as compared to Clonidine group ( $p=0.005$ ). Nishikawa et al [10] found that there was no statistical decrease in heart rate after intubation in patient who received Clonidine 5mcg/kg, which is in accordance with the our results. There was significant decrease in pulse rate in both groups post intubation and intra operatively which is in contrast to previous study by Nishikawa et al [10] and Laurito CE et al [11] who observed an increase in heart rate post intubation, but not significantly after oral Clonidine pre medication 90 min prior to surgery. However, our results are correlated with that of Nair S et al [12] who found significant decrease in overall mean heart rate in Metoprolol group as compared to placebo. This suggested that Metoprolol was much better in controlling heart rate intra operatively when compared with Clonidine.

#### **Blood Pressure:**

SBP, DBP and MAP before drug administration were comparable between the two study groups. Intragroup comparison after premedication showed that there was significant decrease in the parameters as compared to pre operative values in both the groups. There was no significant difference in the SBP, DBP and MAP between the two study groups after premedication. Post-induction, these values increased, but were not statistically significant from pre medication values. Our results were similar to Jakobsen CJ et al [13] who showed that Metoprolol 100 mg 90 min prior to surgery decreases heart rate and MAP in first 45 min of anaesthesia and also attenuates hypertensive response associated with intubation. It also showed decrease in incidence of arrhythmia as

compared to placebo. Clonidine group showed significant decrease in the mean SBP, DBP and MAP as compared to the pre operative values. These results were similar to Marchal JM et al [14], Nishikama t et al [10] and Laurito CE et al [11] who showed attenuation in pressor response to laryngoscopy and intubation after Clonidine pre medication.

The two study groups showed significant difference in their intra operative blood pressure values as compared to their pre operative values, but Clonidine showed significant decrease in intra operative SBP as compared to Metoprolol group. Our results were comparable with the study by Laurito CE et al [11] which showed decrease in SBP and not in MAP with Clonidine 200 mcg as compared to placebo. This suggested that both the drugs were equally good in lowering intra operative blood pressure as compared to their pre operative values, but Clonidine was significantly effective in lowering SBP as compared to Metoprolol. While recording blood pressure in peri operative period, we incidentally found that both drugs were significantly effective in decreasing the pressor response associated with laryngoscopy and intubation, which was not the objective of our study.

Both the drugs were ineffective in constantly maintaining the MAP below 70 mm of Hg intra operatively. Reason behind this may be that the dose used for producing induced hypotension in this study was low oral Clonidine 3mcg/kg as study conducted by M. Jabalameli et al [15] and Kazuhiko Okuyama MD et al [16] both used Clonidine 5 mcg/kg and Marchal et al [14] used 300 mcg Clonidine as premedication. Metoprolol used in this study was 50 mg which in contrast to 100 mg of Metoprolol used by Jakobsen et al [13] in reducing bleeding in hysterectomy patient. Thus for maintaining MAP < 70 mm of Hg higher doses of both the drugs should be studied.

#### **Surgical Field:**

In both the groups surgical field score obtained were 2, 3 and 4, there were no patient scoring less than 2 in both the groups and no patient had score of 5. In Clonidine group there were significant number of patients having score of 2 as compared to Metoprolol group and only one patient having score of 4 as compared to three in Metoprolol group which were statistically significant. Overall comparison of surgical field score between both the group by unpaired t test showed p value of 0.02, which suggested significant difference. Moreover score of 2 in Metoprolol group were associated with a heart rate of <60 bpm. These results were similar to study conducted by Nair S et al [12] which showed surgical field score were significantly better in Metoprolol group with heart rate of <60 bpm.

This study showed significant control of bleeding in Clonidine group as it causes constriction of peripheral blood vessels and reduces nasal mucous blood flow,[17,18] which accounts for the reduction of blood loss. Results of this study showed significant improvement in surgical field with oral Clonidine 3 mcg/kg as compared to the results by M. Jabalameli et al [15] and Kazuhiko Okuyama MD et al [16] who used Clonidine 5 mcg/kg and showed improvement in surgical field as compared to placebo and PGE respectively. Marchal et al [14] showed better surgical field with Clonidine 300 mcg as compared to placebo. Thus it can be stated that oral Clonidine 3 mcg/kg, 90 min prior to surgery can provide surgical field comparable to high doses of Clonidine . [19]

#### **Conclusion**

It can be concluded from this study that single oral doses of 50 mg Metoprolol and 3 mcg/kg Clonidine given 90 minutes before surgery to patients undergoing FESS can effectively produce stable haemodynamics intra operatively. Clonidine is more effective than Metoprolol in reducing intra operative bleeding and maintaining better surgical field even in

low doses of 3 mcg/ kg. Both the drugs emerge as safe premedication for better haemodynamic control intraoperatively in patients undergoing FESS surgery.

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