



## A PROSPECTIVE RANDOMIZED CONTROLLED STUDY OF ORAL CLONIDINE FOR CONTROLLED HYPOTENSION DURING FUNCTIONAL ENDOSCOPIC SINUS SURGERY (FESS)

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### ABSTRACT

controlled hypotension by oral clonidine is used in order to provide a better vision & create a surgical field free of bleed during FESS. Hypotensive anaesthesia is a technique in which the blood pressure is reduced to the optimal level, there by providing the surgeon with bloodless surgical field **AIM-** to analyse oral clonidine given as a premedication in patients along with other regular premedications such as antisialagogues. **MATERIALS AND METHODS-** Sixty ASA class I patients of both sexes between the age of 20 – 40 years weighing between 40 – 65kgs, who were scheduled for elective Endoscopic Nasal Sinus Surgery under General Anaesthesia at Meenakshi Medical College and research Institute were selected for this study. **RESULTS-** Oral Clonidine premedication 4 hours prior to surgery provides a considerable reduction in bleeding during FESS under General anaesthesia (with sevoflurane supplementation). It reduces the need for other hypotensive agents to provide a clear field for surgery. Therefore Oral Clonidine can be used as premedicant as well as a hypotensive agent for FESS.

**KEYWORDS :** clonidine, controlled hypotension, FESS, MAP, bloodless surgical field.

### Introduction

Creating a blood less field during FESS is challenging to the anaesthesiologist and here we are exploring a way of achieving a safer technique of controlled hypotension.

Controlled hypotension by oral clonidine is used in order to provide a better vision & create a surgical field free of bleed during FESS. Hypotensive anaesthesia is a technique in which the blood pressure is reduced to the optimal level i.e MAP not less than 60 mm Hg. there by providing the surgeon with bloodless surgical field and minimum blood loss.

The Technique entails the controlled lowering of blood pressure and is defined as a reduction of the systolic blood pressure to between 80-90 mmhg.

### AIM

To analyse oral clonidine given as a premedicant in patients along with other regular premedicants such as antisialagogues.

- 1) As a hypotensive agent
- 2) On intra operative bleeding using a bleeding severity score.
- 3) In maintaining haemodynamic stability intra operatively
- 4) Precludes the use of intra operative anti hypertensive.
- 5) As a premedicant for sedation, intra operative and post operative analgesia
- 6) To evaluate the various effects and complications. if any that may arise with the use of clonidine.

### Techniques of Hypotensive Anaesthesia

The key equation in the provision of hypotensive anaesthesia is:  
 $MAP = \text{CARDIAC OUTPUT} \times \text{SYSTEMIC VASCULAR RESISTANCE}$   
 Hence MAP can be manipulated by reducing either SVR or Cardiac output or both. Inducing hypotension purely by a reduction in cardiac output is not ideal because the maintenance of tissue blood flow is essential.

SVR can be reduced by peripheral vasodilation ( of the resistance vessels ) whilst cardiac output can be reduced by lowering venous

return, heart rate, myocardial contractility or a combination of these. Mode of action of hypotensive drugs Induced hypotension (in normovolemic patients) can be produced by either a reduction in Cardiac Output (CO) or a decrease in Systemic Vascular Resistance (SVR). The precapillary arterioles contain relatively large amounts of smooth muscle and, thus are the major determinants of resistance.

Complications of controlled hypotension can be avoided by inducing hypotension in a gradual manner, maintaining a Mean Arterial pressure (MAP) above 60 mm Hg and by careful vigilant monitoring methods and protocols.

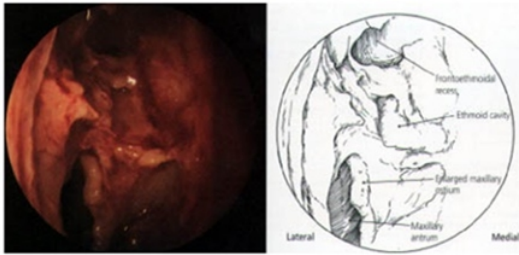
### Clonidine

#### Mode of Action

Clonidine stimulates alpha-adrenoreceptors in the brain stem. This action results in reduced sympathetic outflow from the central nervous system and in decreases in peripheral resistance, renal vascular resistance, heart rate, and blood pressure. Clonidine tablets act relatively rapidly. The patient's blood pressure declines within 30 to 60 minutes after an oral dose, the maximum decrease occurring within 2 to 4 hours. Renal blood flow and glomerular filtration rate remain essentially unchanged. Normal postural reflexes are intact; therefore, orthostatic symptoms are mild and infrequent. Acute studies with clonidine hydrochloride in humans have demonstrated a moderate reduction (15% to 20%) of cardiac output in the supine position with no change in the peripheral resistance: at a 45° tilt there is a smaller reduction in cardiac output and a decrease of peripheral resistance. Slowing of the pulse rate has been observed in most patients given clonidine, but the drug does not alter normal hemodynamic response to exercise. Pharmacokinetics The plasma level of clonidine peaks in approximately 3 to 5 hours and the plasma half-life ranges from 12 to 16 hours. The half-life increases up to 41 hours in patients with severe impairment of renal function. Following oral administration about 40-60% of the absorbed dose is recovered in the urine as unchanged drug in 24 hours. About 50% of the absorbed dose is metabolized in the liver.

**FESS<sup>1</sup>**

Functional endoscopic sinus surgery (FESS) is a minimally invasive technique in which sinus air cells and sinus ostia are opened under direct visualization. The goal of this procedure is to restore sinus ventilation and the normal function of the nasal sinuses.



**PERIOPERATIVE BLOOD LESS SURGICAL FIELD**

**MATERIALS AND METHODS**

Sixty ASA Class I patients of both sexes between the age of 20 – 40 years weighing between 40 – 65kgs, who were scheduled for elective Endoscopic Nasal Sinus Surgery under General Anaesthesia at Meenakshi Medical College and Research Institute were selected for this study.

This study was designed as prospective randomized comparative study. After receiving the institutional ethical committee approval and informed consent, the patients were allocated into two groups, the clonidine group (C) and the placebo group (P), each group comprising of thirty patients respectively.

**INCLUSION CRITERIA**

- (i) ASA PSI.
- (ii) Age 20 – 40 years.
- (iii) Weight between 40-65 kgs.
- (iv) Patients undergoing FESS

**EXCLUSION CRITERIA**

- (i) Sinus bradycardia / heart blocks / conduction defects
- (ii) Hypertension/ Ischaemic Heart Disease (IHD)/ Rheumatic heart disease.
- (iii) H/o CerebroVascular Disease (CVA)
- (iv) Patients on Digitalis, Calcium Channel Blockers and  $\beta$ -blockers
- (v) Chronic renal disease with increased renal parameters.
- (vi) Preoperative Hypotension
- (vii) Patient refusal.

All the patients were informed about the procedure and written consent obtained.

This study was carried out in the theatre where facilities for Induced Hypotension and Resuscitation were available.

**PROCEDURE**

**PRE-OPERATIVE ASSESSMENT**

All the patients were examined prior to surgery. Routine Clinical Examination, Biochemistry Tests, Electrocardiogram and Chest X-Ray were examined thoroughly for the conduct of anaesthesia. Only those patients in the ASA Class I were taken into this study.

**PRE-MEDICATION**

Patients were randomly allocated into two groups, Group C (Clonidine) and Group P (Placebo).

Group C patients received oral Clonidine 100  $\mu$ g with sips of water 90 minutes before surgery. This period ensures maximum plasma concentration after oral ingestion of the drug. Group P patients received placebo drug. All the patients received a nasal packing 2% xylocaine and 1:200000 of adrenaline in order to shrink the nasal mucosal vessels.

Injection Glycopyrolate 0.2 mg i.v was given as an anti-sialogogue

prior to Induction.

**Monitors used were:**

- (i) Electrocardiographic leads,
- (ii) Non-invasive blood pressure – sphygmomanometer cuff, and
- (iii) Pulse oximetry.
- (iv) Capnography.

**CONDUCT OF ANAESTHESIA**

Pre-induction Heart Rate and Blood Pressure both Systolic, Diastolic and MAP were recorded. After Pre-oxygenation with 100% oxygen for 3 minutes, anaesthesia was induced with Thiopental sodium 5mg/kg, Fentanyl 2  $\mu$ g/kg and Vecuronium Bromide 0.1mg/kg. Then laryngoscopy was performed and the trachea was intubated after 3 minutes of mask ventilation with 100% oxygen. In all patients ventilation was controlled manually. Anaesthesia was maintained with Nitrous oxide and oxygen (2:1 ratio) and Sevoflurane 0.8 volume % .Vecuronium top-up doses were given as and when required.

Thereafter the Heart Rate and Blood Pressure were measured at 1 and 3 minutes after induction of anaesthesia and through every 3 minutes thereafter intraoperatively.

To maintain hypotension for producing a bloodless surgical field, mean arterial pressure was proposed to be 75 mm Hg. Sevoflurane was administered with a minimum of 0.8 volume % in both the Groups and later given in escalating doses to a maximum of 1 volume % if necessary. In placebo group Injection Nitroglycerin diluted to a concentration of 100  $\mu$ g/ml and given as a continuous infusion (0.5-10  $\mu$ g/min). Intraoperative bleeding was assessed according to the **Bleeding severity score** (Jabalmeli Et AL)<sup>4</sup>.

Surgeons remarks regarding the field of surgery was also noted. Injection Atropine 0.6mg was planned to give in titrated doses intravenously if the heart rate went below 60 beats/minute. Patients with a MAP below 65 mmHg were planned to treat with Intravenous supplements of Inj. Ephedrine 6mg and infusion of Intra Venous (IV) fluids.

**REVERSAL OF RESIDUAL PARALYSIS AND RECOVERY**

Patients were reversed with Injection Neostigmine 0.05mg/kg body weight and Injection glycopyrolate 0.01 mg/kg body weight at the end of surgery.

**OBSERVATION AND RESULTS**

**Statistics and analysis :**

Sample size of 30 per group was taken for this study data was expressed as mean  $\pm$  SD or absolute values qualitative data were compared with chi square test and fisher's exact test.

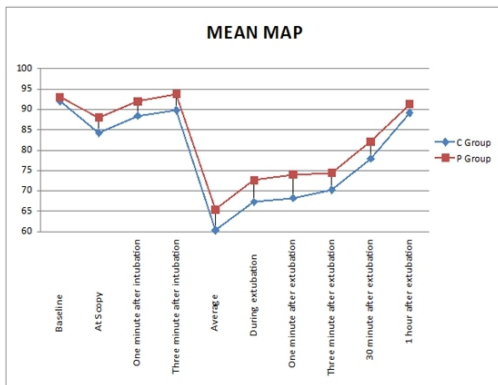
Quantitative variables were compared with the student t test .The level of statistical significance was set at p<0.05.

**HEAMODYNAMICS PARAMETER:**

**TABLE : I MEAN ARTERIAL PRESSURE (MAP)**

S No	Time of observation	MAP (mm/Hg)	SD	P value
1	Baseline	91.97	4.539	0.021
	Group C	93.00	2.464	
	Group P			
2	At Scopy	84.20	2.123	0.000
	Group C	88.00	4.488	
	Group P			
3	One minute after intubation	88.38	3.953	0.001
	Group C	92.00	2.573	
	Group P			
4	Three minute after intubation	89.80	2.552	0.000
	Group C	93.76	4.488	
	Group P			

5	Average Group C Group P	60.32 65.39	3.062 3.181	0.023
6	During extubation Group C Group P	67.29 72.65	3.764 4.068	0.000
7	One minute Group C after extubation Group P	68.22 73.99	2.459 4.518	0.042
8	Three minute Group C after extubation Group P	70.23 74.38	3.271 5.913	0.000
9	30 minute Group C after extubation Group P	77.89 82.11	2.891 5.021	0.000
10	1 hour Group C after extubation Group P	89.20 91.32	4.589 5.458	0.002



Mean values of Arterial Pressure were taken at baseline, at scopy, at one minute and three minutes after intubation, at average, during extubation, at one minute, three minutes, 30 minutes and 1 hour after extubation.

The p values have been calculated on comparing both the groups at each stage and the results are significant in all the stages.

This shows that clonidine drug is highly effective when compared to placebo drug.

**DISCUSSION**

Controlled hypotension is a technique used to reduce bleeding in patients undergoing middle ear surgery, nasal surgery, neuro surgery, orthopaedic surgery, head and neck surgery and plastic surgery. During FESS surgery the single and most common complication is excessive bleeding<sup>3</sup>.

Clonidine an α2 agonist and a potent suppressor of sympathoadrenal activity was given orally 4 hours prior to surgery, in an aim to produce hypotension thereby reducing intra-operative bleeding and the duration of surgery. The need for other hypotensive agents was observed to be reduced with Clonidine. All the patients had a very constant and stable Haemodynamic status intra-operatively<sup>5,6,7,8</sup> Clonidine suppresses central noradrenergic activity with secondary attenuation of perioperative hemodynamic fluctuations and stress response as supported by studies done by Pouuttu et al<sup>5</sup> and Quintin et al<sup>6</sup>. In this study, the effects of oral Clonidine (100ug was studied in 30 patients who underwent FESS **Bleeding severity score of 3 and 4 was seen to be higher in the Placebo Group than with Clonidine.** These findings were similar to that of Marchal et al<sup>7</sup> and Welfringer et al studies.

Although the approach is multifactorial, the principal mechanism employed is reduction of the vascular tone. Sodium nitroprusside<sup>10</sup>, nitroglycerin, hydralazine, trimethaphan, phenolamine, urapidil, esmolol, and labetalol are common drugs used in combination with volatile anesthetic agents<sup>11</sup>.

In the open, controlled, randomized study of Woodcock et al.<sup>2</sup>, single dose oral premedication with clonidine 0.6 mg in patients undergoing middle ear or nasal surgery significantly reduced the vapor requirement for induced hypotension, although it did not entirely obviate the need for further supplementary agents to facilitate induced hypotension. In the prospective study of Welfringer et al.<sup>12</sup>, patients scheduled for ear surgery were randomly assigned to drawback of hypotensive anesthesia. premedication with hydroxyzine alone or combined with clonidine. Anesthesia was maintained with isoflurane and surgical bleeding was assessed on a numerical scale with four values. The comparative assessment of surgical field quality was in favor of the clonidine group. In the present study, we also found that patients in the clonidine group scored significantly lower in the intraoperative bleeding assessment than patients given placebo. For surgeons, what is really disturbing is to have bleeding scores of 2 or higher, at any time. Clonidine has been shown to suppress central noradrenergic hyperactivity with secondary attenuation of perioperative hemodynamic lability<sup>13</sup>. In our study, a more favorable hemodynamic stability in patients treated with clonidine than in controls was also observed. Clonidine premedication has been found to effectively prevent a hyperdynamic response to laryngoscopy and intubation<sup>14</sup> with the additional advantage of a minimum impairment of coronary blood flow and systolic myocardial function<sup>15,16</sup>.

The Induced Hypotension effect by oral Clonidine directly attributed to reduced bleeding and a good surgical field. **Hypotension was produced in the Placebo Group using Sevoflurane and NTG infusion.** There was a statistically significant difference in the Sevoflurane requirement of both the Clonidine and Placebo Group. This was in concert with the study of Marchal et al<sup>9</sup> who observed that the intra-operative consumption of Isoflurane was less in patients premedicated with Clonidine than in control patients undergoing middle ear micro surgery.

Patients who were given oral Clonidine as a premedicant were well sedated and calm pre-operatively, Fentanyl requirement was also significantly reduced Extubation was smooth in all the patients of the Clonidine group who were sedated but arousable. Patients in the Placebo Group were sedated and drowsy in the post-operative period thereby requiring a longer observation in the recovery room.

**SUMMARY**

The advantages of Clonidine as premedicant can be summarized as follows:

- Excellent Sedation and Anxiolysis
- Attenuation of stress response to laryngoscopy and intubation.
- Maintenance of intraoperative cardiovascular stability by maintaining Heart Rate and Blood Pressure.
- Good intraoperative analgesia.
- Postoperative Sedation and Analgesia.
- Devoid of Respiratory depression.
- Less distressing side effects like nausea and vomiting.
- Easy administration.

Clonidine possesses certain limitations in its usage in patients with bradycardia, conduction disturbances and cardiovascular instability as it is likely to worsen the Cardiovascular status.

Clonidine at a dose of 100 g is tolerated well by the patients without major complications. Premedication with oral Clonidine in FESS surgery greatly facilitated controlled hypotension with a clear surgical field which was greatly appreciated by the operating surgeon.

**CONCLUSION**

The present prospective randomized controlled study shows that Oral Clonidine premedication 4 hours prior to surgery provides a considerable reduction in bleeding during Functional Endoscopic Sinus Surgery under General Anaesthesia (with sevoflurane supplementation). It reduces the need for other hypotensive agents to provide a clear field for surgery. Therefore Oral Clonidine can be used as premedicant as well as a hypotensive agent for FESS.

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