

**Evaluation of intravenous Clonidine as a hypotensive agent, when used as a part of balanced anaesthetic technique in functional endoscopic sinus surgery (FESS)**

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**A dissertation submitted in partial fulfillment of M D Branch(Anaesthesiology)  
Examination of the The Tamil Nadu Dr.M.G.R. Medical University, Chennai**

# CERTIFICATE

This is to certify that the dissertation entitled “**Evaluation of intravenous Clonidine as a hypotensive agent as part of balanced anaesthetic technique in Functional endoscopic sinus surgery (FESS)**” is a bonafide work of **Dr. Meghna S. David** in partial fulfillment of M D Anaesthesiology Examination of The Tamil Nadu Dr.M.G.R. Medical University, Chennai, to be held in September 2010.

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## CONTENTS

S.No.	Content	Page. No.
1	INTRODUCTION	1
2	AIMS & OBJECTIVES	3
3	REVIEW OF LITERATURE	4
4	METHODOLOGY	28
5	RESULTS	34
6	DISCUSSION	48
7	CONCLUSIONS	52
8	BIBLIOGRAPHY	
9	APPENDICES:  1. Proforma 2. Informed consent sheet 3. Data entry sheet 4. Key to data entry sheet	

## INTRODUCTION

Functional endoscopic sinus surgery (FESS) is a minimally invasive surgery of the paranasal sinuses.

The main aim of FESS is to restore drainage and aeration of the paranasal sinuses preserving the normal anatomic structures and maintaining the natural mucociliary clearance mechanism (1, 2). As with any other surgery, FESS can also lead to complications, which can be either related injury to the structures surrounding the paranasal sinuses or infection. These complications are rhino-oral fistulas, optic nerve injury, dural injury, cerebrospinal fluid (CSF) rhinorrhoea, meningitis, orbital plate injury, orbital cellulitis etc (3-5).

These complications tend to occur more in the presence of excessive bleeding during the surgery(3), which obscures the field of operation (6). A “bloodless field” would provide the surgeon with a clear field minimizing the risk of injury to the vital structures. This would also minimize the intraoperative blood loss as well as the surgical time.

“Bloodless field” can be achieved by inducing controlled hypotension (7) with various agents like inhalational anaesthetic agents (8-10), beta blockers (5), vasodilators like nitroglycerine (GTN) and sodium nitroprusside (SNP) (5) and intravenous (IV) anaesthetic agent like propofol (11). When inhalational anaesthetic agents are used on their own, they can cause a delay in awakening, shivering etc during the recovery period, which is undesirable. Beta-blockers do not have analgesic

or sedative properties. Propofol needs a continuous infusion throughout the surgery. It lacks analgesic effects and is relatively expensive.

Clonidine (an alpha 2 agonist) has been used as an antihypertensive for many years. Outside anaesthesia, it has been used in hypertensive crisis (12). In addition to its antihypertensive effects, its sedative and analgesic properties have encouraged us to use it as an adjunct in anaesthetic practice. In anaesthesia, it has been used as a premedication to facilitate induced hypotension(13, 14), to reduce the requirement of intravenous & volatile anaesthetics (13, 15) , to suppress pressor response during intubation (16) and to induce hypotension with total intravenous anaesthesia (TIVA) (17). There have not been many studies (18) to delineate its hypotensive effect with inhalational agent together with its other effects, for example analgesia and sedation especially in the Asian population.

In this study we propose to evaluate the hypotensive effect of Clonidine when used as a part of a balanced anaesthetic technique in patients undergoing FESS. In this randomized double blind placebo controlled study, fentanyl and metoprolol have been used as rescue drugs to achieve target blood pressure.

## **AIM AND OBJECTIVES**

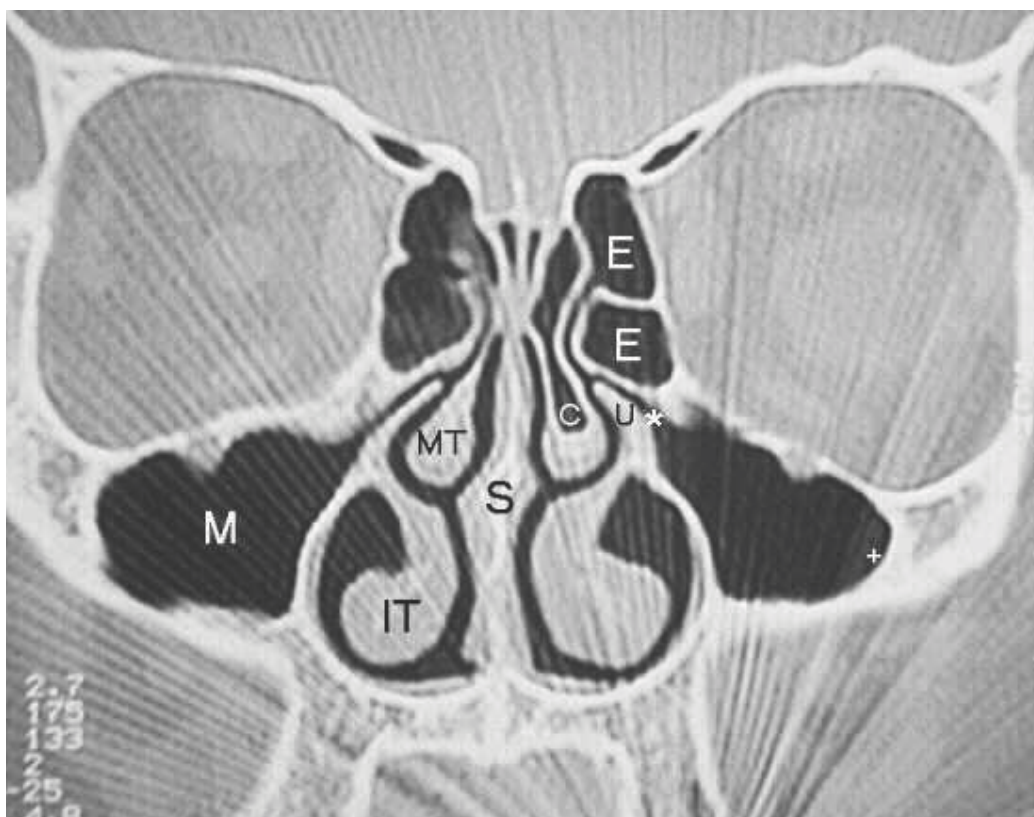
**PRIMARY OBJECTIVE:** To evaluate the hypotensive effect of Clonidine when used as a part of balanced anaesthetic technique in FESS.

**SECONDARY OBJECTIVES:**

1. To assess the reduction in the requirement of metoprolol & fentanyl to achieve hypotension.
2. To aim at 'bloodless field'.
3. To assess blood loss.
4. To evaluate beneficial effects of Clonidine namely reduction in anaesthetic requirements and analgesia.
5. Assess incidence of side effects namely excessive sedation, hypotension & bradycardia.

## REVIEW OF LITERATURE

### FUNCTIONAL ENDOSCOPIC SINUS SURGERY



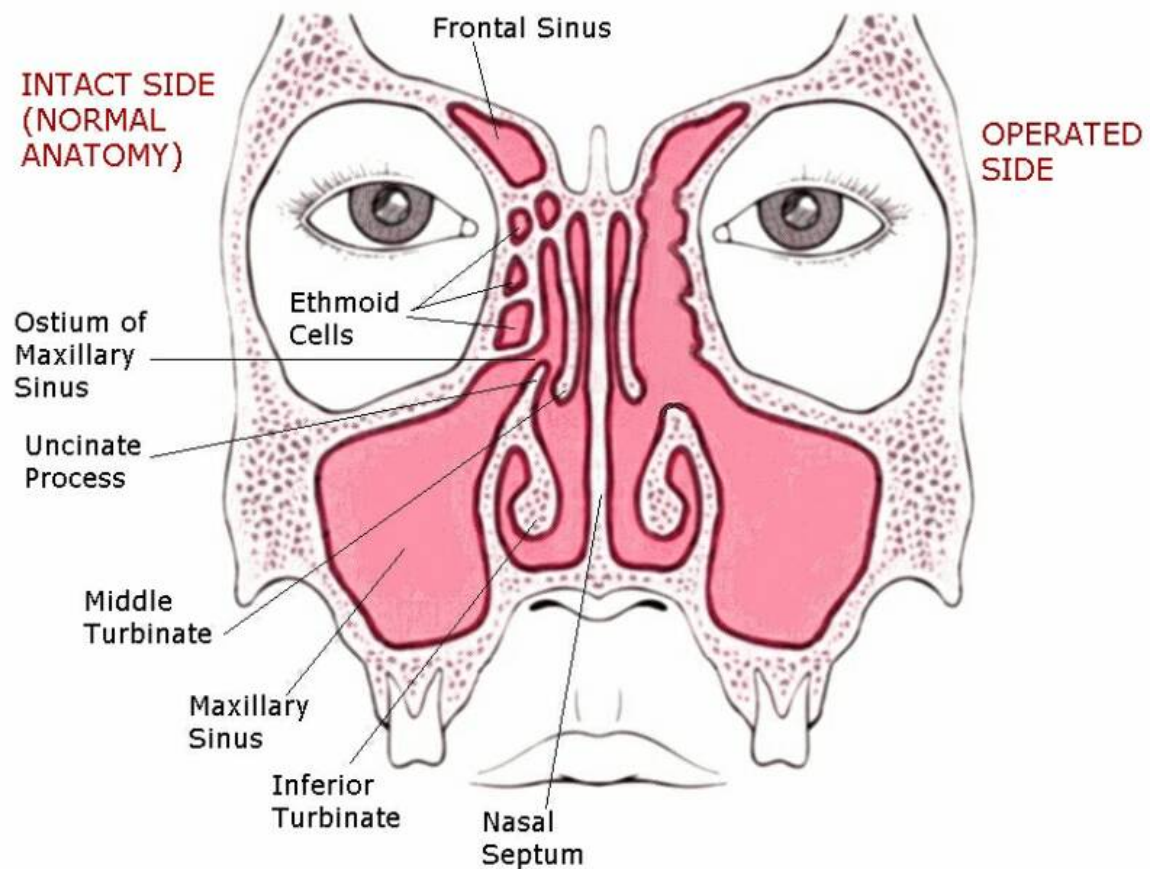
**Figure –1 Normal anatomy of paranasal sinus as seen on CT scan**

E - Ethmoid sinus; M - Maxillary sinus; S – Nasal septum; IT - Inferior turbinate

MT - Middle turbinate; U - Uncinate Process



Removal of the uncinete process of the ethmoid bone allows resection of the anterior ethmoid air cells, with subsequent reestablishment of ventilation and drainage of the maxillary and frontal sinuses through their natural ostia. Surgery is performed through the nostrils and therefore, there are no external incisions.



**Figure –2 Normal anatomy versus operated side in FESS**

FESS is the mainstay in the surgical treatment of chronic sinusitis and nasal polyposis. It is a relatively recent surgical procedure that uses nasal endoscopes to minimise cutting and trauma to the skin (2).

FESS was popularised following the pioneering work of Messerklinger & Stamberger (Graz, Australia). Rhinology & sinus surgery have undergone a tremendous expansion since the discourses of Messerklinger and Wigand in the late 1970's. Improved understanding of the anatomy and pathophysiology of chronic sinusitis, advances in imaging techniques and image guided surgery have allowed surgeons to perform more complex procedures with increased safety.

#### **INDICATIONS:**

The most common indications for endoscopic sinus surgery are as follows:

- Chronic sinusitis refractory to medical treatment
- Recurrent sinusitis
- Nasal polyposis
- Antrochoanal polyps
- Sinus mucoceles
- Excision of selected tumors
- Closure of CSF leak.

- Orbital decompression (e.g. Graves ophthalmopathy)
- Optic nerve decompression
- Dacryocystorhinostomy (DCR)
- Repair of choanal atresia
- Removal of foreign body
- Control of epistaxis

### **COMPLICATIONS:**

Extreme care is required in this surgery due the proximity of paranasal sinuses to the orbits, brain, internal carotid arteries and optic nerves. The complications related to FESS are as follows:

#### **1. Orbital complications:**

- a. Orbital haemorrhage
- b. Abscess and
- c. Optic nerve injury

#### **2. Intracranial complications:**

- a. CSF leak

- b. Meningitis
- c. Abscess and
- d. Intracranial haemorrhage

**3. Nasal complications:**

- a. Adhesions formation
- b. Anosmia
- c. Hyposmia and
- d. Lacrimal duct injury.

**ANAESTHETIC TECHNIQUES:**

FESS can be done under monitored local anaesthesia with topical and infiltration local anaesthesia or under general anaesthesia with inhalational anaesthesia or total intravenous anaesthesia.

**Advantages of monitored local anesthesia:**

- Good hemostasis
- Clear distinction between healthy and diseased mucosa
- Rapid wound healing & short recovery time

**Disadvantages of monitored local anaesthesia:**

- Complicated cases warrant general anaesthesia
- Airway is not protected
- Surgeons need to be gentle & proceed with minimal trauma.
- Anxious patients may need good sedation

## **CONTROLLED HYPOTENSION**

Controlled hypotension or deliberate hypotension during general anaesthesia may be employed to lower the mean arterial blood pressure (MAP) in order to reduce the intraoperative blood loss. This can be achieved by proper positioning of the patient and pharmacological methods.

### **Positioning:**

Appropriate positioning of the patient reduces bleeding. To achieve this, the operative field needs to be elevated above the level of the heart. This reduces the venous pressure and hence the venous bleed. When the head is elevated above the level of heart, there is a reduction in venous return, which results in a reduction in cardiac output and blood pressure and hence the arterial bleed.

### **Pharmacological methods:**

#### **1. Anaesthetic agents:**

##### **a. Volatile anaesthetics**

- i. Halothane,
- ii. Isoflurane and
- iii. Sevoflurane

**b. Intravenous agents:**

- i. Propofol

**2. Vasoactive drugs:**

**a. Vasodilators:**

- i. Nitroglycerine (GTN),
- ii. Sodium nitroprusside (SNP),
- iii. Hydralazine and
- iv. Purine derivatives

**b. Alpha adrenergic blockers**

**c. Beta adrenergic blockers**

**d. Combined alpha and beta adrenergic blockers**

**e. Calcium channel blockers**

**f. Alpha-2 receptor agonists**

A wide variety of drugs have been employed to achieve controlled hypotension in a variety of surgeries. These techniques have resulted in lesser blood loss, shorter operating time etc., which should have reduced the morbidity associated with such

procedures, though they have not been studied. These are relatively non-invasive techniques and can be employed by most practitioners relatively safely.

In a study by Boonmak et al(11) ,the controlled hypotension was given using propofol with general anaesthesia for FESS where mean arterial pressure was lowered in a range of 50 to 65 mmHg,which had shown good results.

Controlled hypotension has been helpful in minimising the blood loss and improving visibility.In a study by Vazeery et al (19)on patients undergoing total hip arthroplasty ,lowering the mean arterial blood pressure by using sodium nitroprusside,had shown significant reduction in blood loss as compared to patients who did not receive the drug.

In a study by PP Kadam et al(20) on patients undergoing spine surgery,there was significant reduction in the mean intraoperative blood loss as well as in the operating time in the group of patients who were started on Nitroglycerine for controlled hypotension.

Positioning and pharmacological methods when employed together will have an additive effect and a good result (23).

### **History of hypotensive anaesthesia:**

Controlled hypotension was first proposed by Cushing in 1917 for intracranial surgeries (21). Eckenhoff and Rich supplied the objective data that deliberate hypotension can indeed reduce the blood loss (22).



In 1950's, ganglion blockade Enderby used pentamethonium was used to achieve hypotension (23). In the early 1980's, volatile agents like halothane as part of balanced anaesthesia was used to achieve hypotension by Enderby (24). There have been extensive studies using isoflurane for hypotensive anaesthesia (25, 26). After the introduction of propofol in anaesthesia, which has good hypotensive potential and has the advantage of rapid reversal, total intravenous anaesthesia with propofol (11) also has been used for the same purpose. Vasoactive drugs such as SNP (19) and GTN (20) and opiates also have been used to achieve deliberate hypotension. Beta blockers (27) like metoprolol and alpha blockers like hydralazine have been used (28).

Centrally acting alpha -2 agonists have also been studied for there hypotensive properties and have shown good results (18, 29). These drugs act by various mechanisms namely increasing the depth of anaesthesia, which blunts the sympathetic response to surgery, cause direct vasodilatation leading to reduced venous return with resultant reduction in cardiac output and blood pressure, cause reduction in systemic vascular resistance with a resultant reduction in blood pressure, cause direct myocardial depression with resultant reduction in cardiac output and consequent hypotension. Centrally acting alpha -2 agonists have many of the above properties on their own and can potentially be more effective in inducing deliberate hypotension under anaesthesia.

## **Indications for hypotensive anaesthesia:**

### **Microsurgery**

Endoscopic sinus surgery

Middle ear surgery

Nerve grafting

Microvascular repair

Plastic surgery e.g. free flap graft

Transnasal transsphenoidal excision

### **Complex arteriovenous malformations**

### **Intracranial surgeries**

### **Craniofacial surgeries**

### **Head and neck surgeries**

### **Spine surgeries**

### **Pelvic surgeries for malignancy**

### **Intraocular surgeries**

## **Contraindications to hypotensive anaesthesia:**

Fixed cardiac output state

Aortic stenosis,

Mitral stenosis

Cardiomyopathy

Renal impairment

Liver dysfunction

Pregnancy

Peripheral vascular disease

Ischaemic heart disease

Glaucoma

Intracranial hypertension

Previous cerebrovascular accident

Untreated / uncontrolled hypertension

## **BALANCED ANAESTHESIA**

Balanced anaesthesia (as defined by Mosby's Medical Dictionary, 8th edition) is a highly variable technique of general anaesthesia that is based on the concept that administration of mixture of small amounts of several neuronal depressants summates the advantages but not the disadvantages of the individual components of the mixture. This comprises of using narcotic analgesics, muscle relaxants, minimal inhalation agent with or without nitrous oxide for anaesthesia balancing the depressant effect on motor, sensory, reflex and mental aspects of nervous system function. When controlled hypotension is desired for surgery, this technique of balanced anaesthesia in combination with various drugs and techniques described earlier will be potentially successful with minimal complications.

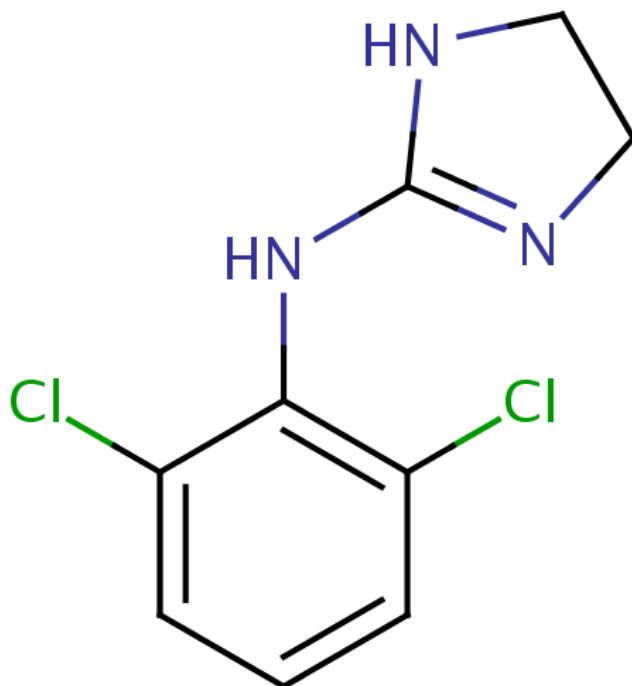
## CLONIDINE

### DRUG DESCRIPTION:

Clonidine is a centrally acting alpha-agonist hypotensive agent. Clonidine hydrochloride was synthesized by Ståhle and associates in 1962 (31). It is a derivative of imidazoline that exists as a mesomeric compound.

### Chemical name:

2-(2,6-dichlorophenylamino)-2-imidazoline hydrochloride



**Physical properties:**

Clonidine is a white, crystalline, odorless, bitter substance, soluble in water and alcohol.

**Chemical pharmacology:**

Clonidine stimulates the alpha adrenoceptors in the brainstem, which results in reduced sympathetic outflow from the central nervous system. This decreases peripheral vascular resistance, renal vascular resistance, heart rate and blood pressure and cardiac output (32). During long term therapy, cardiac output tends to return to control values while peripheral resistance remains reduced (33).

Clonidine when administered on short-term acutely stimulates growth hormone release in both children and adults but does not produce a chronic elevation of growth hormone with long-term use. Other studies in patients have provided evidence of a reduction in plasma renin activity and in excretion of aldosterone and catecholamines (34). The exact relationship of these pharmacological actions to the antihypertensive effect of clonidine has not been fully elucidated. Clonidine is available as tablet for oral administration, injection form for parenteral administration and transdermal strips for transdermal route.

## **Pharmacokinetics:**

Clonidine can be administered via oral, intravenous, intrathecal, epidural and transdermal routes.

- **Absorption:**

- Orally administered clonidine undergoes complete absorption(35) with a Tmax of about 3 to 5 hours. Intravenously administered clonidine has a Tmax of about 19 minutes. When administered Transdermally, therapeutic levels are achieved in 2 to 3 days.

- **Distribution:**

- Volume of distribution (Vd) is about 2.1L/kg. Clonidine is about 20% to 40% protein bound. The distribution half life (t1/2) of clonidine when administered intravenously is about 11 minutes.

- **Onset of action:**

- Orally administered clonidine takes about 30 to 60 minutes for onset of action with peak effect seen between 2 to 4 hours. Intravenously administered clonidine takes 3-15 minutes for onset and the peak effect is seen between 35 to 90 minutes (36).

- **Metabolism:**

- About 50% of the drug is metabolized in the liver. The major metabolite is p-hydroxyclonidine.

- **Elimination:**

- Oral route – elimination  $t_{1/2}$  is 12 to 16 hours. 40% to 60% of the drug is excreted unchanged in urine in 24 hours.
- Intravenous route – elimination  $t_{1/2}$  is about 9 hours. 72% is excreted in urine in 96 hours, out of which 40% to 50% is excreted as unchanged drug. Renal clearance is about 133 minutes.
- Epidural route – elimination  $t_{1/2}$  is 22 hours and clearance is about 190 minutes.
- Transdermal route – after removal, therapeutic levels persists for about 8 hours declining slowly over several days.

- **Special populations:**

The elimination  $t_{1/2}$  increases up to 41 hours in those with severe renal impairment. In such patients dosage adjustment is recommended.



**Indications and usage:**

- Management of hypertension
- Adjunct to opiates for relief of cancer pain
- Unlabeled uses: Treatment of constitutional growth in children, diabetic diarrhea, Tourette syndrome, alcohol withdrawal, methadone/opiate detoxification, ulcerative colitis, diagnosis of phaeochromocytoma, neuralgia, hypertensive emergencies.

**Contraindications:**

Hypersensitivity to clonidine

Pregnancy

**Adverse reactions:****• Cardiovascular:**

Congestive heart failure

Orthostatic symptoms

Palpitations

Bradycardia

- **Central Nervous System (CNS):**

Drowsiness

Delirium

Nightmares

Headache

Fatigue

- **Gastrointestinal:**

Dry mouth

Constipation

Anorexia

Nausea and vomiting

- **Dermatologic:**

Rash and urticaria

- **Miscellaneous:**

Impotence

Nocturia

Muscle cramps

**Drug interactions:**

Clonidine may enhance the depressant effect of alcohol and CNS depressant drugs. Clonidine is highly lipid soluble and it crosses the blood brain barrier (37).

Narcotic analgesics may potentiate the hypotensive effects of clonidine.

Similarly, the sedative effect of narcotic analgesics may be potentiated by clonidine.

There is increased possibility of rebound hypertension in patients who are on beta-blockers, when clonidine therapy is discontinued.

Tricyclic antidepressant may reduce the effect of clonidine.

Clonidine has its effects both at spinal as well as supraspinal levels (38). By virtue of this effect, epidural clonidine may prolong the duration of pharmacological effect of local anesthetics administered into the subarachnoid and epidural space.

In recent years, clonidine has generated considerable interest as an anaesthetic adjuvant. Being a centrally acting alpha-2 agonist, its use in hypertension and hypertensive crisis has been known for many years.

Clonidine has proven to be a very good premedication to facilitate induced hypotension in adults (18) as well as children (29). The hypotension is mainly due to reduction in cardiac output and heart rate without corresponding rise in peripheral resistance (33).

As premedication, clonidine decreases the dose of thiopentone (14) required to induce anaesthesia in children as well as reduction in requirement of volatile agent (29).

Thomas Hackmann et al (29) in his study on adolescent children undergoing maxillo-facial and oral surgery has shown that patients who received clonidine required lesser anesthetics ( $P=0.0004$ ) and less labetalol for control of blood pressure ( $P=0.004$ ). He also showed that the length of stay in the recovery room was significantly shorter in patients who were given clonidine ( $P=0.03$ ). It was also seen that there was no delay in recovery from anaesthesia in patients who received clonidine.

Stocche RM (39) has shown that intravenous clonidine induces hypotension without affecting the anesthetic quality and emergence time in tympanoplasty.

In another randomized, double-blind, placebo-controlled study, Zalunardo et al in 1997 (40), the effects of intravenous and oral clonidine on the hemodynamic and plasma catecholamine response to endotracheal intubation were observed on 33 patients. They found that intravenous clonidine reduced the stress response to endotracheal intubation compared to placebo. Oral clonidine at the dose of 4micrograms/kg was less effective in blunting hemodynamic response than 3mcg/kg of IV clonidine.

Zalunardo et al also concluded in another randomized, double blind, placebo-controlled trial (41) that a single dose preoperative intravenous dose of clonidine (3micrograms/kg) blunts the hemodynamic response during extubation in non-cardiac surgery of intermediate duration.

Clonidine is also known to prolong spinal anaesthesia when added to intrathecal local anesthetics (42) or when administered as oral premedication (43). Rhee et al (42) have shown the efficacy of intravenous clonidine in prolonging the spinal block by approximately 1 hour without any adverse effects.

Intravenous clonidine has been proved to be a good hypotensive agent with inhalation anaesthesia in a double blind, randomized study by Lee et al (18), on 41 patients undergoing middle ear and nose surgery.

Clonidine has shown to be an adjuvant to induce hypotension when used with total intravenous anesthesia (17). With inhalational anaesthesia using isoflurane clonidine has effectively reduced the isoflurane requirement (44) as well as blood pressure (45).

In many studies it has also decreased the requirement of propofol (46), with good cardiovascular stability and postoperative recovery(47). In patients undergoing coronary artery bypass surgery (CABG), clonidine has shown to reduce isoflurane and nitroglycerine requirement with good cardiovascular stability (48). The effect of clonidine in reducing Sevoflurane requirement for anaesthesia and hypnosis is also seen in some studies (49). Thus the requirement of anaesthetic induction agent and the maintenance agent is reduced with the use of clonidine.

Preoperative clonidine in lower limb surgeries has shown to blunt the hyperadrenergic and hyperdynamic responses to prolonged tourniquet pressure during general anaesthesia (50).

Clonidine reduces the presynaptic norepinephrine release, decreases the “set point” around which blood pressure is regulated and has a substantial analgesic and sedative action (32). Clonidine blunts responses to perioperative stress, which has also become a subject of molecular research. In cardiac surgeries like CABG, clonidine use has shown significant blunting of stress response during induction of anaesthesia and surgical field was better, with the hypotension achieved (48). Clonidine has been used as a sedative and as an analgesic too. In mechanically ventilated critically ill patients, clonidine has been used as a sedative (51). This sedative action is mainly due to the central action of the drug. The analgesic property of the drug has been of great benefit in various surgeries for post operative pain relief (52-54) as well as in burn patients (55-57). Clonidine causes analgesia by modulation of nociception via the alpha 2 adrenoreceptors in the spinal cord (58). Peri-operative use of clonidine has also shown adjunctive analgesic effects (59). Clonidine also causes the reduction of delirium during emergence from sevoflurane anaesthesia (60) and also has been used prophylactically in alcohol withdrawal syndrome (61).

Clonidine decreases the incidence, severity and duration of post-operative shivering and therefore the oxygen consumption. It decreases the thermoregulatory threshold for vasoconstriction and shivering as hypothalamus has high density of alpha-2 receptor. It also acts by reducing the spontaneous firing in locus coeruleus, a pro-shivering center in pons (62-64). The effect of reduction in shivering is a decrease in postoperative oxygen consumption, as shown by Delaunay et al (65).

Like other alpha 2 adrenoceptor agonist, clonidine has side effects like bradycardia, hypotension and excessive sedation (47), but these side effects are seen at high doses.

Considering all the above benefits that clonidine provides, it has come up as a very useful adjunct in anaesthesia practice today.

## METHODOLOGY

This study is a randomized, double blind placebo controlled interventional trial. The study was cleared by the research and ethics committee of our institution. The sample size was calculated to detect a difference of 40% in hypotension between the study groups, sample size was calculated to be 30 in each group. Power of the study was assumed to be 80% & level of significance was fixed at 5%

The inclusion criteria being all adults (18years to 65years) ASA grade I and II patients undergoing limited or full FESS.

### **The exclusion criteria were:**

- Hypertension on treatment
- Diabetes with autonomic dysfunction
- Patients on beta blocker or with contraindication for beta blockers
- Heart block of any degree / bradyarrhythmias
- Ischaemic heart disease
- Patients on pacemakers
- Patients already on clonidine / allergic to clonidine
- Pregnant mothers



60 ASA I and II patients who were scheduled for FESS were enrolled in the study. A written consent was obtained from the patient on the night before the study. Pre-operatively, no sedative premedication was prescribed for the patients.

Patients were mobilised into the theatre and basic monitoring namely non-invasive blood pressure, electrocardiogram for heart rate and rhythm and pulse oximetry was established. Intravenous line with lignocaine infiltration was secured and basal vital signs were recorded. These included non invasive blood pressure, electrocardiogram, pulse oximeter and consciousness level. Noninvasive blood pressure was monitored every five minutes, which was the standard practice. ECG and pulse oximetry were monitored continuously.

The patients were randomized into two groups using block randomization. All patients were assigned to the intervention (clonidine, Group A ) group or comparator (placebo Group B) group. Based on randomisation, the patients received 3micrograms/kg of the drug (Group A) or an equal volume of sterile water for injection (Group B) intravenously 30 minutes prior to induction of anaesthesia. The vital signs as mentioned previously were monitored for the next 30 minutes. General anaesthesia was induced with intravenous thiopentone (5mg/kg) after fentanyl (1.5mcg/kg). After ensuring the ability to ventilate with oxygen, air and isoflurane, endotracheal intubation was facilitated with vecuronium (0.1mg/kg). Anaesthesia was maintained with oxygen, air and isoflurane. End tidal anaesthetic concentration was monitored continuously aiming to maintain a minimum alveolar concentration (MAC) of 1.0 of isoflurane during the surgery. If necessary, further doses of fentanyl in 10-20 mcg aliquots was administered upto a total of 4mcg/kg aiming for a mean arterial

pressure (MAP) of 55-65mmHg. Vital parameters were continued to be monitored as described till the end of surgery.

If the target MAP was not achieved after a total of 4mcg/kg of fentanyl and 1.0 MAC of isoflurane, metoprolol was administered as 0.5mg boluses to achieve a MAP of 55-65mmHg. In spite of the above measures, if the target MAP was not achieved and the heart rate was

< 60/minute, 10mg boluses of propofol was given till MAP was in the desired range. This was done to avoid the risk of serious bradycardia with further doses of metoprolol and to standardise the maximum MAC of isoflurane. The side effects which were anticipated were bradycardia, hypotension which were common to both clonidine and metoprolol. If the heart rate was

< 50/minute, atropine (0.02mg/kg) was given to treat bradycardia. If the MAP < 55mmHg, the inspired isoflurane concentration was reduced by 0.5% till MAC reached 0.75. If the blood pressure did not improve with this, ephedrine 3 mg in incremental dosage was administered to treat hypotension.

At the end of the surgery, the anaesthetic was discontinued, throat pack removed and residual paralysis was reversed with neostigmine (0.05mg/kg) and glycopyrrolate (0.02mg/kg). The patients were extubated when awake and were monitored in recovery room.

Blood loss was estimated by measuring the volume in the suction bottle and the number of swabs soaked in blood accounting for any saline used for washing during the procedure. At the end of the surgery, the surgeon was requested to comment on the

quality of the operation field. Clear field of operation with no suctioning required was defined as 'bloodless' field. Surgeon's opinion regarding the field of operation was assessed by using Fromme-Boezaart scale (66). Sedation was assessed using Brussel's sedation score (67) in the immediate post-operative period. When the patient was fully awake, pain was assessed using the visual analogue score (VAS).

### **Fromme-Boezaart scale**

Assessment of intra-operative bleeding

Grade 0: No bleeding.

Grade 1: Slight bleeding, no suctioning of blood required.

Grade 2: Slight bleeding, occasional suctioning required. Surgical field not threatened.

Grade 3: Slight bleeding, frequent suctioning required. Bleeding threatens surgical field a few seconds after suction is removed.

Grade 4: Moderate bleeding, frequent suctioning required, bleeding threatens surgical field after removal of suction.

Grade 5: Severe bleeding, constant suctioning required, bleeding appears faster than can be removed by suction, surgical field severely threatened and surgery impossible.

A : Excellent (grade 0-1)

B : Good (grade 2-3)

C : Poor (grade 4-5)

## **Brussel's Sedation score**

1. Unarousable.
2. Responding to pain stimulation (trapezius muscle pinching) & not to auditory stimulation.
3. Responding to auditory stimulation
4. Awake and calm
5. Agitated

## STATISTICAL ANALYSIS

All normally numerical variables were summarized using mean with SD(standard deviation). Variables with skewed distributions were described using median and range.

The outcome variables were compared between the two study groups using chi-square test.

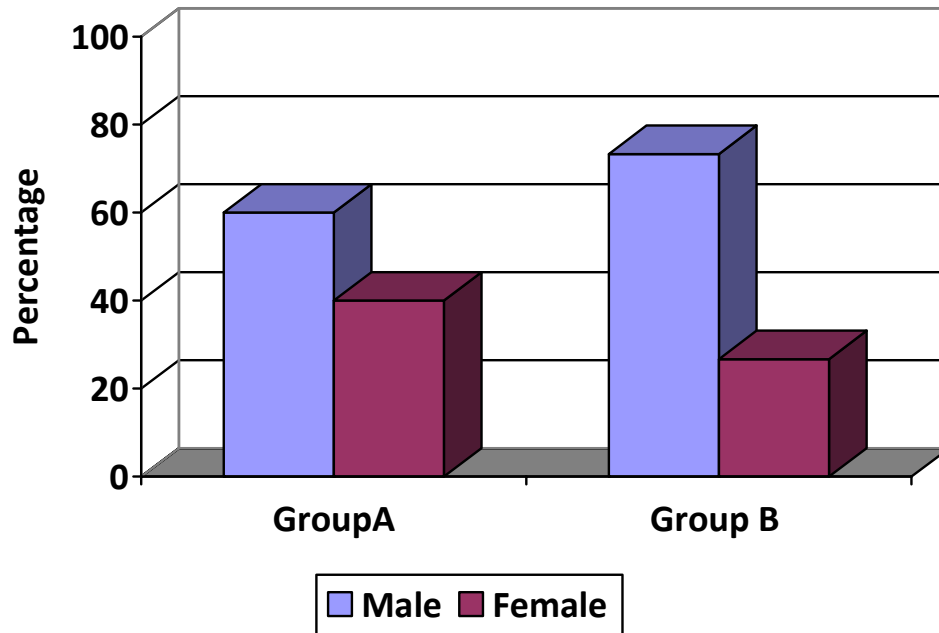
All calculated p-values were two-sided. Analysis was done using STATA 10.0 (Statacorp, College station, TX, USA).

## RESULTS

Sixty patients undergoing (FESS) were included in the study. There were thirty in each group.

Table 1 shows the demographic data of the patients. The age, gender and body weight were comparable between the two groups.

**Figure 1**



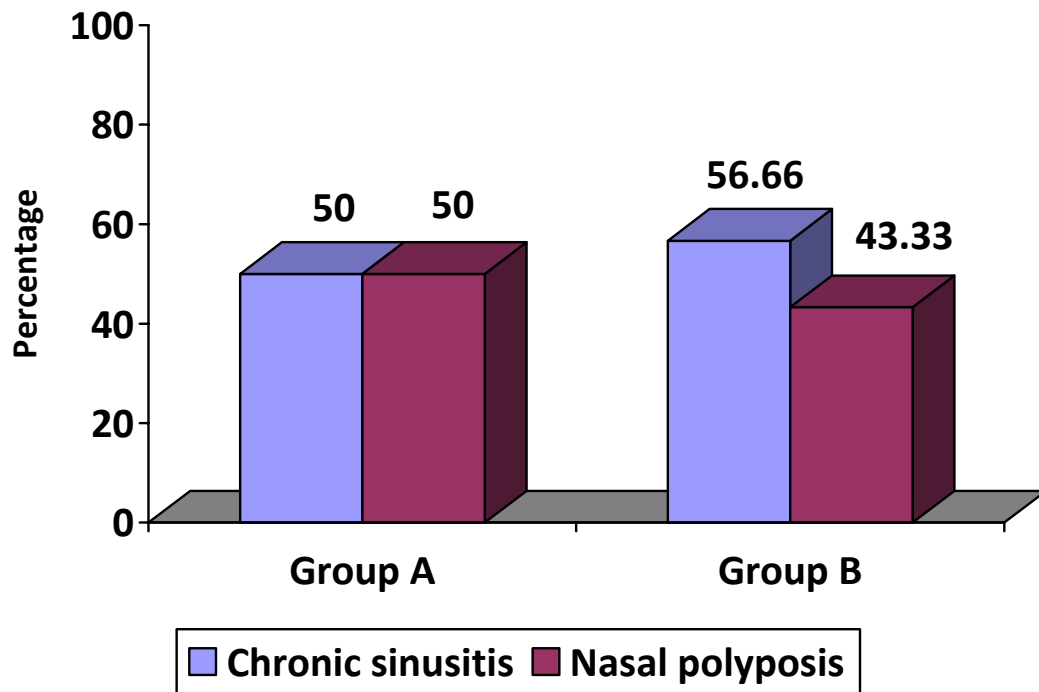
**Table 1****Demographic Data**

<b>Parameters</b>	<b>GROUP A (n=30)</b>	<b>GROUP B (n=30)</b>	<b>P value</b>
Age (years) Mean± S.D.	37.13 ± 10.78	37.4 ± 12.82	0.93
Sex: Male Female	18 (60%) 12 (40%)	22 (73.33%) 8 (26.67%)	0.273
Body weight (kg) Mean± S.D.	60.13 ± 11.91	60.76 ± 12.38	0.85

The above table shows male predominance in both the groups respectively 60% and 73.33%. The p value is 0.273.

Figure 2

Preoperative Diagnosis:





**Table 2**

**Preoperative Diagnosis:**

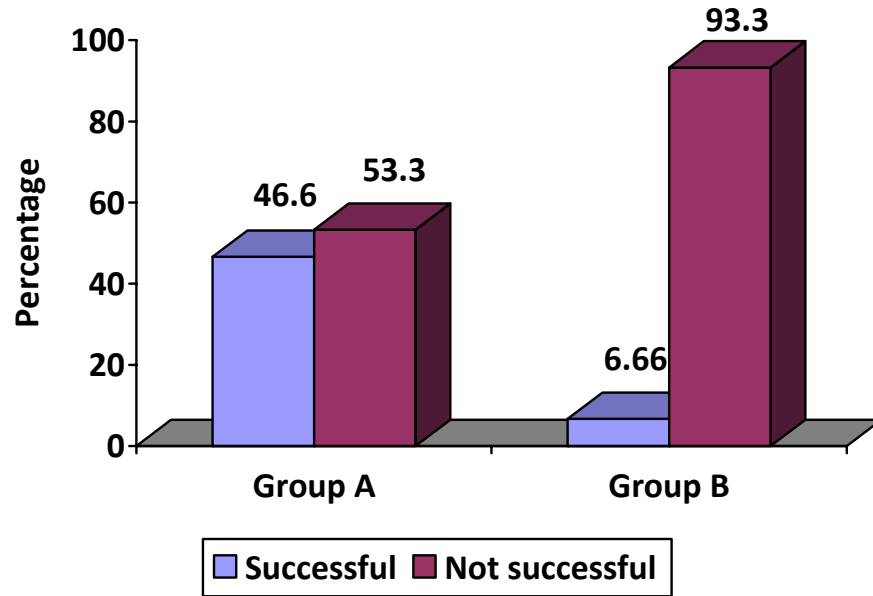
<b>DIAGNOSIS</b>	<b>GROUP A</b>	<b>GROUP B</b>
Chronic sinusitis	15 (50%)	17 (56.66%)
Nasal polyposis	15 (50%)	13 (43.33%)

Fisher's exact = 0.8

- There were equal number of patients in group A with the preoperative diagnosis of chronic sinusitis and nasal polyposis, whereas in group B chronic sinusitis was seen more than nasal polyposis.
- There was no statistical difference in the number of patients with the two diagnoses in group B.

Figure 3

Success of achievement of controlled hypotension with clonidine alone



**Table 3**

**Success of achievement of controlled hypotension with clonidine alone**

	<b>GROUP A</b>	<b>GROUP B</b>
Successful	14 (46.6%)	2 (6.66%)
Not successful	16 (53.3%)	28 (93.3%)

“P” value < 0.001

- At induction 1.5 mcg/kg of fentanyl was administered to all the patients. In 14 out of 30 patients (46.6%) in the clonidine group, target blood pressure was achieved without additional fentanyl and metoprolol. In the placebo group, target blood pressure was achieved only in 2 (6.66%) out of 30 patients with the induction dose of fentanyl. 28 (93.3%) patients needed additional fentanyl and metoprolol. This difference was statistically significant.

**Table 4**

**Requirement of additional fentanyl to achieve target blood pressure**

	<b>GROUP A</b>	<b>GROUP B</b>
Required	16 (53.3%)	28 (93.3%)
Not required	14 (46.6%)	2 (6.66%)

(P value <0.001)

- 16 (53.3%) patients out of 30 who received clonidine, required additional fentanyl (after the 1.5mcg/kg induction dose) up to a total 4mcg/kg for achieving blood pressure within the target range. In the placebo group, 28 (93.3%) patients out of 30 needed fentanyl up to 4mcg/kg to achieve target blood pressure. This difference was statistically significant.

**Table 5**

**Requirement of Metoprolol**

<b>Metoprolol</b>	<b>GROUP A</b>	<b>GROUP B</b>
Required	3 (10%)	22 (73.3%)
Not required	27 (90%)	8 (26.6%)

(P value < 0.001)

- Metoprolol was administered if the target blood pressure was not achieved after administration of a total of 4mcg/kg of fentanyl and MAC of isoflurane was 1.0. In the placebo group 22 (73.3%) out of 30 patients required metoprolol as an additional drug to achieve hypotension within the target range, which was significantly higher than the clonidine group where only 8 (26.6%) of the patients needed metoprolol.

**Table 6**

**“Bloodless” field during the surgery**

	<b>GROUP A</b> <b>(n = 30)</b>	<b>GROUP B</b> <b>(n = 30)</b>	<b>P</b> <b>Value</b>
Bloodless Field	11 (36.67%)	3 (10%)	0.05

- There was significant difference in successful achievement of bloodless field between the two groups with more success in the clonidine group.

**Table 7**

**Intraoperative blood loss (millilitre)**

	<b>GROUP A</b>	<b>GROUP B</b>	<b>P</b>
Median blood loss	63.5	180	0.0449
(Range)	(40-200)	(70-300)	

- Median blood loss in the patients who received clonidine was 63.5 ml, which was significantly lower than the placebo group with a median blood loss of 180 ml.

**Table 8**

**VAS (visual analogue scale) for assessment of pain**

	<b>GROUP A</b>	<b>GROUPB</b>	<b>P value</b>
Mean (SD)	0.27 (0.73)	0.93 (1.28)	
Median (Range)	0 (0-3)	0 (0-5)	0.01

- Patients who received clonidine had significantly better analgesia in the immediate post-operative period.



**Table 9**

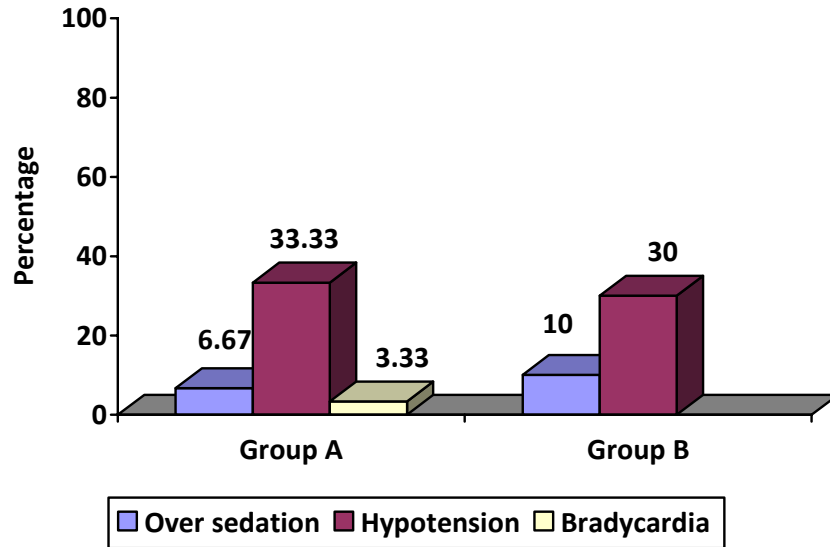
**MAC (minimum alveolar concentration) of isoflurane**

	<b>GROUP A</b>	<b>GROUP B</b>	<b>P value</b>
MAC (60min) i.e. < 1	5 (16.6%)	1 (3.3%)	0.0837

- Out of 60 patients, only 6 patients required the anaesthetic at a lower concentration at one set point of time.
- Therefore there was no significant difference in the requirement of anaesthetic agent in both the groups.

**Figure 10**

**Complications**



- Over sedation was seen in 6.67% of patients in group A whereas 10% of patients in Group B.
- Hypotension requiring treatment was seen in 33.33% of patients in Group A whereas 30% of patients in group B.

**Table 10**

**Complications**

	<b>GROUP A</b>	<b>GROUP B</b>	<b>P value</b>
Over sedation	2 (6.67%)	3 (10%)	0.640
Hypotension	10 (33.33%)	9 (30%)	0.781
Bradycardia	1 (3.33%)	0 (0%)	0.313

- The complication rate of excessive sedation, bradycardia and hypotension requiring treatment was not significant between both the groups.

## DISCUSSION

Controlled hypotension is a very useful technique in surgeries where a bloodless field is expected. Hypotensive techniques are used widely in anaesthesia practice in cases where major blood loss may occur or to aid a “bloodless surgical field”. Volatile anaesthetic based anaesthetic techniques and total intravenous anaesthetic technique has been in use for many years.

However, the need of better results and improvement in the surgical field has always been a reason for further research. This has led to studies on many other drugs for achieving controlled hypotension. Clonidine, a hypotensive agent belonging to alpha 2 agonist class of drugs, has come up with promising results in achieving bloodless field when used with balanced anaesthesia. It also has other benefits like analgesia, sedation and reduction in anaesthetic requirement. This study was designed to evaluate the hypotensive effect of clonidine when used with balanced anaesthesia, along with its other benefits, especially in our Asian population.

In our study, target MAP of 55-65mmHg was achieved in 46.6% of the patients in the clonidine group versus 6.7% the placebo group with just the induction dose of fentanyl (1.5 mcg/kg). Moreover, only 53.3% of patients in the clonidine group versus 93.3% in the placebo group needed extra fentanyl (up to a total dose of 4mcg/kg) to achieve the target MAP. The use of rescue drug metoprolol was 10% in clonidine versus 73.3% in the placebo group. Thus clonidine is effective to achieve controlled hypotension as part of balanced anaesthetic technique. These observations are similar to the study done by Lee et al (18) and Hackmann et al (29). However there were few patients in both the (2 in clonidine and 3 in placebo) groups, who required propofol for

achieving the target MAP, despite using metoprolol. In a study by Lee et al(18) 46 patients were studied to compare the hypotensive effect of clonidine with placebo in middle ear and nose surgery. Their aim was to achieve a systolic blood pressure of 80mmHg. It was seen that there was no difference in MAP in the two groups before and during anaesthesia, except in the values at the 45 minute of surgery in both groups where reduction in MAP was found to be significant.

As regard to the requirement of additional fentanyl, there were only 16 patients in clonidine group that required fentanyl whereas in placebo group 28 patients out of 30 required fentanyl. This is similar to the studies done on clonidine to emphasize its effect in reducing the requirement of fentanyl, isoflurane and beta blockers (study by Hackmann et al(29) on adolescent children to investigate whether clonidine lessened the requirement of fentanyl, isoflurane and labetalol) except that our study did not show significant reduction in isoflurane requirement.

In a study by Mandal et al(8), hypotensive anaesthesia was achieved in 30 patients undergoing FESS using isoflurane. MAP of 55-60mmHg was aimed in this study for which mean inspired isoflurane used was 3.8%.

We had set a maximum MAC of 1.0 for isoflurane whereas other studies have used a higher MAC. There was no reduction in the requirement of isoflurane for maintenance of anaesthesia with the use of clonidine. This may be due to the maximum limit we had set.

There was no significant difference between the two groups in terms of heart rate measured at different time intervals as opposed to the study done by Nair, Salil et al (27) where beta blockers were used for hypotension in FESS. Their study showed a significant difference in overall mean heart rate between the placebo and the beta-blocker groups ( $p < 0.0001$ ).

Concomitant use of fentanyl was seen somewhat equally in both the groups without any large difference.

In our study, the blood loss was less in the clonidine group. As seen in a study by Mandal et al there was significant difference in the intraoperative blood loss. Mandal et al found that hypotensive anaesthesia with isoflurane resulted in less bleeding compared to normotensive anaesthesia provided by isoflurane. In our study, it was seen that many patients achieved controlled hypotension in clonidine group with mean blood loss of 63.5ml(40-200ml), whereas in placebo group with mean blood loss of 180ml(70-300ml), which was statistically significant.

Though the target blood pressure was achieved in both the groups, the placebo group needed more fentanyl and metoprolol to achieve the target MAP. Thus the MAP in the placebo group was higher most of the time (though it was brought to target level ultimately) causing more blood loss. We classified the grading of surgical field as poor, good and excellent based on the Fromme-boezaart scale of surgical field grading. Clonidine group had significantly excellent surgical field of operation when compared to the placebo group ( $P = 0.05$ ).

Post-operative analgesia was better in patients who received clonidine. It was found that patients who received clonidine had much lesser pain score than the ones

who did not receive the drug. Clonidine group demonstrated the range of (0-3) on VAS whereas placebo group had VAS score range of (0-5), which was significant.

Sedation score was found to be comparable in both the groups. The anaesthetic concentration was titrated using the anaesthetic gas analyzer, towards the time of extubation. Excessive sedation was seen in very few patients in both the groups, results of which did not show any significance. The other complications like hypotension and bradycardia requiring treatment were comparable in both the groups.

## CONCLUSIONS

Clonidine when used in a dose of 3mcg/kg intravenously 30 minutes prior to induction of anaesthesia in FESS

- Is effective in achieving controlled hypotension when used with balanced anaesthesia in FESS.
- Is effective in reducing the intra-operative requirement of additional fentanyl and metoprolol.
- Effectively reduces the intraoperative blood loss and offers a conducive operating field.
- Provides good analgesia property.
- Is devoid of serious hypotension, bradycardia and does not cause over sedation prolonging the recovery time.



## BIBLIOGRAPHY

1. **Stammerger H , Posawetz W.** Functional endoscopic sinus surgery.concept,indications and results of the Messerklinger technique. . *Eur Arch Otorhinolaryngology*. 1990;247:63-76.
2. **Robert Slack, Grant Bates.** Functional endoscopic sinus surgery. . *Laryngoscope*. 1990;100:986-88.
3. **Stankiewicz J A.** Complications of endoscopic intranasal Ethmoidectomy. *Laryngoscope*. 1987;97:1270-3.
4. **Maniglia AJ.** Fatal and other complications of endoscopic sinus surgery. *Laryngoscope*. 1991;101:349-54.
5. **Boezaart A P , Vander Merwe J, Coetzee A.** Comparison of sodium nitroprusside and esmolol-induced controlled hypotension for functional endoscopic sinus surgery. *Can.J. Anaesth* 1995;42:373-6.
6. **G Tirell et al.** Total intravenous anaesthesia in endoscopic sinus nasal surgery. *Acta Otolaryngol ITAL*. 2004;24:134-144.
7. **Garder J W.** Control of bleeding during operation by induced hypotension. *JAMA*. 1946;132:572.
8. **P.Mandal.** Isoflurane anaesthesia for functional endoscopic sinus surgery. *Indian J Anaesth*. 2003;47(1):37-40.
9. **Prys-Roberts C, Lloyd J W, Fisher A , .** Deliberate profound hypotension induced with halothane:Studies of hemodynamics and pulmonary gas exchange. *Br. J Anaesth*. 1974;46:105.
10. **Ronald D Miller, Hugo Van Aken, Edward D Miller, .Jr eAYCL.** 2000:1472.
11. **Boonmak S, Boonmak P, Laopaiboon M.** Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery(FESS). *Cochrane database of Systematic Reviews*. 2007(3).

12. **Maze M, Tranquilli W.** Alpha-2-adrenoceptors agonists.defining the role in clinical anaesthesia. *Anesthesiology*. 1995;74:581-605.
13. **Woodcock E T, Millard R K, Dixon J, Prys-Roberts C, .** Clonidine pre-medication for isoflurane-induced hypotension. . *Br.J Anaesth*. 1988;60:388-94.
14. **Toivonen J, Kaukinen S.** Clonidine premedication:a useful adjunct in producing deliberate hypotension. *Acta Anaesth.Scand*. 1990;34:653-7.
15. **Leslie K, Mooney P H, Silbert B S, .** Effect of intravenous clonidine on the dose of thiopental required to induce anesthesia. *Anesthesia Analg*. 1992;75:530-5.
16. **Carbine U A, Wright PMC, Howe JP, Moore J, .** Cardiovascular effects of intravenous clonidine: partial attenuation of the pressor response to intubation by clonidine. *Anesthesiology*. 1991;46:634-7.
17. **Maroof M, Khan RM, Bhatti TH, .** Clonidine premedication for induced hypotension with total intravenous anesthesia for middle ear microsurgery. . *Can J Anesth*. 1994;41:164-5.
18. **J Lee, A T Lovell, M G Parry, H R Glaisyer , L M Bromley.** IV Clonidine: does it work as a hypotensive agent with inhalation anaesthesia? . *Br J Anaesth*. 1999;82:639-40.
19. **Vazeery AK, Lunde O.** Controlled hypotension in hip joint surgery.An assessment of surgical hemorrhage during sodium nitroprusside infusion. *Acta Orthop Scand* 1979;50:433.
20. **PP Kadam, SG Saksena, SR Jagtap, SM Pantavaidya.** Hypotensive anaesthesia in spine surgery-nitroglycerine vs halothane. 1993;49:26-8.
21. **Cushing H.** Tumours of nervus acusticus. *Philadelphia(W B Saunders)*. 1917.
22. **Eckenhoff JE, Rich JC.** Clinical experience with deliberate hypotension. *Anaesth Analg*. 1966;45:21-28.

23. **Enderby GEH.** Controlled circulation with hypotensive drugs and posture to reduce bleeding during surgery. Preliminary results with pentamethonium iodide. *Lancet.* 1950;1:1145.
24. **Enderby GEH.** Halothane and hypotension. *Anaesth.* 1960;15:25.
25. **VanAkenH, Fitch W, Graham DI.** Cardiovascular and cerebrovascular effects of isoflurane-induced hypotension in the baboon. *AnaesthAnalg.* 1986;65:565.
26. **Lam AM, Gelb AW.** Cardiovascular effects of isoflurane-induced hypotension for cerebral aneurysm surgery. *Anesthesia Analg.* 1983;62:742.
27. **Nair, Salil et al.** The effect of beta blocker premedication on the surgical field during endoscopic sinus surgery. *Laryngoscope.* 2004;114(6):1042-1046.
28. **Vladimir Nekhendzy et al.** The effect of deliberate hypercapnia and hypocapnia on intraop blood loss and quality of surgical field during functional endoscopic sinus surgery. *Anaesth Analg.* 2007;105(5):1404-1409.
29. **Hackmann T, Friesen M, Suzanne Allen, David S.Precious.** Clonidine Facilitates Controlled Hypotension in Adolescent Children. *Anaesth Analg.* 2003;96:976-81.
30. **Oddby Muhrbeck E, Jakobsson J, Enquist B.** Implicit processing and therapeutic suggestion during balanced anaesthesia. *Acta Anaesthesiol Scand.* 1995;39:333-7.
31. **P BMW Timmermans, W Hoefke, H Stahle, P A van Zweitan.** *Best practice & Research Clinical Anaesthesiology.* 2000;14(2):237-246.
32. **Kobinge W, Pichler L.** Evidence for direct alpha adrenoreceptors stimulation of effector neurons in cardiovascular center by clonidine. *Euro.J Pharmacol.* 1974;27:151-154.
33. **McRaven D R, Kroetz F W, Kioschos J M, Kirkendall W M.** The effect of clonidine on haemodynamics in hypertensive patients. *Amer.Heart J* 1971;81:482-489.

34. **Onesti G, Bock KD, Heimsoth U, Kim KE, Mergnet P.** Clonidine, a new antihypertensive agent. *Amer J Cardiology*. 1971;28:74-83.
35. **Reid J L, .** The fourth Lilly Prize Lecture, University of Aberdeen, September 1980. The clinical pharmacology of oral clonidine and related central antihypertensive agents. *Br J Clin. Pharmacol*. 1981;12:295-302.
36. **Davies D S, Wing L M, Reid J L, et al.** Pharmacokinetics and concentration effect relationships of intravenous and oral clonidine. *Clin Pharmacol Ther*. 1977;21:593-601.
37. **Timmermans P B, Brands A, Van Zweitan P.** Lipophilicity and brain disposition of clonidine and structurally related imidazolines. *Naunyn-Schmiedeberg Arch Pharmacol* 1977;300:217-26.
38. **Klimcsa W, Tong C, Eisenach J C, .** Intrathecal alpha 2 adrenoceptors agonist stimulate acetylcholine and norepinephrine release from the spinal cord dorsal horn in sheep. An in vivo microdialysis study. *Anaesthesiology*. 1997;87:100-6.
39. **Stocche RM, Garcia LV, Reis MP, Miranda Junior O.** [Intravenous clonidine in the induced arterial hypotension technique for tympanoplasty] *Rev Bras Anestesiol*. 2003;53(4):457-66.
40. **Zalunardo M P, Zollinger A, Spahn DR, et al.** Effects of intravenous and oral clonidine on hemodynamic and plasma-catecholamine response due to endotracheal intubation. *J Clin Anaes*. 1997;9(2)(March):143-7.
41. **Zalunardo M.** Preoperative clonidine attenuates stress response during emergence from anesthesia. *J Clin Anaes*. 2000;12(5):343-349.
42. **Rhee K, Kang K, Kim J, Jeon Y.** Intravenous clonidine prolongs bupivacaine spinal anaesthesia. *Acta Anaesthesiol Scand*. 2003;47:1001-1005.
43. **Liu S, Chiu AA, Neal JM, Carpenter RL, Bainton BG, Gerancher JC.** Oral clonidine prolongs lidocaine spinal anesthesia in human volunteers. *Anaesth*. 1995;82(6):1353-9.

44. **Gabriel AH, Faryniak B, Sojka G, Czech T, Freye E, Spiss CK.** Clonidine: an adjunct in isoflurane N<sub>2</sub>O/O<sub>2</sub> relaxant anaesthesia. Effects on EEG power spectra, somatosensory and auditory evoked potentials *Anaesthesia* 1995;50(4):290-6.
45. **Ghignone M, Calvillo O, Quintin L, .** Anaesthesia and hypertension:the effect of clonidine on preoperative hemodynamics and isoflurane requirements. *. Anaesthesiology.* 1987;67:3-10.
46. **Fehr SB, Zalunardo MP, Seifert B, et al.** Clonidine decreases propofol requirements during anaesthesia: effect on bispectral index . . *Br J Anaesth.* 2001;86(5):627-32.
47. **Gugliel Minotti J, Descraques C, Petitmaire L, Almenzi L, Grenapin O, Mantz J.** Effects of premedication on dose requirement of propofol;comparison of clonidine and hydroxyzine. *Br J Anaesth.* 1998;80:733-6.
48. **Mandke A, Mevada H, Borkar S, Mandke N.** Clinical efficacy of clonidine as an adjunct to anaesthesia for coronary artery bypass graft surgery. *AnnCard Anaesth.* 1999;2(1):22-7.
49. **Katoh T, Ikeda K.** The effect of clonidine on sevoflurane requirements for anaesthesia and hypnosis *Anesthesia* 52(4):377-81.
50. **Zalunardo M P, Serafino D, Szelloe P, et al.** Preoperative clonidine blunts hyperadrenergic responses to prolonged tourniquet pressure during general anaesthesia. *Anaesth Analg.* 2002;94:615-618.
51. **Koleff MH, Lery NT, Ahrens TS, Schaiff R, Prentice D, Sherman G.** The use of continuous intravenous sedation is associated with prolongation of mechanical ventilation. *Chest.* 1998;114:541-8.
52. **Bonnet, Franis, Olga B, Sylvie Rostaing, Loriferne, Saada M.** Clonidine induced analgesia in postoperative patients:Epidural versus Intramuscular administration. *Anaesthesiology.* 1990;72:423-27.

53. **Curletta J D, Coyle R J, Ghignone M.** Systemically administered clonidine enhances postop epidural opiate analgesia. *Anaesth Analg* 1989;68(supp):661.
54. **Gordh T Jr.** A study on the analgesic effect of clonidine in man. *Acta Anaesth.Scand.* 1983;78:72.
55. **Kariya N, Shindoh M, Nishi S, Yukioka H, Asada A.** Oral Clonidine for sedation and analgesia in a burn patient. *J Clin Anaes.* 1998;10:514-7.
56. **Ostadalipour A, Jamshidi M, Zamani A, Jamshidi M, Tavasoli AA.** Analgesic and antisympathetic effects of clonidine in burn patients. *Indian J Plast Surg.* .2007;40:29-33.
57. **Lyons B, Casey W, Doherty P, McHugh M, Moore KP.** Pain relief with low dose intravenous clonidine in a child with severe burns. *Intensive Care Med.* 1996;22:249-51.
58. **Sullivan A F, Dashwood M R, Dickenson A H.** Alpha 2 adrenoreceptors modulation of nociception in rat spinal cord:location,effects and interactions with morphine. *Eur J Pharmacol*1987;138:169-177.
59. **Segal IS, Jarvis DA, Duncan SR, White PF, Maze M.** Perioperative use of transdermal clonidine as an adjunctive agent. *Anaesth Analg.* 1989;68:250.
60. **P J Kulka.** Clonidine prevents Sevoflurane -induced agitation in children. *AnaesthAnalg.* 2001;93(2):335-338.
61. **I Dobrydnjov et al.** Intrathecal and oral clonidine as prophylaxis for alcohol withdrawal syndrome:A randomised double blinded study. *AnaesthAnalg.* 2004;98(3):738-744.
62. **Marwaha J, Kehne JH, Commissaris RL, Lakoski J, Shaw W, Davis M.** Spinal clonidine inhibits neural firing in locus coeruleus. *Brain Res.* 1983;276:379-82.
63. **Mao CC, Tsou MY, Chia YY, Chow LH, Chan KH, Lee TY.** Pre anaesthesia oral clonidine in effect to prevent post spinal shivering. *Acta Anaesthesiol Sin.* 1998;36:137-42.

64. **Powell RM, Buggy DJ.** Ondansetron given before induction of anaesthesia reduces shivering after general anaesthesia. *AnaesthAnalg.* 2000;90:1423-7.
65. **Delaunay L, Bonnet F, Duvaldestin P.** Clonidine decreases postoperative oxygen consumption in patients recovering from general anaesthesia. *Br J Anaesth.* 1991;67(4):397-401.
66. **Theodore Athanasiadis, Achim Beule, Jose Embali, Elke Steinmeier, John Field, PJ Wormald.** Standardized video-endoscopy and surgical field grading scale for endoscopic sinus surgery( ESS):A multicentre study. *Laryngoscope.* 2008;118(2):314-319.
67. **O Detriche, J Berre, J Massaut, Vincent J.** The Brussel's sedation scale:use of a simple sedation scale can avoid excessive sedation in patients undergoing mechanical ventilation in the intensive care unit. *Br J Anaesth.* 1999; 83(5):698-701.

# PROFORMA

Serial number:

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(INTRAVENOUS CLONIDINE AS HYPOTENSIVE AGENT IN ACHIEVING CONTROLLED HYPOTENSION IN FUNCTIONAL ENDOSCOPIC SINUS SURGERY)

Name:

Hospital no.:

Age:

Sex:

Weight:

**Clinical diagnosis:**

NO PREMEDICATIONS.

**MONITORS :** Pulse oxymetry

Non invasive bloodpressure(NIBP)

Electrocardiogram(ECG)

End tidal carbondioxide

Gas analyzer for minimum alveolar concentration(MAC)

**IV CLONIDINE /PLACEBO :** 3mcg/kg to be administered 30 minutes before induction

in anaesthesia room

**PREOXYGENATION:** with 100% oxygen

**IV INDUCTION :** Fentanyl 1.5mcg/kg

Thiopentone 5 mg/kg

Vecuronium 0.1mg/kg

Endotracheal intubation with appropriate size tube



**MAINTENANCE:**

- O<sub>2</sub> + AIR +ISOFLURANE(maintaining MAC as 1.0)
- IV Paracetamol 15mg/kg
- IV Fentanyl to be administered in aliquots of 10-20 mcg(upto a total of 4mcg/kg) for control of MAP between 55-65mmHg
- If MAP control is not achieved after a total of 4mcg/kg of fentanyl then Metoprolol in 0.5mg boluses to be administered to achieve MAP of 55-65mmHg
- If MAP<55mmHg inspired isoflurane to be reduced by 0.5% till MAC reaches 0.75
- If blood pressure does not improve,ephedrine 3mg in incremental dosage will be given
- If the heart rate <50/minute,atropine(0.02mg/kg)will be given
- IV Ondansetron 0.1mg/kg to be administered just before extubation

**EXTUBATION:**

- Anaesthetic to be discontinued at the end of the procedure
- Reversal agent:Neostigmine(0.05mg/kg)

+

Glycopyrrolate(0.01mg/kg)

- Patient to be extubated when he/she is awake

**MONITORING:**

baseline      pre-induction    (Q 5 min till 30 min.)

	0min	5min	10min	15min	20min	25min	30min
SBP							
DBP							
MAP							
HR							
	At induction				Q 5 minutes till extubation		
	10	15	20	25	30	35	40
	45	50	55	60	65	70	75
SBP							
DBP							
MAP							
HR							
MAC							
	80	85	90	95	100	105	110
	115	120	Postextubation				
SBP							
DBP							
MAP							
HR							
MAC							

INTRAOP BLOOD LOSS: swabs soaked in blood =  
Suction blood =  
Total =

PAIN SCORE : (Visual analogue score)

SEDATION SCORE: 1)Unarousable.  
(Brussel's ) 2)Responding to pain stimulation(trapezius muscle pinching)

& not to auditory stimulation.

3) Responding to auditory stimulation

4) Awake and calm

5) Agitated

COMPLICATIONS: (if any, please tick )

1. Hypotension requiring ephedrine
2. Bradycardia requiring atropine
3. Sedation score of 3

Surgeon's opinion about the surgical field-Fromme-Boezaart scale : (please tick)

- a. Excellent(grade 0-1)
- b. Good(grade 2-3)
- c. Poor(grade 4-5)

Total dose of metoprolol in milligrams (if used):

Total dose of fentanyl in micrograms :

(SBP:systolic blood pressure DBP:diastolic blood pressure

HR:heart rate

MAP:mean arterial pressure

MAC:minimum alveolar concentration)

Total dose of propofol used in milligrams(if used):

## **Christian Medical College, Vellore**

### **Department of Anaesthesia**

A randomized trial comparing the hypotensive effect of clonidine with placebo in patients undergoing Functional endoscopic sinus surgery (FESS).

### **Information sheet**

You are being requested to participate in a study to see if a drug called clonidine is able to reduce your blood pressure successfully within a given range during the sinus surgery which you will be undergoing.

This surgery involves blood loss that can make visibility of the surrounding structures difficult for the operating surgeon and thereby can lead to complications. Lowering the blood pressure can minimize this blood loss and thus offers good result.

### **What does clonidine do?**

Clonidine lowers the blood pressure and heart rate .It has been in use for the treatment of high blood pressure patients. This drug also has pain relief quality as well as provides mild sedation.

### **Does it have any side effects?**

Clonidine has been in use for many years in the treatment of high blood pressure. The side effects have been noticed when it has been stopped suddenly after a long term therapy or if taken in a very high dose than what we plan to use in this

study. These side effects are like drowsiness, dry mouth, low heart rate, low blood pressure, nausea and headache.

**If you take part what will you have to do?**

If you agree to take part in this study, then on the day of the operation you will be given either clonidine or an identical looking drug i.e. a dummy drug through an intravenous cannula which will be introduced in one of your hand veins and will also be used to give saline or other drugs. This cannula is routinely put for all patients undergoing any type of surgeries. Using this dummy drug will help us to know that successful lowering of blood pressure within a given range has been by clonidine and not due to chance.

However patients who will be subjected to the dummy drug will also not suffer harm because another drug called Metoprolol will be used as a rescue medication in both the groups in case the fall in BP is not possible within a given range. Neither you nor your doctor giving anaesthesia will have a choice in whether you get clonidine or dummy drug as this will be decided by a computer generated program. Also neither you nor your doctor will know which drug you got out of the two till the study is over.

Once you are given the assigned drug your BP, heart rate and breathing will be under continuous monitoring. After this you will be subjected to general anaesthesia in a usual way that is applied for this surgery during which your BP, heart rate oxygen saturation and breathing will be strictly monitored by an anesthetist. Once your operation is over you will be woken up and shifted to recovery room where you will be again kept under monitoring till you are fully awake and then will be sent back to your respective ward.

If you choose to withdraw from the study, then, clonidine or the dummy drug will not be administered to you prior to anaesthesia, instead you will be subjected to anaesthesia in the usual way which is practiced routinely for FESS patients and other drugs like metoprolol etc. will be used for lowering the blood pressure during the surgery.

**Can you withdraw from this study after it starts?**

Your participation in this study is entirely voluntary and you can withdraw from this study anytime before you are subjected to anaesthesia. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any serious side effect or your condition worsens, the study drug will be stopped and you may be given additional treatment.

**What will happen if you develop any study related injury?**

We do not expect any injury to happen to you but if you do develop any side effect or problems during the study, these will be treated at no cost to you. We are unable to provide any monetary compensation, however.

**Will you have to pay for the study drug?**

Both clonidine and the dummy drug will be given free of cost to you. The other expenses related to the surgery and the anaesthesia will have to be paid by you as usual.

**What happens after the study is over?**

You may benefit from the study that your blood loss would have got minimized and complications would have been avoided. The result however will however help us to know that clonidine can be used in future for lowering the BP within a given range in patients undergoing FESS

**Will your personal details be kept confidential?**

You will never be identified by name in any publications or presentation of the results of this study. However your medical notes may be reviewed by people associated with the study without your additional permission, should you decide to participate in this study.

## CONSENT FORM

**Study title:** A randomized trial comparing hypotensive effect of clonidine with placebo in patients undergoing functional endoscopic sinus surgery (FESS).

Study no.:

Participant's name:

Date of birth/Age(in years):

I \_\_\_\_\_ son/daughter of  
\_\_\_\_\_

(Please tick boxes)

Declare that I've read the information sheet provided to me regarding this study and have clarified any doubts that I had. ( )

I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at anytime prior to administration of anaesthesia without affecting my usual treatment or my legal rights. ( )

I also understand that neither I, nor my doctors ,will have any choice or knowledge of whether I will get clonidine or the identical looking dummy drug. ( )

I understand that I will receive free treatment for any study related injury or adverse event but I will not receive any other financial compensation. ( )



I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access.

( )

I understand that my identity will not be revealed in any information released to third parties or published. ( )

I voluntarily agree to take part in this study. ( )

Name:

Signature:

Date:

Name of witness:

Signature:

Date:

## KEY TO DATA ENTRY SHEET

Group A = Clonidine

Group B = Placebo

Hosp.No.= Hospital number

MAP-PB = mean arterial blood pressure-preinduction(baseline)

P ( 0 to 30 min)=preinduction MAP at different time intervals

INDUC= Induction

EXTUB=Extubation

SBP-B=Systolic blood pressure(baseline)

DBP-B=Diastolic blood pressure(baseline)

HR-B=Heart rate(baseline)

HR-IND=Heart rate at induction

MAC-ind=Minimum alveolar concentration at induction

Bl.loss=Blood loss(ml)

VAS=Visual analog score

Sed.score= Sedation score

Metop=Metoprolol(mg)

Fenta=Fentanyl(mcg)

Addtn.fenta=Additional fentanyl

Profol=Propofol(mg)

FIELD=Surgical field grading

CompEph=complication(hypotension requiring ephedrine)

CompAtr=complication(bradycardia requiring atropine)

CompSed=complication(over sedation)

S.NO.	GROUP	H.No.	AGE	SEX	WEIGHT	DIAGNOSIS	MAP - PB	P-5min	P-10min	P-15min	P-20min	P-25min	P-30min	INDUC	5min	10min	15min	20min	25min	30min	35min	40min	45min	50min	55min	60min
1	A	754763	39	F	60	b/lsinonasal polyp	87	88	84	83	73	73	73	72	68	69	62	66	59	61	64	62	63	63	63	67
2	A	524441D	45	F	51	b/lsinonasal polyp	75	72	66	65	63	63	62	65	56	54	58	55	63	54	55	60	63	63	63	58
3	B	515971D	52	M	52	b/lsinonasal polyp	85	82	82	83	87	88	87	85	95	73	91	77	78	70	73	75	72	71	70	65
4	B	526743D	53	M	51	Chronic Sinusitis	78	80	86	84	85	84	86	86	94	69	54	76	67	74	67	59	63	65	64	64
5	A	556634D	49	M	63	b/lsinonasal polyp	98	92	84	86	77	77	83	84	69	62	78	65	54	60	54	72	64	66	60	77
6	B	917280C	18	M	94	b/lsinonasal polyp	89	86	92	83	83	88	92	83	105	91	79	64	65	81	69	67	68	66	72	66
7	B	479114D	32	M	55	Chronic Sinusitis	68	71	67	67	68	66	75	73	75	70	67	70	61	64	63	67	63	62	63	66
8	A	126299A	30	M	78	Chronic sinusitis	93	89	87	84	76	83	83	85	60	84	72	64	64	58	56	50	67	61	55	56
9	A	542656d	25	M	75	Chronic sinusitis	77	74	74	74	70	74	78	88	66	75	71	69	60	61	58	65	64	68	61	58
10	B	136251D	27	M	63	Chronic sinusitis	74	74	72	72	74	72	71	86	54	91	68	68	64	59	64	56	55	60	65	64
11	A	398343d	33	F	40	b/lsinonasal polyp	76	76	71	68	67	68	68	76	68	57	67	65	70	67	69	64	63	60	59	70
12	A	398474D	53	M	50	Chronic sinusitis	70	70	68	68	64	64	63	70	80	68	67	64	60	59	54	48	52	53	50	54
13	B	485009D	24	M	74	Chronic Sinusitis	67	68	68	64	68	65	64	74	71	68	96	72	87	70	70	65	66	71	70	83
14	B	772502D	22	M	57	Chronic Sinusitis	78	78	78	76	76	79	78	79	66	100	79	75	71	74	69	68	66	66	63	62
15	A	579524C	43	M	80	Chronic Sinusitis	99	98	89	88	88	86	84	84	89	112	86	82	76	75	79	84	83	85	79	76
16	B	492729D	38	M	54	Chronic Sinusitis	74	70	72	73	72	72	71	73	80	77	72	66	74	70	56	56	54	58	59	57
17	A	091878C	24	M	64	Chronic Sinusitis	78	80	76	72	70	68	68	73	65	68	65	64	64	65	64	60	60	60	60	60
18	B	445949D	26	M	60	Chronic Sinusitis	85	85	90	81	72	99	85	80	103	93	79	81	92	72	69	71	72	112	72	64
19	B	430354D	28	M	55	Chronic Sinusitis	102	102	95	96	93	93	104	86	81	76	66	63	64	65	65	67	64	63	75	59
20	A	527025D	26	M	54	Chronic Sinusitis	83	72	77	71	64	70	65	76	74	70	86	66	59	57	60	59	58	62	62	65
21	A	273723D	56	F	54	Chronic Sinusitis	112	101	84	82	79	78	78	95	78	57	57	64	58	57	43	54	55	55	59	60
22	B	119201D	37	M	80	Chronic Sinusitis	79	72	75	73	73	78	80	84	70	65	75	70	67	64	68	70	55	58	66	65
23	A	713802C	49	M	55	Chronic Sinusitis	95	85	79	78	79	70	71	79	60	67	73	70	63	61	52	60	59	50	67	65
24	A	585410D	40	F	45	b/lsinonasal polyp	89	89	81	82	76	75	73	76	56	80	71	59	61	59	57	62	63	61	67	62
25	B	575831D	32	M	70	Chronic Sinusitis	99	90	90	91	95	91	90	90	90	90	82	75	68	62	63	60	68	62	57	62
26	A	165237C	43	M	50	b/lsinonasal polyp	84	84	82	71	68	62	68	70	59	74	56	58	60	61	55	58	57	64	55	54
27	B	538422d	33	M	63	b/lsinonasal polyp	76	72	71	76	76	70	80	94	85	78	79	61	61	65	78	63	65	61	59	61
28	B	575671d	18	M	60	Chronic Sinusitis	79	75	78	79	78	75	75	76	61	60	73	57	60	54	59	55	55	53	52	57
29	B	587385d	60	F	44	b/lsinonasal polyp	100	100	98	98	96	98	98	108	63	62	62	62	63	64	56	60	64	60	61	58
30	A	579548d	22	M	50	Chronic Sinusitis	82	82	90	77	73	71	67	71	56	77	75	58	66	58	56	57	58	64	60	63
31	A	619236d	22	M	64	b/lsinonasal polyp	66	65	66	64	63	64	68	79	75	64	61	63	63	67	63	58	60	61	57	64
32	B	547810D	49	M	63	b/lsinonasal polyp	90	94	89	94	86	93	94	94	54	73	58	52	71	60	74	89	53	77	66	63
33	A	797256C	40	F	75	b/lsinonasal polyp	79	74	82	66	69	67	69	78	59	83	69	70	67	68	66	63	63	64	63	64
34	B	251319d	21	M	55	Chronic Sinusitis	100	97	97	95	98	98	100	100	72	97	80	100	60	56	52	57	55	56	66	55
35	B	618755D	47	F	50	b/lsinonasal polyp	114	108	106	111	109	104	100	114	55	100	72	53	65	48	47	52	65	55	49	76
36	B	389191D	42	M	80	b/lsinonasal polyp	112	108	102	105	101	99	101	128	98	112	95	81	83	75	66	64	61	60	69	69
37	A	602186d	50	M	63	b/lsinonasal polyp	87	81	77	77	71	72	71	80	59	69	64	45	55	47	49	55	48	53	53	51

S.NO.	GROUP	H.No.	AGE	SEX	WEIGHT	DIAGNOSIS	MAP - PB	P-5min	P-10min	P-15min	P-20min	P-25min	P-30min	INDUC	5min	10min	15min	20min	25min	30min	35min	40min	45min	50min	55min	60min
38	A	523226d	45	F	61	Chronic Sinusitis	82	82	64	61	64	65	68	75	53	71	56	61	58	58	56	58	65	70	66	58
39	A	594165d	23	M	41	b/lsinonasal polyp	74	74	74	71	70	71	71	79	62	61	57	58	59	54	59	53	57	60	60	59
40	B	849853C	26	F	50	b/lsinonasal polyp	71	68	62	68	66	65	73	70	74	78	62	63	65	60	49	59	59	62	58	61
41	A	534234d	32	M	55	Chronic Sinusitis	74	68	68	65	71	71	62	61	55	72	58	56	56	64	62	58	56	64	61	59
42	B	623581d	31	M	60	b/lsinonasal polyp	82	82	82	82	80	82	94	83	75	89	80	74	75	88	88	77	92	77	92	88
43	B	496928D	28	M	50	b/lsinonasal polyp	79	77	77	70	73	77	78	90	98	79	72	65	62	63	60	65	63	54	57	57
44	A	720668C	40	F	76	Chronic Sinusitis	77	73	72	78	78	80	80	68	75	75	67	57	55	48	48	68	69	56	56	55
45	B	523237D	48	M	46	Chronic Sinusitis	63	58	63	62	62	65	58	80	55	42	63	64	58	55	53	50	55	55	56	55
46	A	628473D	28	F	50	b/lsinonasal polyp	76	63	63	56	58	64	60	62	61	55	56	55	55	62	61	56	55	60	59	65
47	B	640177d	33	F	50	b/lsinonasal polyp	89	88	80	78	74	70	70	69	59	66	65	63	62	61	67	59	60	60	60	59
48	A	624734D	32	M	80	Chronic Sinusitis	70	63	63	63	64	63	64	69	78	77	76	74	67	68	68	64	66	67	65	54
49	A	538342D	33	M	78	Chronic Sinusitis	88	64	64	65	63	73	67	85	70	105	102	76	74	63	60	60	55	70	84	66
50	B	334070C	56	F	64	Chronic Sinusitis	90	88	90	86	89	88	88	85	90	75	54	69	71	79	69	63	66	65	52	55
51	B	624250D	59	F	73	Chronic Sinusitis	105	100	100	100	104	101	101	124	88	67	60	64	64	60	59	56	55	61	79	78
52	A	610172D	45	F	70	b/lsinonasal polyp	93	87	87	85	84	80	76	73	86	86	78	56	66	64	64	64	52	65	65	64
53	B	073389B	48	F	68	Chronic Sinusitis	104	100	100	98	99	96	90	96	70	69	71	80	65	65	66	62	57	64	63	54
54	A	482703D	20	M	51	Chronic Sinusitis	74	67	64	64	76	67	60	56	64	64	76	67	60	56	56	55	61	60	63	56
55	B	636380D	57	M	48	b/lsinonasal polyp	89	88	89	90	86	88	88	89	74	103	77	74	70	68	70	64	63	62	57	55
56	B	299970D	41	F	50	Chronic Sinusitis	70	68	69	69	70	70	68	74	70	66	63	60	56	54	67	66	66	66	65	63
57	A	566125D	30	F	50	b/lsinonasal polyp	84	87	80	78	64	69	69	72	64	64	54	56	57	60	62	62	64	70	64	60
58	A	619796D	56	F	56	b/lsinonasal polyp	103	104	116	102	98	96	96	107	100	72	92	68	65	64	78	74	59	63	62	62
59	A	577878D	41	M	65	b/lsinonasal polyp	82	71	68	66	64	64	64	72	70	69	71	72	68	66	65	65	66	65	67	68
60	B	571758D	36	M	84	b/lsinonasal polyp	106	104	100	98	104	104	100	112	114	112	100	69	65	76	66	77	65	65	65	57

S.NO.	65min	70min	75min	80min	85min	90min	95min	100min	105min	110min	115min	120min	EXTUB	SBP - B	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	INDUC	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	40MIN	45MIN	50MIN
1	69	64	63	63	64	64	64	63	63	67			86	133	129	102	109	99	99	99	90	82	99	9	74	80	93	88	97	104	86
2	63	64	65	69	76	77	77	76					80	110	103	100	99	95	95	95	90	86	80	76	79	82	80	80	80	86	86
3	62	72	74	68	66	65	77	74	77	78	78	77	78	108	107	108	110	117	117	116	112	115	99	116	107	103	110	97	106	100	107
4	63	65	65	55	52	73	68	70	61	60	61	62	84	110	107	110	108	110	108	110	110	129	83	70	98	86	94	87	80	77	85
5	66	60	65	63	69	77	56	58	58	65	69	68	74	119	128	126	117	116	102	102	99	95	95	89	89	88	86	84	90	89	88
6	71	65	66	83	81	73	62	62					92	125	120	118	121	121	120	124	115	130	119	105	96	92	111	105	103	101	105
7	65	63	63	63	64	63	66	67					71	103	106	105	100	101	101	107	106	97	95	102	97	87	95	91	91	91	95
8	57	63	56	57	65	61	62	56	60	65	62	65	85	125	125	119	128	119	108	117	126	85	111	96	92	82	82	75	79	79	77
9	60	68	65	68	68	70	63	61	61				77	117	111	109	103	102	110	110	114	91	103	107	98	103	95	94	86	87	80
10	67	69	62	57	58	70	64	55	73	69	61	61	84	114	114	110	110	112	110	110	119	101	124	107	119	105	102	99	94	94	106
11	80	73	70	65	69	68	69	69					73	109	109	98	87	87	90	90	109	93	83	91	100	90	90	92	90	90	88
12	58	65	57	57	57	54	64	55	62	65	65	66	76	104	104	102	99	98	98	99	108	116	95	88	86	86	84	70	74	76	78
13	84	70	67	67	65	65	64	70					83	105	105	107	108	106	101	104	122	106	103	134	108	127	113	107	103	102	110
14	62	65	66	66	65	65	65	64	65	65	65	74	91	117	113	112	109	109	117	117	122	105	105	131	114	110	106	110	111	104	100
15	76	71	70	69	66	66	65	65	68	66			83	138	129	121	105	105	112	114	118	119	13	113	108	112	108	112	114	119	113
16	56	60	67	60	60	60	65	66	66	65			72	114	117	116	114	114	116	116	114	105	106	88	87	97	88	82	78	72	82
17	58	60	62	64	65	65	65	68					80	112	108	107	103	103	100	100	101	93	89	100	95	95	92	109	95	95	92
18	70	70	76	66	65	65	65	65	70	74			87	129	120	124	112	105	123	123	116	121	107	112	105	123	104	103	103	103	158
19	61	60	61	73									80	153	142	13	148	131	147	147	121	116	108	100	104	103	103	99	101	96	94
20	59	59	59	70	74	74							77	122	115	116	113	109	106	105	111	93	97	111	113	90	87	92	87	84	93
21	56	51	54	53	57	70	90						104	155	139	107	106	101	100	99	124	102	78	78	90	78	78	68	77	77	77
22	67	42	52	76	55	66	61	69	63	55			77	120	112	118	115	115	117	119	122	104	94	108	99	95	105	115	102	105	98
23	63	62	59	56	61	61							88	135	119	112	111	112	100	101	112	89	95	105	99	81	82	72	87	88	70
24	64	64	64	63	65	65							89	117	118	109	108	98	98	100	98	76	104	92	82	84	82	77	83	84	84
25	69	63	71	59	60	62	62	69					84	113	111	110	112	113	112	111	112	134	119	109	98	102	89	90	90	92	85
26	61	58	55	54	55	62	64	64					88	114	114	109	104	98	92	92	98	88	101	88	80	94	89	86	88	85	93
27	60	65	65	64	65	65							88	114	112	104	115	114	104	116	116	138	118	110	104	92	92	97	97	100	94
28	61	58	56	76	68	61	64	65	67	59	60	62	80	111	104	110	110	111	104	104	105	97	101	91	85	86	85	87	81	79	88
29	64	68	64	78	87	64	66	62	63	66	75	66	100	128	128	120	124	118	120	120	130	83	82	84	85	95	97	87	94	96	86
30	62	61	59	58	52	58							64	127	127	118	114	110	110	104	108	88	113	103	89	95	93	84	86	87	81
31	62	60	63	61	59	62	63	65					72	105	102	101	106	102	97	109	109	115	103	100	101	105	104	105	98	98	95
32	34	51	65	58	51	75	86	86					88	116	117	116	115	111	115	115	116	71	90	79	76	90	82	96	117	74	103
33	65	61	65	67	75	68	65	67	68				111	109	102	112	88	99	97	98	99	81	108	94	89	93	86	82	85	87	81
34	54	58	57	57	58	67	69	70					90	140	131	130	128	136	137	137	140	112	131	121	86	97	90	96	96	100	95
35	73	72	66	61	60	68	73	57	59	56	64	55	79	181	170	178	171	172	165	162	186	85	158	114	85	84	82	100	78	85	94
36	62	78	69	66	61	62	67	61	50	50	50	63	83	153	152	142	143	137	138	141	156	136	152	130	111	122	96	91	93	89	92
37	59	57	60	58	57	53	56	59	59	57	56		86	120	112	110	94	96	94	94	108	79	90	62	80	70	69	79	70	76	78

S.NO.	65min	70min	75min	80min	85min	90min	95min	100min	105min	110min	115min	120min	EXTUB	SBP - B	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	INDUC	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	40MIN	45MIN	50MIN
38	58	58	57	58	57	60	60	58	58	58	58		80	126	126	98	93	91	94	100	100	72	95	79	78	79	83	77	76	86	97
39	54	59	65	62	57	61	57	57	53	62			66	124	124	120	114	112	112	111	111	97	100	98	98	94	88	90	100	98	93
40	57	69	55	67	62	68	60	70	68	69	57	60	73	103	100	100	94	100	98	104	97	116	108	93	93	91	90	88	92	92	89
41	50	58	59	60	60	64	64	65					92	112	100	10	99	98	97	90	95	83	100	85	78	90	87	90	85	79	86
42	73	80	73	67	66	66	65	69	64	62	61	57	100	114	114	128	118	113	117	130	128	107	98	104	106	124	111	126	125	111	118
43	57	54	53	53	54	50	53	55	64	53	54	55	79	113	107	104	107	106	111	109	127	138	111	105	89	89	94	90	88	100	79
44	60	53	53	56	67	67	52	60	60	60	70	72	90	110	103	104	105	107	121	98	102	90	88	77	79	107	111	86	100	98	105
45	55	57	60	60	57	57	57	58					69	90	95	95	85	84	86	84	94	104	72	63	88	86	83	82	80	77	72
46	55	62	61	65	64	64							67	90	100	100	90	94	100	96	105	102	96	94	106	100	105	102	90	96	110
47	59	56	61	59	5	63	59	56	61	62	61	62	74	118	112	114	110	112	111	99	96	95	88	90	90	86	86	90	87	90	90
48	63	66	66	63	55	49	57	59	58	61			77	115	113	107	105	105	106	111	131	112	116	115	109	100	106	107	99	106	99
49	59	63	66	62	58	55	50	49	57	53	68	88	102	122	108	94	95	94	95	99	100	112	105	144	138	111	109	93	95	99	97
50	59	56	77	78	60	80	70	63	79	71	62	59	88	128	124	128	118	124	124	124	123	110	95	89	80	90	88	126	100	88	87
51	55	58	56	52	56	43	56	55	78	53	63	64	78	166	160	156	156	160	156	156	190	127	94	94	90	94	91	73	86	123	104
52	70	68	69	65	63	63	57	60					72	137	136	130	127	124	124	110	109	105	94	91	93	94	94	93	93	90	92
53	69	68	70	78	66	65	66	64	64	66			87	166	148	148	150	144	140	140	100	108	102	114	92	79	83	96	97	80	92
54	66	60	56	53	53	59	61	58	59	60			71	118	105	96	96	109	107	98	86	96	109	107	98	86	91	90	95	94	99
55	58	60	60	60	58	60	60	57	58	60			84	120	95	132	99	90	90	88	90	81	81	77	75	69	76	74	76	80	88
56	60	56	69	66	67	66	66	70	69	66			72	128	127	128	124	120	120	118	118	104	100	108	98	99	100	87	88	88	88
57	60	64	66	65	65	63	64	65	67				92	127	114	94	99	99	99	105	88	88	74	84	86	85	89	89	89	87	103
58	57	60	67	61	61	70	67	65	65	65	70		94	167	171	194	164	155	155	160	177	159	92	153	103	95	95	118	111	94	89
59	68	69	70	70	69	70	73	69	65	65	65		73	113	94	94	99	95	94	110	99	98	95	97	97	95	93	90	89	88	87
60	68	80	68	68	68	68	68	66	65	65			80	137	130	135	134	135	135	130	125	106	100	120	113	113	102	9	89	97	99

S.NO.	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	DBP - B	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	INDUC	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	40MIN
1	114	99	80	93	93	102	99	81	89	90	99	95			102	73	79	79	79	73	70	70	62	76	55	55	48	59	44	67	56
2	85	81	81	80	78	78	77	80	88	88					96	70	63	55	56	52	50	52	52	52	47	47	57	57	57	47	48
3	95	93	88	96	100	100	99	98	98	98	99	102	107	107	99	78	74	74	74	74	80	80	77	88	65	68	70	58	65	65	63
4	73	72	92	88	93	78	81	76	80	86	81	80	82	84	108	68	71	78	75	74	74	77	77	82	65	49	70	62	67	60	51
5	93	94	90	91	95	90	90	90	95	95	90	95	96	97	122	77	80	83	74	73	63	64	64	59	61	53	58	51	55	58	57
6	101	103	98	98	105	116	111	106	104	104					124	72	75	83	83	70	74	74	84	83	82	78	78	80	80	80	83
7	97	97	93	100	98	99	96	99	100	98					114	56	61	55	57	58	55	57	64	60	60	58	55	57	58	59	56
8	79	87	78	81	82	88	92	98	93	86	77	83	90	92	109	82	78	72	71	67	73	73	73	53	75	65	58	58	50	49	40
9	86	98	98	106	106	103	103	99	99	96	93				108	64	61	63	60	64	62	62	71	49	58	51	50	37	43	38	51
10	106	105	102	97	99	95	90	116	106	88	112	107	101	99	121	70	70	71	74	70	70	70	78	38	80	56	53	50	45	54	46
11	83	92	100	95	96	96	86	88	96	96					96	65	65	65	60	58	48	58	65	63	50	60	57	60	60	60	65
12	78	94	90	85	76	93	77	89	94	88	92	93	93	93	101	59	59	57	48	48	48	50	58	66	51	48	43	42	43	37	40
13	107	120	108	108	99	96	96	97	95	108					120	56	54	45	51	56	53	53	74	59	57	85	63	75	57	59	55
14	105	97	97	101	103	106	106	97	104	107	106	107	107	113	123	67	69	68	67	68	69	69	66	55	90	70	63	59	60	59	54
15	124	109	107	105	100	97	97	90	89	92	90	90			126	89	88	78	83	82	80	78	73	79	105	77	74	66	65	70	73
16	88	79	80	80	91	80	87	88	80	86	86	86			112	62	57	59	60	60	58	59	60	66	59	56	52	55	58	55	41
17	92	90	89	90	90	93	94	92	92	92					114	68	71	68	58	56	52	53	57	50	53	49	46	60	47	47	45
18	109	94	94	90	94	90	90	90	100	103	105	112			126	65	68	72	63	53	62	65	61	77	62	63	53	65	50	54	56
19	106	91	89	89	91	104									118	86	84	81	88	78	80	90	73	70	67	56	50	53	55	54	56
20	90	92	96	91	84	96	99	104							111	71	59	64	58	53	59	53	65	68	64	52	49	47	50	51	52
21	84	83	79	70	76	74	84	97	104						136	97	90	75	74	70	68	68	84	69	50	52	56	51	50	42	47
22	91	88	96	97	71	88	91	97	92	101	94	87			104	69	61	65	61	60	66	70	74	63	58	66	63	57	54	53	61
23	88	87	92	92	87	81	93	93							113	75	68	59	58	59	54	55	60	43	50	55	53	49	46	51	44
24	88	81	86	86	86	84	88	90							122	81	81	74	80	69	68	64	69	50	75	64	52	55	52	50	54
25	82	85	100	92	100	90	92	92	99	95					108	94	82	82	88	90	87	82	80		80	80	71	68	58	52	52
26	88	86	92	80	83	83	82	93	90	90					115	74	74	75	60	60	53	53	60	50	65	46	52	52	52	46	49
27	98	93	98	94	94	94	104	99							118	65	62	61	66	66	60	70	72	66	62	63	46	45	48	64	44
28	87	90	87	87	106	97	95	98	94	100	91	92	95	96	116	62	58	60	62	60	59	59	57	44	57	44	44	34	42	36	37
29	94	89	93	101	87	111	124	92	99	90	90	95	96	96	142	88	88	84	83	82	84	89	96	48	46	46	46	45	47	39	42
30	99	90	93	88	85	83	85	90							90	59	59	72	57	63	51	50	60	37	57	58	40	47	39	40	40
31	104	104	102	100	106	99	101	103	101	103					110	53	54	53	53	51	54	56	58	75	50	48	51	49	57	49	47
32	92	81	70	70	88	76	74	100	115	115					120	80	87	80	87	77	88	88	87	48	69	51	43	66	54	63	80
33	83	85	87	90	82	90	97	90	90	88	93	91			136	70	64	73	60	58	61	61	71	52	78	61	64	59	62	62	57
34	92	98	90	90	92	100	104	104	104	106					135	80	86	86	84	88	88	88	80	58	86	65	100	52	43	43	46
35	91	82	113	114	109	98	98	97	105	108	91	93	89	97	117	94	89	87	93	90	87	81	82	38	74	51	33	49	29	52	27
36	100	100	88	106	100	96	88	89	91	86	73	73	73	90	110	102	95	92	94	90	89	93	113	77	92	77	64	68	62	49	47
37	76	83	78	84	84	80	76	76	77	81	82	83	80		118	68	64	64	60	60	60	60	62	46	54	59	32	39	32	34	34

S.NO.	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	DBP - B	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	INDUC	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	40MIN
38	92	88	88	88	90	92	88	89	89	88	88	90	90		113	69	69	56	51	56	59	60	65	47	63	49	54	51	50	54	58
39	96	94	104	99	92	106	95	95	92	103	99	98			107	51	51	53	54	49	48	50	48	60	42	40	36	37	37	34	42
40	98	84	87	90	87	90	97	95	100	102	96	88	95	95	99	55	51	57	55	55	64	60	74	68	54	56	57	51	52	34	48
41	85	88	70	82	89	89	90	90	90	94					121	67	57	59	56	62	63	52	55	47	64	49	50	56	57	52	49
42	99	96	96	96	97	97	98	98	98	88	92	93	93	94	130	72	73	70	73	69	73	74	72	58	69	67	67	58	59	68	78
43	80	83	81	79	74	73	74	80	95	75	81	80	80	82	110	69	68	68	59	64	67	78	85	68	63	57	55	53	52	57	53
44	90	89	89	87	104	79	99	95	100	98	98	98	102	102	118	69	64	63	65	68	70	59	67	67	60	69	59	55	47	49	38
45	72	77	77	79	80	80	80	88	88	88					100	55	50	56	52	56	50	57	54	66	34	38	47	48	44	40	40
46	100	106	96	100	100	110	108	108							110	70	45	45	40	42	46	40	40	40	33	36	45	36	40	38	40
47	88	88	95	86	88	88	89	90	90	88	90	90	90	88	102	72	70	59	60	60	62	68	60	52	53	50	45	48	48	44	53
48	100	99	99	85	105	87	90	100	100	96	98	98			126	57	48	49	51	49	50	56	55	57	55	51	46	51	49	42	46
49	102	107	107	96	97	90	100	95	84	82	77	93	99	102	148	90	62	55	55	57	58	66	56	77	61	99	95	64	63	54	51
50	91	84	82	81	100	100	81	86	86	100	100	97	93	80	117	74	74	76	70	75	74	74	72	86	71	45	61	51	65	59	53
51	78	84	99	84	92	84	93	100	83	85	82	95	94	95	124	86	86	83	84	85	86	86	104	77	70	56	52	56	53	55	56
52	103	100	86	95	90	90	90	93	93	96					98	83	80	82	77	78	78	70	63	74	70	72	57	65	60	60	37
53	96	104	104	102	106	106	110	112	100	104	108	108			118	83	90	87	80	80	79	79	80	60	60	60	75	57	47	49	57
54	86	90	96	92	86	89	97	99	95	93	96	96			112	52	47	44	46	59	47	40	37	44	46	59	47	40	37	37	43
55	90	88	88	88	88	80	86	85	88	88	90	90			105	80	93	67	70	70	69	63	64	61	58	57	52	50	50	53	57
56	89	90	90	96	96	95	95	95	90	90	90	100			122	67	67	65	66	68	67	67	67	56	56	55	47	47	48	50	50
57	88	88	88	88	89	96	96	96	90	97	97				122	77	78	74	56	60	60	60	65	59	59	59	48	50	50	54	50
58	90	100	92	94	94	87	85	90	99	98	90	99	105		170	82	84	95	89	80	78	78	80	88	65	73	55	65	55	65	63
59	86	90	94	94	96	97	98	99	97	99	99	98	97		105	66	56	56	56	57	58	65	56	53	52	54	57	51	49	48	49
60	99	99	100	107	102	102	98	99	90	98	98	98	98		123	98	97	94	98	96	96	98	70	70	59	50	57	57	57	58	68



S.NO.	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	HR-B	5MIN	10MIN	15MIN	20MIN	25MIN	HR-30MIN	HR-IND	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	
1	64	66	56	58	50	56	56	58	58	58	60	60	60	60			61	84	80	78	71	71	68	66	68	70	70	70	61	60	66	66	
2	49	50	54	54	55	55	56	44	47	48	50	56					58	92	92	89	84	84	84	70	71	65	65	65	66	66	65	66	
3	58	62	56	54	65	64	64	60	60	60	62	57	58	60	60	60	56	86	85	85	88	90	88	88	80	90	110	98	88	88	102	98	
4	59	59	49	49	68	60	63	55	57	56	57	46	56	56	56	56	76	98	98	96	98	88	88	97	97	94	94	90	76	76	92	73	
5	56	58	59	62	57	58	56	56	57	58	60	60	60	58	55	57	76	81	78	72	71	68	70	83	80	80	83	80	67	67	63	57	
6	91	82	71	55	56	57	57	60	57	63	56	54					73	88	86	92	83	84	83	84	94	99	94	88	83	79	81	82	
7	57	57	57	56	56	55	55	54	58	59	59	59					70	80	70	69	69	70	67	70	82	62	67	72	71	63	62	58	
8	63	57	47	59	51	58	49	47	56	46	50	59	55	61	53	54	75	103	104	112	116	105	103	102	113	100	103	94	91	88	88	81	
9	47	54	46	37	54	38	43	49	49	52	44	41	41				58	88	70	75	72	80	92	92	93	72	90	79	73	69	61	60	
10	42	46	54	52	56	59	50	45	48	74	54	45	60	56	49	49	89	71	71	68	69	62	62	63	61	57	70	61	64	62	62	64	
11	46	43	48	46	64	74	65	61	57	65	65	65					65	63	63	61	60	60	60	61	63	72	70	81	92	90	85	85	
12	32	34	49	38	38	38	46	40	46	47	48	48	49	46	46	48	50	59	59	59	53	54	54	54	56	54	69	60	58	59	61	56	
13	54	59	59	76	54	52	54	54	50	56	54	60					76	57	60	58	58	57	55	54	61	68	99	70	62	61	58	58	
14	55	56	51	51	55	53	55	53	56	53	59	59	59	58	56	59	81	79	84	70	77	77	80	80	88	84	90	79	80	74	71	70	
15	74	79	70	66	67	64	62		61	59	59	58	56	61			78	74	74	73	74	79	75	75	77	77	80	82	112	86	82	76	
16	41	43	43	44	44	45	53	53	53	50	50	55	55	55			70	64	64	64	65	60	68	60	68	91	91	8	88	76	70	70	
17	45	50	50	48	48	50	50	48	52	51	51	52					77	64	66	58	57	55	54	54	58	58	58	60	67	58	55	70	
18	56	106	52	64	71	71	70	70	76	73	73	73	72	74			75	91	89	90	84	80	82	107	89	102	98	98	88	84	80	80	
19	54	55	66	51	53	52	51	63									67	120	120	130	107	107	112	104	90	99	101	105	102	107	200	99	
20	53	55	57	54	51	50	50	50	56	56							70	68	65	65	65	59	59	58	90	96	96	96	64	66	66	66	
21	47	48	53	62	48	45	47	46	51	63	70						86	83	74	68	68	66	66	65	72	73	68	73	73	72	75	75	
22	59	45	63	58	56	40	49	72	41	57	51	61	55	44			63	71	69	70	70	70	74	79	84	89	99	99	89	85	84	80	
23	43	51	51	49	44	45	42	44	44	44							74	77	70	68	68	67	65	65	76	75	80	90	90	87	85	80	
24	57	53	60	56	58	58	58	56	60	59							78	87	88	78	82	78	72	72	81	69	78	77	69	72	68	68	
25	50	60	55	49	55	59	53	62	51	51	60	60					79	92	93	93	90	92	92	93	90	113	104	88	82	90	93	94	
26	49	56	47	47	51	50	45	46	48	54	56	56					75	64	64	61	62	64	65	65	64	94	64	89	64	65	57	59	
27	47	40	39	40	40	50	50	50	44	46							76	72	70	72	88	87	80	89	110	96	97	99	102	101	94	90	
28	37	37	33	40	44	39	37	59	50	43	44	49	49	41	40	43	74	66	65	67	67	70	69	69	72	71	84	85	85	74	85	74	
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30	40	52	45	44	44	37	43	32	40	45							52	86	86	85	78	80	85	80	85	83	89	89	80	90	86	70	
31	48	49	43	52	50	48	51	48	46	50	51	53					64	55	58	57	55	54	57	60	90	83	70	66	65	68	66	67	
32	47	68	59	55	28	44	58	54	43	67	77	77					78	85	82	79	80	80	82	80	85	85	93	89	75	70	73	80	
33	56	61	58	59	58	52	60	59	68	62	57	62	59	60	83		103	89	86	73	80	77	77	78	92	92	90	84	90	82	81	78	
34	43	48	60	47	43	48	46	46	48	62	68	68					88	99	89	89	88	90	90	90	89	110	109	106	99	111	101	105	
35	33	49	36	30	57	53	52	48	40	41	50	54	38	40	37	46	59	97	96	96	96	96	92	90	93	78	78	85	77	61	71	70	52
36	43	41	52	52	45	60	52	48	44	44	51	44	34	45	45	44	68	74	79	70	68	70	71	72	73	73	106	75	69	68	66	63	
37	39	34	38	38	37	42	42	44	42	42	42	36	40	41	44		74	80	74	73	73	70	69	69	80	84	83	88	80	94	83	84	

S.NO.	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	HR - B	5MIN	10MIN	15MIN	20MIN	25MIN	HR - 30MIN	HR - IND	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN	
38	67	58	58	58	58	55	56	58	58	60	58	56	55	58	55		79	95	95	79	78	79	77	82	84	80	81	73	68	67	67	67	
39	33	35	40	43	39	40	43	39	32	40	43	37	37	37			52	120	120	116	112	110	110	110	109	109	109	110	110	111	105	98	
40	49	55	49	51	47	63	43	57	57	58	47	60	58	57	51	62	64	84	80	83	80	84	86	81	100	85	84	88	85	84	86	89	
41	48	57	55	53	44	50	50	50	54	54	55	57					82	62	62	56	56	55	52	52	60	56	55	65	57	59	59	51	
42	58	73	68	53	62	48	49	48	47	47	50	46	45	38	41	42	88	62	65	68	74	65	69	67	90	70	84	58	71	57	59	55	
43	46	49	49	49	47	47	47	41	47	47	54	46	54	45	46	50	64	66	59	66	60	60	67	63	65	86	90	86	75	65	65	61	
44	51	43	43	46	58	48	50	50	56	56	55	66	67	66	66	68	79	65	66	67	67	68	76	78	70	70	75	75	73	66	70	57	
45	33	49	50	50	56	48	48	47	48	46	46	46					56	61	55	63	58	56	59	66	66	73	63	77	66	70	64	65	
46	33	45	45	45	36	40	40	40	42	42							46	100	110	92	90	100	108	110	110	112	114	106	110	102	106	100	
47	42	42	42	44	45	51	40	48	44	48	48	48	48	50	50	50	57	77	73	70	66	68	70	70	90	86	86	80	73	83	80	80	
48	48	46	30	44	46	54	42	36	28	35	38	38	44	45			52	76	66	67	72	69	70	76	70	88	86	75	73	74	73	70	
49	50	43	58	76	51	47	51	60	51	45	48	40	42	44	38	57	88	84	76	74	75	76	74	75	75	79	83	83	102	94	89	86	
50	59	58	49	50	47	69	69	55	73	66	58	71	62	53	53	48	86	80	82	80	80	82	81	80	73	62	59	67	66	68	73	64	
51	67	48	47	53	43	47	34	47	44	47	59	59	44	44	47	50	67	72	72	72	69	66	69	66	68	72	63	52	60	53	60	70	
52	57	57	53	59	70	67	61	58	56	57	42	47					70	84	88	80	78	78	77	78	84	90	90	81	73	86	84	84	
53	50	46	55	51	58	59	61	69	70	67	67	67	66	56			77	80	70	69	68	68	68	70	70	85	77	85	75	72	70	64	
54	41	36	39	42	43	38	33	34	39	41	39	40	42	42			78	64	80	75	89	67	73	75	69	75	89	67	73	75	69	65	
55	52	57	57	55	55	55	55	53	55	55	55	55	55	50			78	69	70	88	69	68	68	68	68	68	64	64	64	63	62	60	63
56	50	50	58	55	56	57	38	44	44	44	46	48	50	50			65	84	84	80	84	82	85	85	90	90	90	94	100	87	88	88	
57	55	57	57	56	63	59	53	52	52	60	62	62	60				82	85	72	70	78	77	77	88	70	73	86	89	78	78	78	78	
58	47	54	63	53	50	45	48	58	53	55	62	53	54	55	56		84	88	86	80	75	73	72	74	74	75	67	74	73	71	73	76	
59	51	48	52	53	53	52	57	57	55	62	54	59	59	57	56		61	81	81	78	78	77	70	87	75	70	70	73	75	76	73	72	
60	66	65	59	53	80	64	56	56	56	60	61	60	57	56	57		70	72	70	70	63	62	63	62	61	61	72	71	70	70	70	70	68

S.NO.	40MIN	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	MAC- Ind	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN
1	66	66	69	70	72	72	69	70	74	73	73	74	74	74	74	74		86	0.85	0.85	0.9	0.95	1	1	1	1
2	66	66	66	66	69	66	62	65	67	67	61	66	76	76				80	0.95	1	1	1	1	1	1	1
3	98	97	93	90	87	87	78	78	76	75	72	74	74	75	78	78	74	78	0.85	0.85	0.9	1	1	1	1	1
4	73	73	64	64	64	64	73	70	70	70	72	72	70	72	72	72	72	84	0.9	0.9	0.9	1	1	1	1.1	1.1
5	57	57	58	60	77	77	67	67	81	75	64	62	61	62	66	66	68	74	0.9	1	1	1	1	1	1	1
6	79	72	75	77	80	78	70	74	69	69	77	77	78					90	0.95	1.7	1.1	1.1	1.1	0.9	1	1
7	63	63	63	62	70	68	66	66	66	66	65	68	68					90	0.9	1	1	1	1.2	1.2	1	1
8	80	85	86	86	85	88	90	90	90	98	98	105	102	102	102	102	106	90	0.9	0.95	1	1	1.1	1.1	1.1	1.1
9	64	59	62	68	65	69	65	68	68	70	63	61	61	61				76	0.8	0.9	1	1	1	1	1	1
10	67	66	67	68	70	70	73	70	68	68	70	74	75	71	71	75	75	84	0.8	1	1	1.05	1.1	1.1	1.2	1.1
11	80	80	78	89	92	86	89	83	88	88	89	92	92					74	0.9	0.9	0.9	0.9	1	1	1	1
12	56	56	58	57	58	58	60	61	61	62	65	66	60	60	59	58	59	69	0.9	1	1	1	1	1	1	1
13	57	57	57	57	57	58	58	58	58	60	56	58	66					82	1.2	1.1	1	1	1	1	1	1
14	70	70	73	70	70	70	70	73	75	70	70	70	70	70	75	75	75	75	1	1	1	1	1	1	0.9	1
15	99	100	97	96	90	98	90	88	86	82	80	83	80	80	80			83	0.9	0.9	0.9	0.9	1.1	1	1	1
16	70	68	70	70	69	70	74	70	70	69	70	69	68	79	80			78	0.9	1	1	1	1	1	1.2	1.2
17	64	64	64	59	60	60	60	60	60	62	64	60	62					65	1	1	1	1	1	1	1	1
18	88	80	100	68	78	70	64	70	68	68	69	68	70	70	70			90	1.2	1.2	1.15	1.15	1.15	1.15	1.2	1.2
19	99	92	94	99	92	102	92	98	98									100	0.9	1	1.1	1	1	1	1	1
20	69	69	68	69	60	70	70	72	72	72	74							88	1.05	1	1	1	1	1	1	1
21	75	73	77	85	73	71	73	74	74	74	89	91						108	0.9	0.8	0.8	0.8	0.8	0.9	0.8	0.8
22	77	72	70	64	65	63	68	67	56	57	63	67	66	70	72			72	0.9	1	1	1	1	1	1	1
23	88	82	78	90	87	87	85	83	82	94	94							100	0.9	1	1	1	1	1	1	1
24	70	73	71	73	74	77	77	77	75	78	80							80	0.8	0.9	1	1	1	1.1	1	1
25	90	89	93	90	87	86	85	85	84	84	88	90	90					94	1	1	1	1.1	1.2	1.2	1.3	1.3
26	60	61	62	57	60	57	58	59	59	59	59	58	61					80	0.95	0.8	0.8	0.8	0.9	0.9	1	1
27	89	89	89	84	85	84	84	83	87	84	84							114	0.9	1	1	1	1	1.1	1.2	1.2
28	72	70	74	75	75	69	70	78	77	78	78	78	78	83	80	81	81	101	0.9	1	1.1	1	1.1	1.2	1.1	1
29	77	80	80	80	83	83	87	87	86	77	77	77	78	78	79	80	80	87	0.9	1.1	1.1	1	1	1	1.2	1.2
30	69	79	75	78	76	76	74	70	69	70	70	70						72	0.9	1	1	1	1	0.9	0.8	0.9
31	62	61	62	62	60	62	65	64	63	67	67	66	66					68	0.9	1.2	1.2	1.2	1.3	1.2	1.2	1.2
32	82	74	74	70	67	63	68	70	68	688	76	80	80					88	1.2	1.1	1.1	1.05	0.75	0.8	0.9	0.9
33	81	81	80	78	81	83	81	87	108	87	88	86	85	84	85	84		114	1	1	1	0.9	1	1	1	1
34	101	99	102	99	96	96	95	95	96	108	114	114	114					104	1.2	1	1.1	1.2	1	1	1	1-Jan
35	58	55	70	69	67	75	74	68	67	68	71	71	69	68	68	69	69	83	1	1	1	1.2	1.1	1.1	1.2	1.2
36	62	64	66	72	62	65	76	69	70	68	68	72	62	64	66	72	75	76	1.2	1	1	1	1	1	1	1.1
37	80	82	78	78	84	83	80	80	80	81	82	80	80	83	84	82		80	1	1.1	1	1	1	1	1	0.8

S.NO.	40MIN	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	EXTUB	MAC- Ind	5MIN	10MIN	15MIN	20MIN	25MIN	30MIN	35MIN
38	72	70	68	68	71	69	64	64	66	67	67	68	68	70	68	68		79	0.9	1	1	1	1	0.9	1	1
39	94	109	112	107	100	98	100	105	103	118	118	120	112	112	120			124	0.9	0.9	1	1	1	1	1.1	1
40	82	89	82	80	78	76	81	76	81	84	83	83	88	87	89	85	81	85	1	1	1	1.1	1.1	1.1	1.1	1
41	51	57	62	60	56	58	57	58	60	60	60	59	60					81	1	1	1	1	1	1	1	1
42	60	87	55	58	61	62	64	65	62	64	64	68	62	66	70	64	66	88	1	1	1	1	1.2	1.2	1.2	1.2
43	77	63	64	64	64	64	60	60	65	65	63	66	67	68	68	68	70	83	1	1	1	1.2	1.1	1	1	1
44	70	70	73	67	67	69	69	70	68	90	69	69	64	70	69	68	69	81	1		1	1.2	1.2	1.2	1.1	1.1
45	60	60	60	63	62	77	77	77	69	68	68	70	70					70	1	1	0.9	0.9	0.9	0.9	0.9	0.8
46	100	108	102	102	102	100	100	101	100	106	106							110	1	1	1	0.9	0.9	0.8	0.8	0.8
47	76	78	70	78	83	86	78	83	86	86	97	97	86	94	90	92	93	88	1	1	1	0.9	0.9	0.9	0.9	0.9
48	76	87	70	71	73	73	75	79	72	77	83	81	83	84	79			88	1	1	1	1	1	1	1	1.2
49	93	75	76	74	79	77	71	72	75	75	73	75	70	70	71	75	75	104	1	1	1	1	1	1.2	1.2	1.2
50	60	60	58	59	55	61	62	60	56	60	56	61	57	56	58	66	63	88	0.8	0.9	0.9	0.9	0.7	0.8	0.9	0.9
51	73	73	77	79	80	82	79	79	80	81	79	77	75	73	74	73	77	90	1	1	1	1.2	1.3	1.2	1.2	1
52	73	70	68	66	67	70	70	61	67	68	67	68	68					74	1	1	1	1	1	0.9	0.9	0.9
53	65	58	62	62	62	62	64	61	60	63	68	68	68	68	68			68	1	1	1	1	1	1	1	1
54	61	63	67	66	72	61	79	70	67	66	63	71	70	74	76			80	1	1	1	1	1	1	1	1
55	60	60	60	62	63	64	64	64	64	64	64	64	66	62	65			66	1	1	1	1	1.2	1.2	1.2	1.1
56	88	90	90	90	67	60	68	74	74	74	75	75	75	77	78			78	1	1	1	1	1.2	1.2	1.2	1.1
57	78	77	77	74	73	72	70	71	75	78	75	75	75	74				71	1	1	1	1	1	1	0.9	0.9
58	74	73	74	65	68	67	68	65	67	60	60	76	7	76	76	76		100	1	1	1	1	1	1	1	1
59	72	72	73	76	78	78	80	82	83	85	85	88	85	85	85	80		84	1	1	1	1	1	1	1	1
60	63	67	68	70	70	74	73	72	72	70	70	70	70	70	70	70		73	1	1	1	1.2	1.2	1.1	1.2	1

S.NO.	40MIN	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	Fl.Loss	VAS	Sed.score	Metop	Fenta	Addn.Fenta	PROFOL	FIELD	CompEph
1	1	1	1	1	1	1		1	1	1	1	1	1	0.9	0.9			160	0	4	0	140	40	0	B	0
2	1	1	1	1.05	1							1	0.9					5	0	4	0	100	0	0	A	YES
3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	280	3	2	6.5	200	120	0	C	0
4	1.1	1.1	1	1	1	1	1	1	1.1	1.1	1	1	1	1	1	1	1	580	1	4	0	180	80	0	B	YES
5	1	1	1	0.9	1	1	1	1	1.2	1.2	1	1	1	1	0.9	0.9	0.9	740	0	4	0	240	140	0	B	YES
6	1	1	1	1	1.2	1.2	1.2	1.2	1.3	1.3	1.2	1.2	1.3					320	0	4	5	360	200	0	C	0
7	1	1	1	1	1	1	1	1	1	1	1	1	1					40	0	4	0	140	40	0	B	0
8	1	0.8	0.85	1	1	1	1	1	1.1	1.1	1	1	1.1	1.1	1.1	1.1	1	500	0	4	0	140	40	0	C	YES
9	1	1	1	1	1	1	1	1	1	1	1	1	1	1				65	0	3	0	160	60	0	A	0
10	1.1	1.2	1.2	1.3	1.3	1.2	1.3	1.15	1.3	1.3	1.2	1.2	1.2	1.3	1.4	1.4	1.3	300	1	3	1.5	240	140	0	B	0
11	1	1	1	1	1	1	1	1	1.1	1.1	1.2	1.1	1					200	0	4	0.5	160	100	30	B	0
12	1	1	1	1	1	0.9	0.9	1	1	1	1	1	1	1	1	1	1	200	0	3	0	140	40	0	A	YES
13	1	1	1	1	1	1	1	1	1	1	1	1	1	0.9				70	0	4	2	300	200	0	B	0
14	1	1.25	1.12	1.2	1.2	1.2	1	1	1	1	1	1	1		1	1	1	100	0	3	1	230	130	0	A	0
15	1.2	1	1	1	1	1.2	1	1	1	1	1	1	1	1	1	1	1	230	0	3	4	240	140	50	C	0
16	1.1	1.1	1	1	1	1	1	1	1	1	1.1	1	1	1	1	1	1	66	0	4	1	200	100	30	B	YES
17	1	1	1	1	1	0.9	0.9	1	1	1	1	1	0.95					70	0	4	0	170	70	0	B	0
18	1.2	1	1	1	1	1	1.1	1	1	1	1	1	1	1	1	1	1	75	2	4	3	240	140	0	C	0
19	1.2	1	1	1	1	1	1	1	1	1								180	0	3	2	200	100	0	B	0
20	1	1	1	1	0	1	1	1	1	1	1							50	0	4	0	120	0	0	B	0
21	0.8	0.7	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8	0.8						65	2	3	0	140	40	0	B	0
22	1.2	1	1	1	1	1.1	1.1	1	1	1	1	1	1	1	1	1	1	510	0	4	4.5	240	120	0	C	YES
23	1.1	1	1	1	1	1	1	1	1	1	1	1						50	2	4	0	140	40	0	B	YES
24	1	0.9	1	1	1	1.1	1	1	1	1	1	1						62	0	4	0	100	0	0	A	0
25	1.1	1	1	1	1	1	1	1	1	1	1	1	1					480	5	2	3	250	150	70	C	0
26	1	1	0.8	0.8	0.9	0.8	0.9	0.8	0.9	0.9	0.9	0.9	0.8					20	0	4	0	100	0	0	A	0
27	1.1	1	1	1	1	1	1	1	1	1	1	1						20	0	3	0	200	100	0	A	0
28	1	1	1	1	1.1	1	1	1	1	1	1	1	1	1	1	1	1	200	2	3	4	240	140	0	B	0
29	1.1	1	1	0.9	1	1	1.11	1	1	1	1	1	1	1	1	1	1	120	2	4	2	160	80	0	B	0
30	0.9	0.9	0.9	0.9	0.9	0.8	0.8	0.8	0.8	0.8	0.8							40	0	3	0	130	0	0	A	0
31	1.2	1.1	1	1	1	1	1	1	1.1	1	1	1	1	1				40	0	2	2	240	140	0	B	0
32	0.9	1.1	1.15	1.2	1.05	0.9	0.9	0.9	0.9	1	1	1	1	1				180	0	4	4	220	120	0	B	YES
33	1	1	1	1	1.15	0.9	1.1	1	1	1	1	1	1	1	1	1	1	60	1	4	0	130	0	0	B	0
34	1.2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	20	2	3	3	200	100	0	B	0
35	1.2	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	140	1	3	4	220	120	150	C	YES
36	1.2	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1000	0	3	3	320	200	0	C	YES
37	0.8	0.9	0.9	1	1	1	1	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	40	0	2	0	100	0	0	A	0

S.NO.	40MIN	45MIN	50MIN	55MIN	60MIN	65MIN	70MIN	75MIN	80MIN	85MIN	90MIN	95MIN	100MIN	105MIN	110MIN	115MIN	120MIN	Fl. Loss	VAS	Sed. score	Metop	Fenta	Addn. Fenta	PROFOL	FIELD	CompEph
38	0.9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	60	0	4	0	140	0	0	B	0
39	0.9	0.9	0.9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	250	0	3	0	160	100	0	C	YES
40	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	650	0	3	2	200	125	0	B	0
41	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	150	0	4	0	120	0	0	B	0
42	1.1	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	100	0	4	3	240	140	0	B	0
43	1	1	1	1.1	1.1	1	1	1	1	1	1	1	1	1	1	1	1	210	0	3	2	200	100	0	B	YES
44	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	40	0	4	0	200	100	0	B	YES
45	0.8	0.8	0.8	1	1	1	1	1	1	1	1	1	1	1	1	1	1	50	2	4	0	100	0	0	A	YES
46	0.8	0.9	0.9	0.9	0.9	0.9	0.9	0.91	1	1	1	1	1	1	1	1	1	10	3	4	0	100	0	0	A	YES
47	0.9	0.8	0.8	0.8	1	1	1	1	1	1	1	1	0.9	0.9	0.9	0.9	0.9	300	2	3	0	100	0	0	B	0
48	1.2	1.2	1.2	1.1	1.1	1	1	1	1	1	1.1	1.1	1	1	1	1	1	200	0	4	0	180	60	0	C	YES
49	1.1	1.1	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	0.9	150	0	3	0	260	140	0	C	YES
50	0.9	1	1	1	0.9	0.85	0.9	0.9	0.8	0.8	0.9	0.9	0.9	0.9	0.9	0.9	0.85	180	3	3	0	200	100	0	C	0
51	1	1	1	1	1	1	1.1	1.1	1	1	1	1	1	1	1	1	1	90	0	3	0	200	100	0	B	YES
52	0.9	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	220	0	4	0	160	0	0	A	0
53	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	15	0	3	0	200	100	0	B	0
54	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	30	0	4	0	100	0	0	A	0
55	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	15	0	3	2	200	100	0	B	0
56	1.1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	200	0	3	3	200	100	40	B	0
57	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	10	0	4	0	100	0	0	A	0
58	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	40	0	4	0	100	0	0	B	0
59	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	320	0	2	0	250	150	0	C	0
60	1	1	1	1	1	1	1.2	1.2	1.3	1.3	1	1	1	1	1	1	1	240	2	2	2	320	200	0	B	0

S.NO.	CompAtrro	CompSed
1	0	0
2	0	0
3	0	YES
4	0	0
5	0	0
6	0	0
7	0	0
8	0	0
9	0	0
10	0	0
11	YES	0
12	0	0
13	0	0
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	0	0
20	0	0
21	0	0
22	0	0
23	0	0
24	0	0
25	0	YES
26	0	0
27	0	0
28	0	0
29	0	0
30	0	0
31	0	YES
32	0	0
33	0	0
34	0	0
35	0	0
36	0	0
37	0	0

S.NO.	CompAtrr	CompSed
38	0	0
39	0	0
40	0	0
41	0	0
42	0	0
43	0	0
44	0	0
45	0	0
46	0	0
47	0	0
48	0	0
49	0	0
50	0	0
51	0	0
52	0	0
53	0	0
54	0	0
55	0	0
56	0	0
57	0	0
58	0	0
59	0	YES
60	0	YES