ORAL BISOPROLOL IMPROVES SURGICAL FIELD IN FESS

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

APRIL 2015

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

TAMILNADU

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled **"ORAL BISOPROLOL IMPROVES SURGICAL FIELD IN FESS"** is a bonafide record work done by **Dr. JEYAKKUMAR. R** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of University regulation for MD, Branch X –Anaesthesiology

PROF. Dr .S.C. GANESH PRABU, M.D, D.A,
Director,
Institute Of Anesthesiology,
Govt. Rajaji Hospital &
Madurai Medical College
Madurai.

CERTIFICATE FROM THE GUIDE

This is to certify that this dissertation entitled **"ORAL BISOPROLOL IMPROVES SURGICAL FIELD IN FUNCTIONAL ENDOSCOPIC SINUS SURGERIES"** is a bonafide and genuine research work done by **Dr. JEYAKKUMAR.R.,** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University, in partial fulfilment of the requirement for the degree of MD in Anaesthesiology.

Date:

Place:

DR .T.THIRUNAVUKKARASU,MD.,DA
PROFESSOR,
INSTITUTE OF ANAESTHESIOLOGY,
GOVT. RAJAJI HOSPITAL &
MADURAI MEDICAL COLLEGE,
MADURAI.

DR .S. SENTHILKUMAR,MD.,DA
ASSISTANT PROFESSOR,
INSTITUTE OF ANAESTHESIOLOGY,
GOVT. RAJAJI HOSPITAL &
MADURAI MEDICAL COLLEGE,
MADURAI.

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Date:

Place:

(Capt) Dr.B.SANTHAKUMAR, M.Sc (F.sc), M.D (F.M).
PGDMLE, D.N.B (F.M),
DEAN,
GOVT. RAJAJI HOSPITAL &
MADURAI MEDICAL COLLEGE,
MADURAI.

DECLARATION

I **Dr. JEYAKKUMAR.R.,** solemnly declare that this dissertation entitled **"ORAL BISOPROLOL IMPROVES SURGICAL FIELD IN FESS"** has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other University or board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfilment of the rules and regulations for the award of Doctor of Medicine degree Branch –X (Anesthesiology) to be held in April 2015.

Place: Madurai **Dr. JEYAKKUMAR.R**

Date:

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ORAL BISOPROLOL IMPROVES SURGICAL FIELD IN FESS

ABSTRACT

Background:

The success of functional endoscopic sinus surgery (FESS) depends on visual clarity of the surgical field, through the endoscope. The objective of this double-blind, randomized, controlled study was to determine if a pre-operative dose of Bisoprolol (2.5 mg) would reduce the bleeding during FESS and improve the visualization of the operative field.

Materials and Methods:

Sixty American Society of Anesthesiologists I or II patients, scheduled for FESS were randomized to receive either a Placebo (Group A) or 2.5 mg of Bisoprolol (Group B) 90 min prior to the surgery. All the patients received standard anesthesia and monitoring. The aim was to maintain the mean arterial pressure (MAP) of 60-70 mmHg, by titrating dose of Sevflurane and Fentanyl. The concentration of Sevoflurane used was recorded every 10 min. At the end of the surgery, the volume of blood loss was measured and the surgeon was asked to grade the operative field as per the Fromme-Boezaart Scale.

Result:

The blood loss was significantly ($P < 0.0001$) more in the Control group (97 ± 16.75 ml) as compared with that in the Bisoprolol group (58.3 ± 13.9 ml). The surgical field was graded better in those who received Bisoprolol as compared with those in the Control group ($P - 0.0001$). The volume percent of Sevoflurane and the dose of Fentanyl used was significantly lower in those who received Bisoprolol. During the operative period, the MAPs were 92.87 ± 6.39 (Group A) and 78.25 ± 3.5 mmHg (Group B) and the heart rate was 94.75 ± 3.14/min (Group A) and 67.97 ± 1.84/min (Group B). These differences were statistically significant ($P < 0.001$).

Conclusion:

This clinical trial has demonstrated that administration of a single pre-operative dose of bisoprolol (2.5 mg) can significantly reduce the blood loss during FESS and improve the visualization of the operating field.

Keywords:

Beta-blocker, bisoprolol, blood loss, functional endoscopic sinus surgery, surgical field

INTRODUCTION

One of the mainstay of surgical treatments of sinusitis and nasal polyps is Functional Endoscopic Sinus Surgery. This includes bacterial, fungal, recurrent acute or chronic sinus problems. Ample researches have supported the record of safety and success of FESS. Advanced imaging techniques, better and increased understanding of the anatomy and the pathophysiology of the disease processes like chronic sinusitis, and image-guided surgery have allowed surgeons to perform more complex procedures with increased safety and reduced complications.

FESS is a relatively recent and advanced surgical procedure which uses nasal endoscopes through the nostrils to visualize the inner aspect and to avoid cutting the skin. Its introduction associated with enhanced illumination and visualization has dramatically improved surgical dissection. FESS came into existence through the pioneering work done by **Dr.Messenklinger** and his assistants in 1960 to 1970's.

Remarkable short- and long-term results have been reported extensively in the literature. A report by Senior et al says that symptoms improved in 66 of 72 (91.6%) patients following functional endoscopic sinus surgery, with a mean follow-up time of 7.8 years. In addition to the relief of symptoms, endoscopic sinus surgery also significantly influences quality of life. **Damm et al** reported an improvement in quality of life for 85% of the chronic sinusitis patient population, with a mean follow-up time of 31.7 months.

But the very success of the use of endoscope for sinus surgeries depends on the visual clarity of the operating field. The sinonasal mucosa is very vascular and poor visualization due to excessive bleeding has been blamed for complications associated with this procedure. There is general agreement that bleeding can be reduced by maintaining a low blood pressure during the surgery. This can be achieved using high concentrations of anesthetic agents or administration of vasodilators like sodium nitroprusside.

Controlled hypotension is a technique used to limit intraoperative blood loss to provide the best possible field for surgery. Benefits of controlled hypotension for FESS include reduction in blood loss with improved quality of surgical field. Various agents e.g., magnesium sulphate,vasodilators (sodium nitroprusside) nitroglycerine, high doses of potent inhaled anesthetics, and beta adrenergic antagonist have been used to achieve controlled hypotension. Some disadvantages have been reported of these techniques including delayed recovery from inhaled anesthetics, resistance to vasodilators, tachyphylaxis, and cyanide toxicity for nitroprusside.

However, these pharmacological techniques are associated with tachycardia which, apart from being an undesirable side effect, can increase the venous oozing and therefore obscure the surgical field. β-adrenergic receptor antagonist such as labetalol, metoprolol and esmolol have been shown to be useful in lowering the blood pressure and provide a relatively bloodless field for

surgery, but because of their short duration of action, this benefit does not last throughout the surgery

The present work was designed to compare the efficacy of Bisoprolol as a hypotensive agent in FESS with attention on the amount of blood loss, quality of the surgical field and anesthetic requirements with Placebo.

Indications for Endoscopic Sinus Surgery

Endoscopic sinus surgery is most commonly performed for inflammatory and infectious sinus disease. The most common indications for endoscopic sinus surgery are as follows:

- Chronic sinusitis refractory to medical treatment
- Nasal polyposis
- Antrochoanal polyps
- Sinus mucoceles
- Excision of selected tumors
- Cerebrospinal fluid (CSF) leak closure
- Orbital decompression (eg, Graves ophthalmopathy)
- Optic nerve decompression
- Dacryocystorhinostomy (DCR)
- Choanal atresia repair
- Foreign body removal
- Epistaxis control

AIMS AND OBJECTIVES

1. To compare the efficacy of BISOPROLOL 2.5 mg orally in reducing the bleeding during Functional Endoscopic Sinus Surgery and improving the visualization of the operating field with PLACEBO.

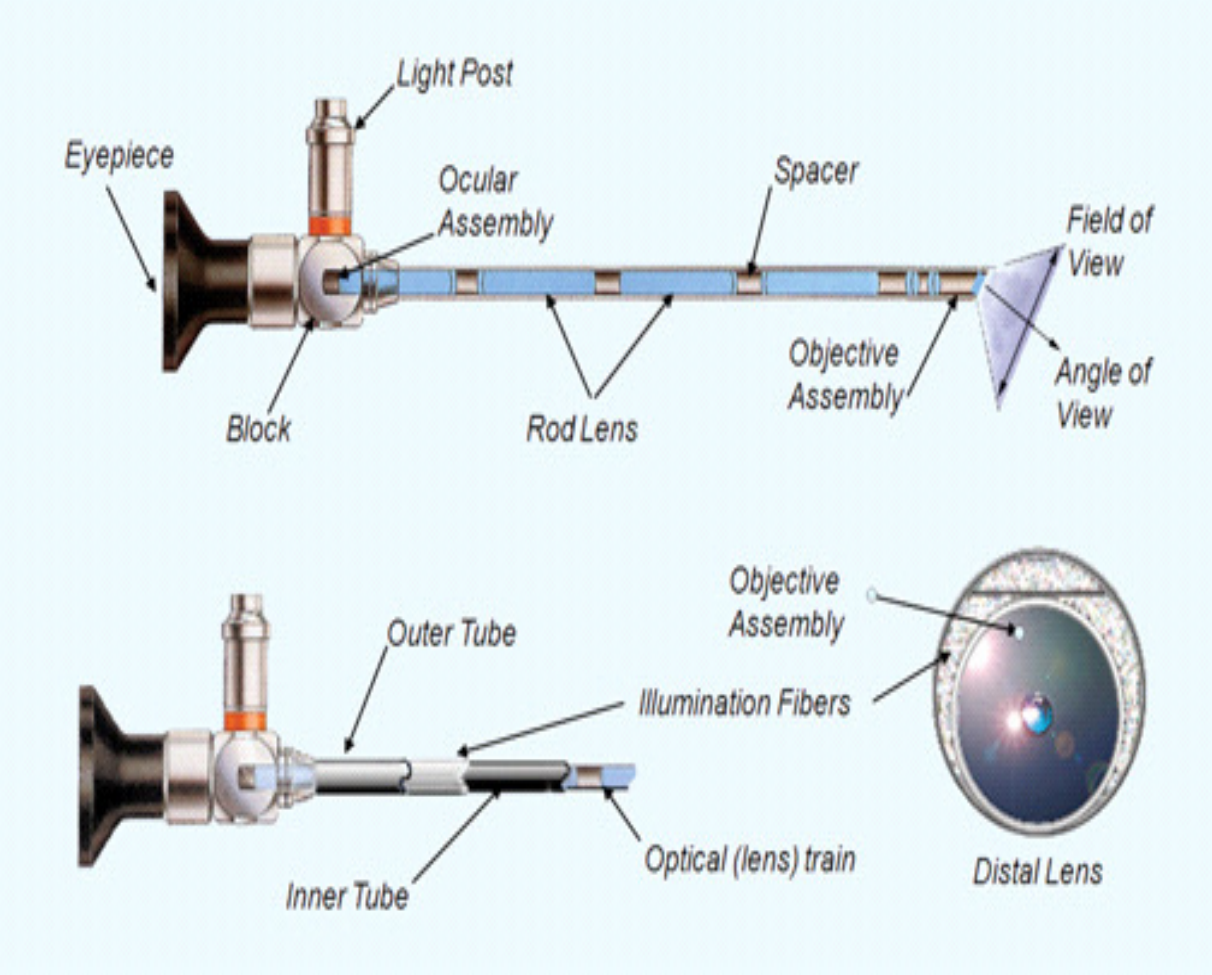
2. To compare the requirements of anesthetics like Sevoflurane and Fentanyl during the procedure with BISOPROLOL and PLACEBO.

HISTORY

Rhinology and sinus surgery have undergone a tremendous expansion since the discourses of **Messerklinger** and **Wigand** in the late 1970s.

In 1901, **Hirschmann** was the first to attempt endoscopic examination of the sinonasal cavity using a modified cystoscope (Hirschmann, 1903). This was followed by **Reichert**, who performed the first endonasal sinus surgery with a 7-mm endoscope for closure of oroantral fistulas (Imhofer, 1910). In 1925, **Maltz** promoted the use of nasal endoscopes for diagnostic evaluation of the sinonasal cavity and coined the term sinuscopy, describing methods for visualizing the maxillary sinus by placing endoscopes through the canine fossa or inferior meatus (Maltz, 1925). However, inadequate illumination and difficulties with depth of field discouraged their widespread use until the 1960s, when Professor **H. H. Hopkins'** recently developed rod optic system was manufactured, dramatically improving resolution, widening the field of vision, and increasing light intensity sixfold over prior endoscopes. It was Messerklinger who was the first to use these nasal endoscopes to systematically analyze the anatomy of the lateral nasal wall and the mucociliary patterns of the paranasal sinuses (Messerklinger, 1978). Through his studies and detailed endoscopic photodocumentation, he determined

that widespread infection of the sinonasal cavities often appeared to originate from pathology within the narrow recesses of the lateral nasal wall. This led to the concept that minor endoscopic surgical removal of disease within this region and enlargement of natural sinus ostia should result in spontaneous resolution of pathology within the adjoining sinuses. Messerklinger compiled all of his endoscopic observations and published his findings in 1978. However, Messerklinger's work did not include the potential endoscopic surgical resolution of these diagnostic observations and therefore did not receive widespread recognition.

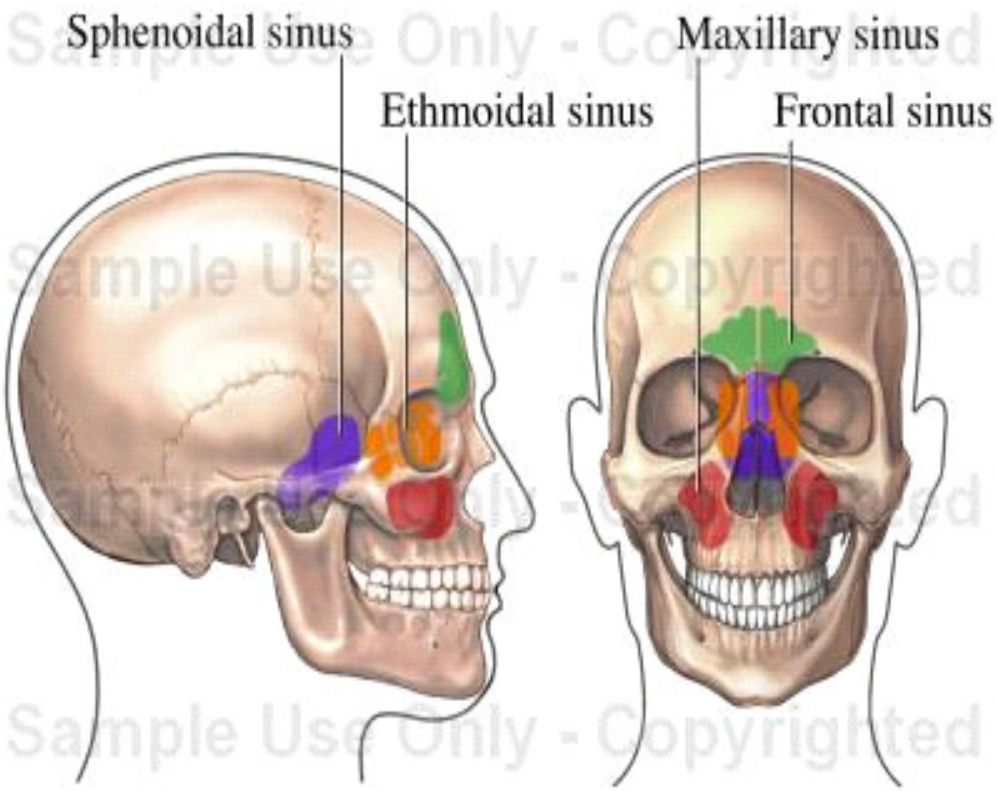


Later, in 1984, **Kennedy**, who had also previously performed animal studies on mucociliary clearance and microscopic endonasal ethmoidectomies, had the opportunity to witness a video demonstration of Messerklinger's work on cadaveric mucociliary transport while attending a conference in Dubrovnik.

The presentation prompted him to visit Stammberger and Messerklinger in Graz, where he had the opportunity to observe Messerklinger's endoscopic diagnostic and operative techniques firsthand. Visits also to Wigand in Erlangen and Draf in Fulda provided further experience with endoscopic surgical approaches and enabled him to begin incorporating these endoscopic techniques into his own operative procedures and to begin working with **Karl Storz** to develop a set of instruments for endoscopic sinus surgery. **Zinreich**, working with Kennedy at Hopkins, developed computed tomography (CT) parameters for sinus imaging and demonstrated the superiority of this modality over the previously available plain films and polytomograms for imaging sinonasal disease, particularly within the ethmoid sinus and ostiomeatal complex.

They termed these new endoscopically guided diagnostic evaluations, and more focused therapeutic and surgical techniques, **"Functional Endoscopic Sinus Surgery."** In 1985, the first instructional course on endoscopic sinus surgery was organized at Hopkins and the use of endoscopic sinus surgery has only grown more widespread with the passage of time.

SURGICAL ANATOMY OF NOSE AND PARANASAL SINUSES



HISTORY

The literary evidence of paranasal sinus way back to **Galen** (AD 160-201). He described the ‘’porosity” of bone in the head. **Leonardo Da vinci** illustrated the maxillary antrum and the fronal sinus from his classical sections of head. He also recognised these as individual functional cavities. Maxillary sinus has been referred as a cavity bone that supports the cheek. First detailed description of maxillary antrum was given by **Highmore** in 1651. Since then maxillary antrum is referred as “Antrum of Highmore”.

But only in 19th century paranasal sinuses were described anatomically and pathologically in a detailed manner, by **Zuckerkandl** who also published that all these descriptions are more valuable that it can be applied to the patients problem directly.

X-ray invention did not contribute much to the knowledge of sinus anatomy. But in mid 1970s, availability of CT clearly showed the relationship of ethmoids with the largest sinus.Since 100 years this knowledge has been developed and applied.

Drawings by **Onodi, Grenwald** and **Zuckerkandl** are compared with CT which demonstrated the accurate knowledge of these pioneers. At the upper airway entrance four pairs of air filled cavities forms a complete unit. During 8th week of embryogenesis, paranasal sinuses develops from the lateral nasal wall.

Pneumatisation of paranasal sinuses continue till adulthood. Each paranasal sinus are named after the bone in the skull where it is located. While

development, involvement of adjacent bones is seen during pneumatisaion, as with the case of ethmoid sinus which is developed into frontal, maxillary or sphenoid, and extension of maxillary sinus in zygomatic bone. The lining of paranasal sinus is by pseudostratified epithelium which also lines the respiratory tract.

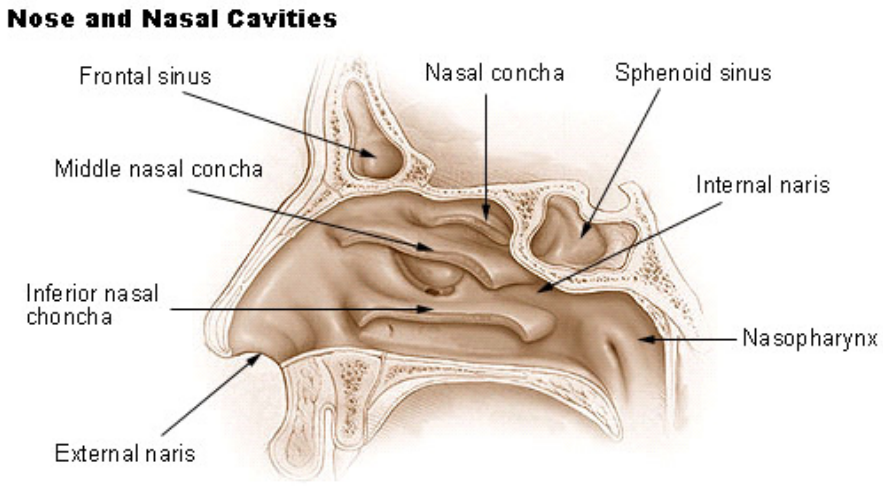
It is composed of,

- Ciliary column
- Nonciliary column
- Goblet , mucous and basal cells

When the mucosa is attached to bone, it is referred as mucoperiosteum. The mucoperiosteum of sinuses are in continuity with the nasal cavity via the ostia and sinuses. An ostium is a opening via which sinuses drains into airway, either into nasal cavity directly or by complex structures indirectly.

When compared to older surgical for paranasal sinus the new concept of FESS acknowledged that sinus ostium and its lining mucosa has an essential role in inflammatory process involving paranasal sinus. So, the diseases of mucosa and its symptoms can be reversible by obtaining proper drainage via the ostium.

NASAL CAVITY:

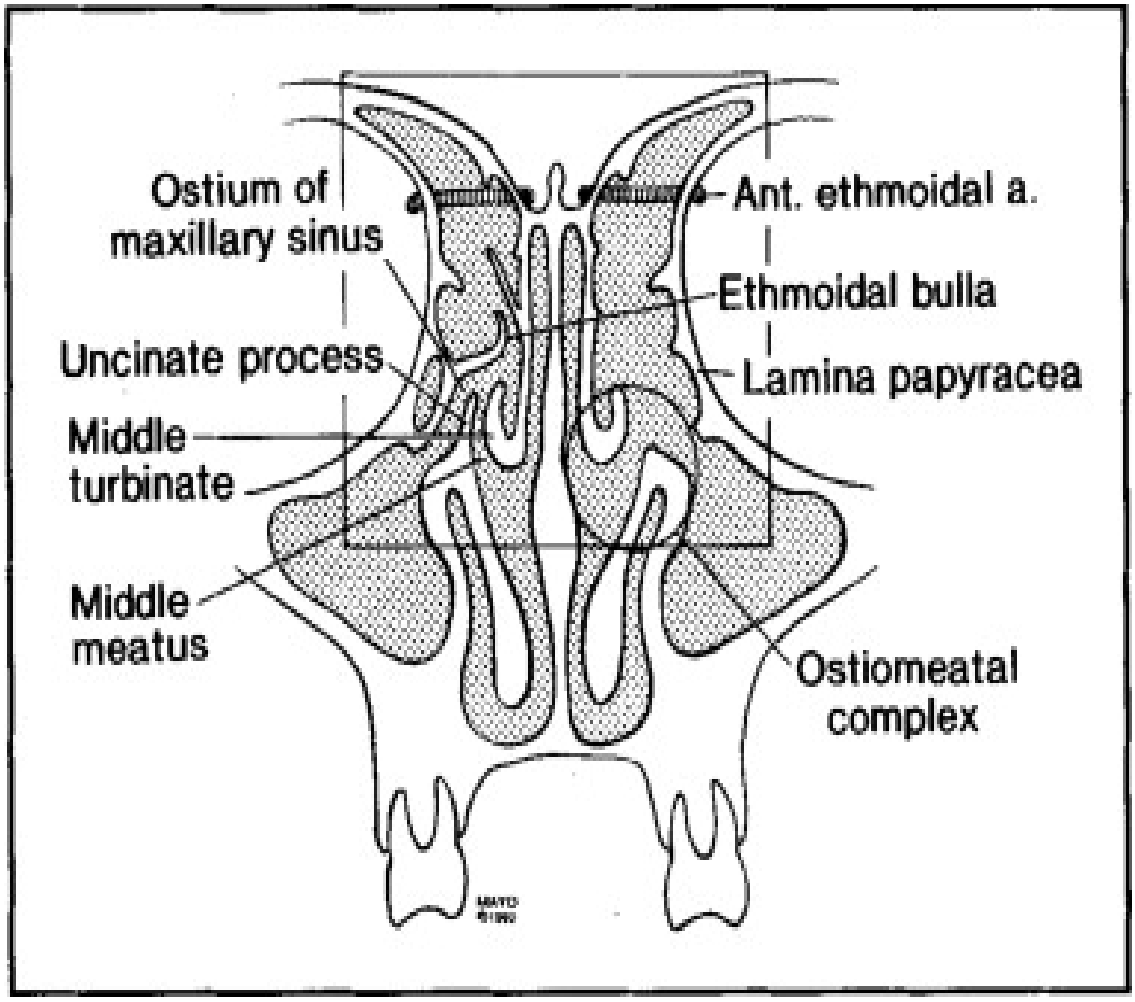


The first cavity encountered during FESS is the nasal cavity. Paranasal sinus opens into the posterosuperior and lateral walls of nasal cavity. Through choanna, nasopharynx is reached by the posteroinferior walls.

In the beginning of FESS surgery, identifying the relationship of choana with the posterior nasal sepum and the Eustachian tube is very important. When nasal airway is obstructed in the inferomedial part by the polyps ,nasal cavity patency must be re-established first. For visualising the choana and providing route for the drainage of blood into the nasopharynx. Conchae or turbinates forms the ridges in the lateral wall of nasal cavity. Embryologically the inferior turbinate is derived from maxilloturbinate. It is inserted on the maxilla anteriorly and on the palatine bone posteriorly.

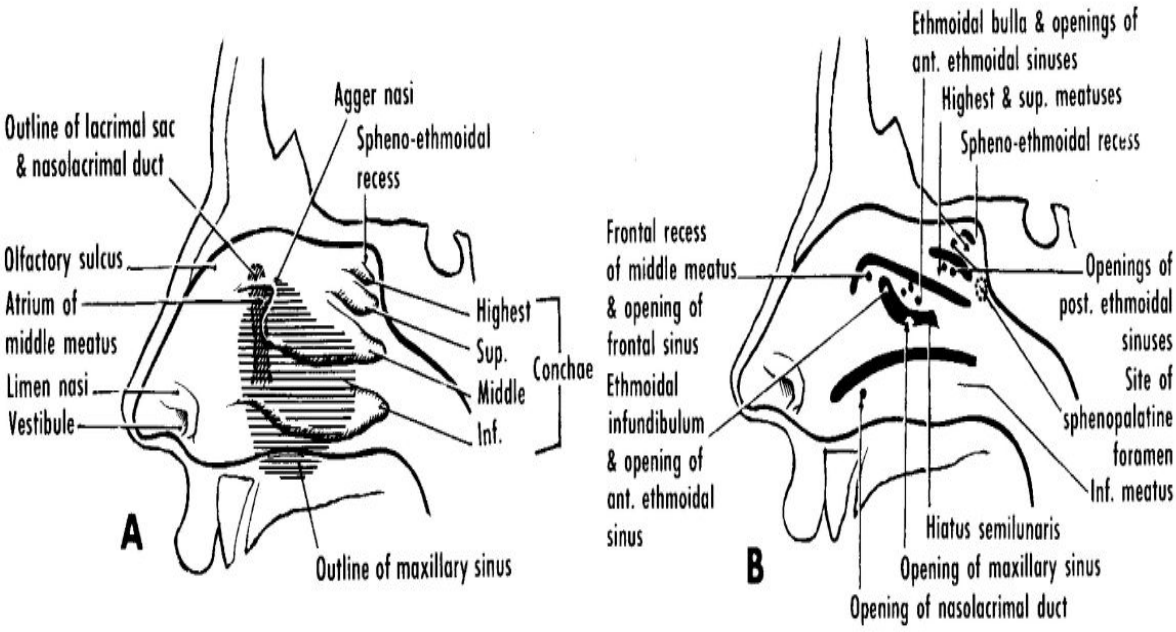
Mourett in1922 described conchal lamina, from which ethmoid turbinates develops(superior and middle). It is a bony plate which is attached between the cribriform and the roof of ethmoid. The turbinates subdivides the nasal cavity in

the lateral part into meati which are four in number. Inferior meatus lies between the lateral wall and inferior turbinate and the medial wall and maxillary sinus. Its distal opening leads to nasolacrimal duct, covered by Hasner's valve. Space between lateral and middle turbinate by middle meatus. Functionally it is known as osteomeatal complex. It contains pathways of drainage for anterior ethmoid, frontal and maxillary sinus. Chronic rhinosinusitis is most commonly involved in the area of middle meatus.



In the middle meatus, the structures seen from anterior side to posterior side are;

- Cells of agar nasi
- Uncinate process
- Hiatus semmilunaris
- Ethmoid bulla
- Sinus lateralis
- Posterior fontanelle



SUPERIOR MEATUS:

It is the lateral space between middle and superior turbinates. Post ethmoid cells are drained by it. Area which drains the post ethmoid cells is the supreme meaus which is the space above the superior turninate.

Nasal cavity is divided as superior part by olfactory cleft in the anterior space, posteriorly by sphenoethmoid recess. The location of olfactory cleft under olfactory fossa between the nasal septum and the insertion of middle turbinate. Just inferior to cribriform plate is its location. Depending on how low the cribriform plate is located in relation with the roof of ethoid,keros classified olfactory fossa into 3 types.

Keros classification:

Type 1 is 1 – 3 mm deep in relationship to the roof of ethmoids and it corresponds to an olfactory fossa.

Type 2 is 4 – 7 mm deep.

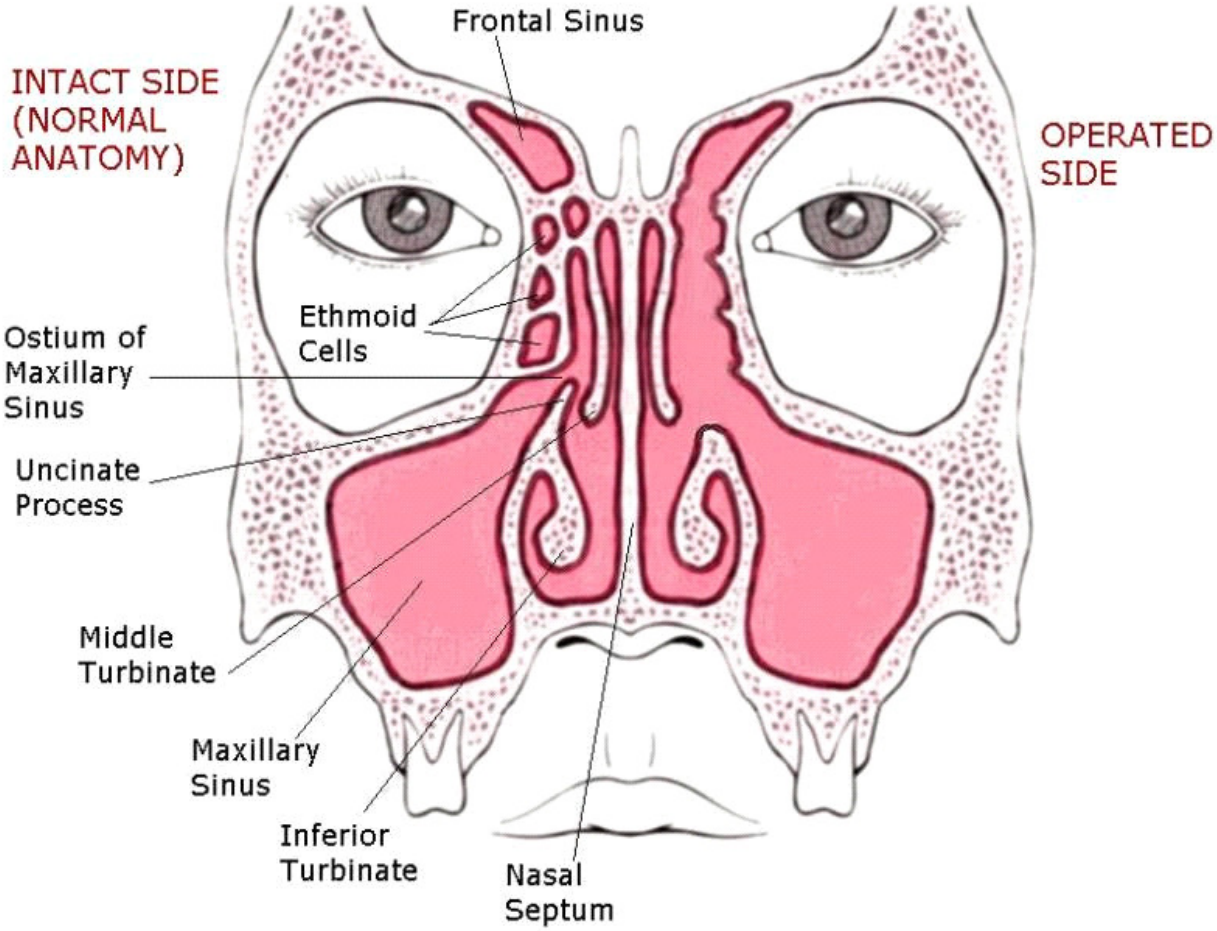
Type 3 refers to a depth of 8 mm and above.

To avoid breaking into the skull base anteriorly, relationship between fovea ethmoidalis, cribriform plate and insertion of superior and middle turbinates are important.

Especially in the least resistant zone, where anterior ethmoid lies between ethmoid roof and conchal lamina. The roof of nasal cavity is very inferior in the posterior part of olfactory cleft, where the sphenoethmoid recess curves in between the posterosuperior septum and the tail of superior turbinate above choana. Posterior ethmoids and ethmoid sinus are drained by this recess through supreme and superior meati. This area is also referred functionally as “posterior” osteomeatal complex, in par with “anterior” osteomeatal complex of middle meatus.

Sphenoid recess constitutes an important surgical landmark which is the tail of superior turbinate, since it is pointed medially to the sphenoid sinus.

MAXILLARY SINUS AND UNCINATE PROCESS:



In endonasal sinus surgeries, Uncinate process is the important landmark which is located in the lateral wall of the nose. Though it is derived from the 1st ethmoturbinal and considered as a part of ethmoid labrynth, typically it is discussed with maxillary sinus due to its close relationship with its ostium.

Uncinate process is a bony structure which is crescent in shape.It is projected posteroinferior to anterosuperior and runs across the lateral wall and nose where it is attached to the maxilla, skull bone and lacrimal bone.It is not attached to any of the bony part anteroinferiorly.It is attached to the inferior turbinate (ethmoid process) posteriorly. Anteriorly it forms the boundary for osteomeatal complex.It hides hiatus semilunaris endoscopically which is represented as a space between ethmoid bullae and uncinate.Polypoid disease and maxillary sinus hypoplasia displaces the uncinate process medially and laterally.

In most of the endoscopic sinus surgeries removal of the uncinate process is the first step. During surgery, the insertion of uncinate process anteriorly should be considered to avoid injury to the medial side and the orbital wall. In this step the ostium and the maxillary sinus is revealed. The orbital floor level is identified by the superior and the ostium of maxillary sinus. The most constant and the largest of the paranasal sinuses is the maxillary sinus. It is the first one to be developed in utero. It undergoes rapid growth at two phases of life. One upto 3 years of life and another between 7 and 18 years.The facial surface of maxilla corresponds to the anterior wall of the maxillary sinus.

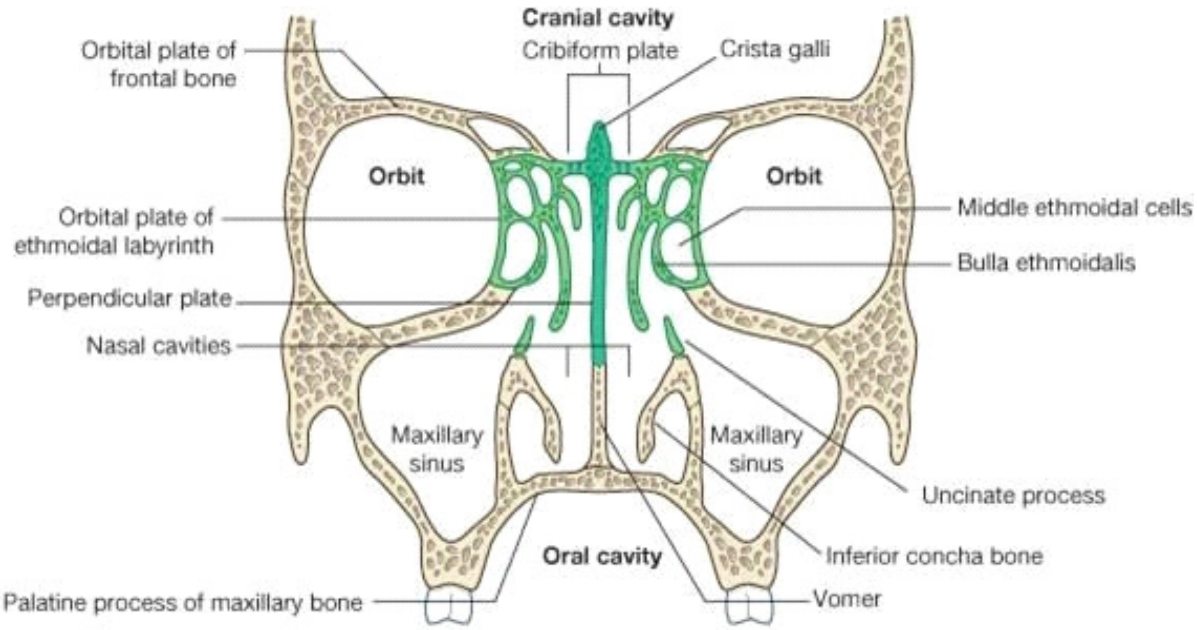
A bony wall present posteriorly seperates it medially from pterygomaxillary fossa and laterally from infratemporal fossa. Medial wall is formed by mucosa of the middle meatus,sinus mucosa and connective tissue. The posterior fontanalle can also have an accessory ostium which opens into the

maxillary sinus. During FESS surgery if uncinectomy is incomplete this could be mistaken for the natural ostium. The location of anterior fontanelle is between the inferior turbinate inferiorly and uncinate superiorly. Hard palate and the alveolar process in the maxillary bone forms the floor of the sinus.

In children it lies in the same level to the nose and in adults it is located 5 – 10 mm beneath the floor of the nose. In maxillary sinus floor of the orbit forms the roof and it houses a bony canal for the 2^{nd} branch of Trigeminal nerve. The prescence of Haller cells (infraorbital ethmoid cells) are the anatomical variation most commonly found. The Ethmoid cells that are pneumatised projects along the orbital floor and most commonly arises from anterior ethmoids. In some cases it can be involved in polypoidal diseases and in others and the patency and the maxillary sinus infundibulum can be compromised.

Clear identification of the floor of orbit and the posterior wall of the maxillary sinus can be done by removing infraorbital ethmoids. Often it is an important and most reliable surgical landmark in case of advanced diseases and distorted anatomy of middle meatus.

ETHMOID LABRYNTH



Ethmoid sinus is located between the nasal wall laterally and the orbital wall medially and lateral to olfactory cleft. It is compartmentalised. Pneumatization occurs with only few cells at birth and it goes beyond 15 cells in adulthood.

The fromtal bone extends posteriorly to cover the roof of ethmoid sinus,forming the fovea.Along the roof of ethmoid sinus runs the anterior and posterior branches of Internal Carotid artery,from lateral to medial side.Due to the cone like structure of the orbit the width increases feom anterior to posterior.Complex anatomy due to honeycomb appearance of air cells with blind alleys and intricate passageways made ethmoid sinus to be referred as

ethmoid labrynth.This complex anatomy is simplified by rhinologists by describing the sinus as 5 paralell lamelles oriented obliquely.

These lamelles are easily recognised intraoperatively since their consistency.The first anterior lamella represents the basal lamella of the first ethmoturbinal embryologically.Most of this corresponds to the uncinated process. The second lamella is called the "ethmoid bulla". Zuckerkandl reffered it as bulla ethmoidalis and it is found to be the largest and most consistent anterior ethmoidal cell. It is round in shape and it extends from laminae papyracea on the lateral side and bulges into the middle meatus medially. The third lamella is the most important which is the basal lamellae and the middle turbinate that anatomically seperates the anterior and posterior ethmoidal cells and also creates a septa which dictates the drainage of the anterior ethmoidal cells into the middle meatus and the posterior ethmoidal cells into the superior meati. Thus it represents as the posterior limit while doing anterior ethmoidectomy. The 4^{th} and the 5^{th} lamellae are the basal lamellae of the superior and supreme turbinates respectively.

In addition to the bony lamellae there are particular groups of ethmoidal cells, recognising of them helps in understanding the pathophysiology of the disease process and helps in doing a near complete ethmoid surgery that is associated with least number of complications.With endoscopy agger nasi cells which are the most important anterior ethmoidal cell are visualised prominently anterior to the middle turbinate.Agger meaning eminence or mound in Latin and

agger nasi is referred to the first ethmoturbinal which is a pneumatised superior remnant.

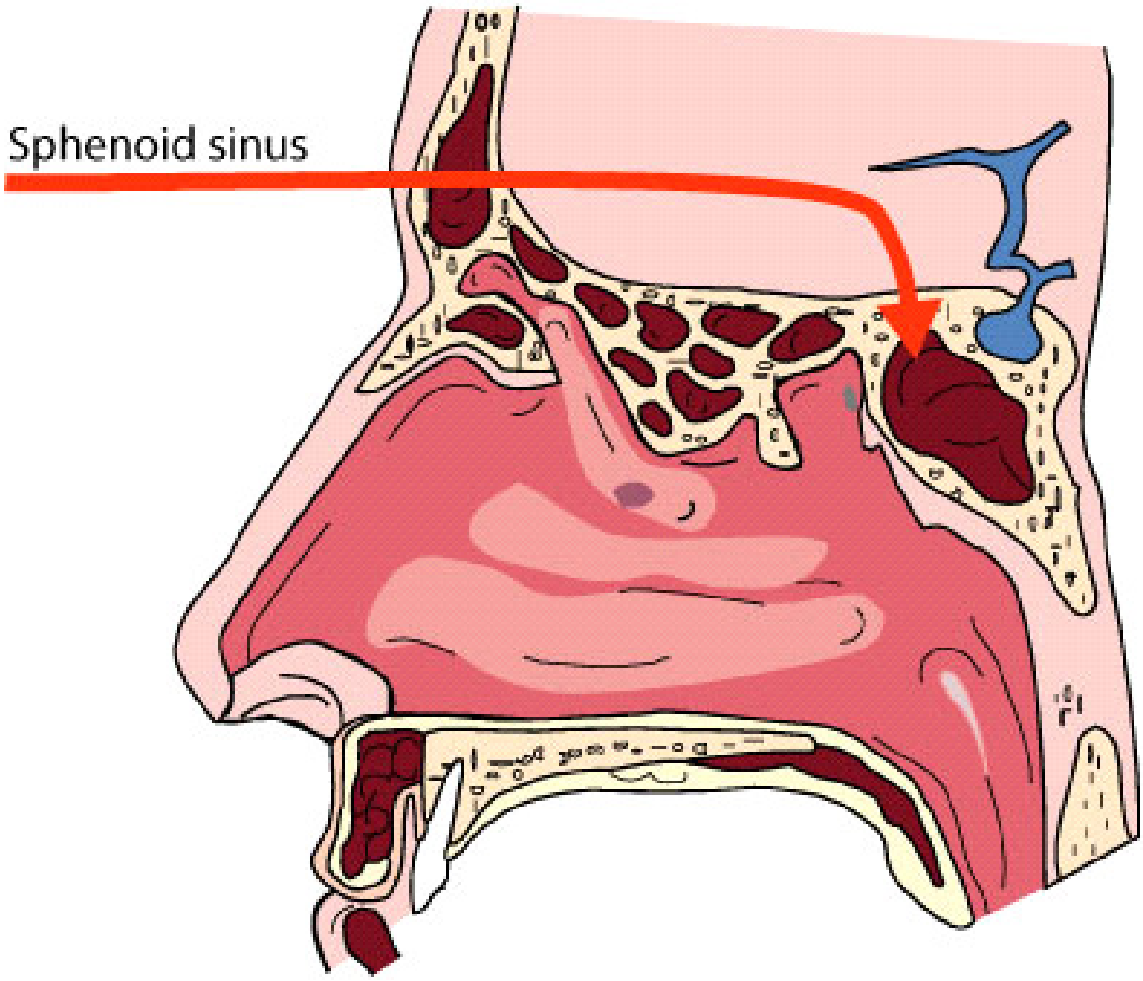
It persists as mound superior and anterior to the middle turbinate. Inferiorly pneumatisation extends to involve the uncinated process which is very rare. Pneumatization of agger nasi significantly has impact on the frontal recess pateny and the insertion of the uncinated process. Frontal recess is accessed surgically with accurately identifying the agger nasi. Sometimes middle turbinate is pneumatised forming circular bullosa. Pneumatization originates uasually from tha agger nasi or the frontal recess.

The concha bullosa usually does not require surgery since it is a normal variant.But when the pneumatisation is extensive narrowing of the osteomeatal complex may occur leading to sinus diseases.Conchal cells which invades the middle turbinate anteriorly are ethmoidal cells but lamellar cells arises due to pneumatisation of the middle turbinate from superior meatus. These conchal cells are described by **Grunwald.**

The supraorbital ethmoidal cells also known as suprabulbar cells are anterior ethmoidal cells that extends upon the orbit by orbital plate pneumatisation.They arose behind the frontal recess.They compromise the drainage of the frontal sinus posteriorly like agger nasi cells in the anterior part.Inexperienced surgeons usually mistakes the supraorbital cells for the frontal sinus.With transillumination using a telescope, these can be differentiated.

In frontal sinus the inner canthal area is illuminated.Yet another important group of cells are the sphenoethmoid cells. They are referred to as Odoni cells, since **Adoff Odoni** studied the relation between ethmoid and optic nerve. The extent of posterior ethmoidal cells are up to the superior and lateral part of sphenoid sinus and the pneumatisation can extend up to the clinoid process. The sphenoethmoid cell has intimate relationship with the optic nerve in the lateral wall.

THE SPHENOID SINUS:



The location of sphenoid sinus is at the junction of middle and anterior cerebral fossa which is located at the base of the skull. While fetal development it starts its growth in the 3rd and 4th month. It starts as an invagination of mucosa of the nasal cavity into the cartilaginous part of the nasal capsule. It is present as a pit in spheno ethmoidal recess a birth upto 3 years. At three years o age pneumatisation starts, at seven years of age extension into the sella turcica occurs. At middle of the teens its final form is reached. First it is developed as

sinuses that are two in number which are asymmetrical. A bony septum separates both the sinuses. Since they are asymmetrical, bony septum is not exactly in midline and can be inserted posteriorly on the carotid canal, which is situated in the lateral wall of sphenoid.

So great care is taken while removing the septum, rupture of carotid can happen on avulsion of the bone. The clinoid processes as the vomer which constitutes the posterior part in the nasal septum can be invaded when pneumatisation of sphenoid occurs. The drainage of sphenoid is into the spheno ethmoidal recess via a single ostium. The ostium is located at the base of columella which measures around 7 cm and situated at 30 degree angulation. The posterior and inferior end of superior turbinate is pointed medially and superiorly to the ostium.

This is the most important landmark to identify the ostium in endoscopic view. Distortion of the normal anatomy can occur during polypoid changes, then the location of ostium can be adjacent to the septum of nasal cavity in level with posterior part of the orbital floor through sinusotomy of the middle meatus. This location is approximately 10-12 mm to the superior arch of choana and 7 cm of columella. The floor of sella turcica forms the superior wall. Sphenoid sinus is classified depending on the extent to which pneumatisation occurs.

- Conchal-It is located below sella. It is a solid block of bone in which pneumatisation has not occurred.

- Presellar – when pneumatisation of sphenoid is upto the frontal plan of sella turcica.
- Sellar – here extention of pneumatisation occurs upto and beyond the body of sphenoid. This is the most common type.

The prominences of optic canal and carotid canal is located in the sphenoid sinus in its lateral wall.

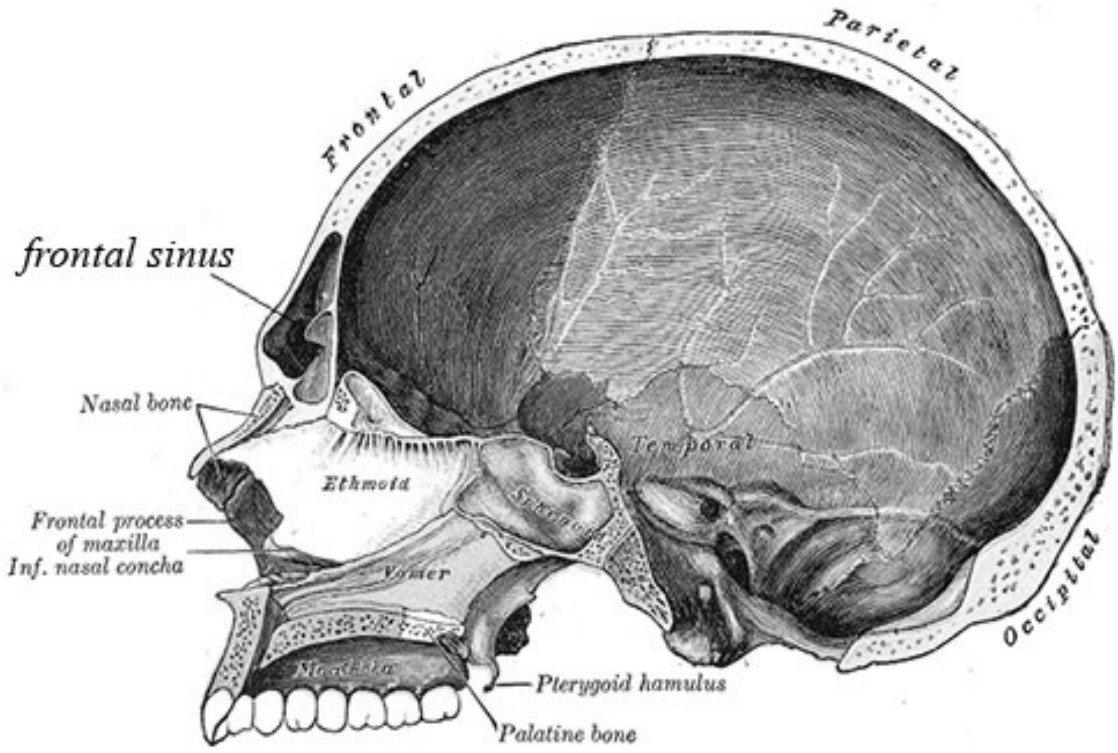
The medial most structure in cavernous sinus is the internal carotid artery which rests on the lateral part of sphenoid bone. Its prominence varies within the sphenoid sinus. It can be simple local bulge to a serpigenously elevated which masks the full course of(posteroinferior to posterosuperior) the carotid artery within the sphenoid sinus. Dehiscence of bony margin should be looked for in the CT scan even when the disease is not advanced. The location of optic canal is present between superior, lateral and posterior walls of the sphenoid sinus at an angle poserosuperiorly. It crosses the carotid canal lateral to medially. In sphenoid when pneumatisation occurs blow and above the optic canal it results in opticocarotid recess. The location of infraoptic recess is between the carotid canal in the inferior portion and superiorly the optic nerve. Sometimes pneumatisaion of clinoid process occurs.

In the lateral wall canals for 2 more nerves can be present.

- Trigeminal nerve(2^{nd} branch) passes superiorly through foramen rotandum.

- Inferiorly the viridian nerve which passes through the pterygoid canal when the sphenoid sinus is extensively pneumatised these nerves are identified easily in a coronal CT scan which defines the both (superior and inferior) borders of entry into lateral recess.

THE FRONTAL SINUS:



The frontal sinus is related intimately to the anterior ethmoid both embryologically and anatomically. The frontal sinus is developed from the anterior ethmoid cells which extends upwardly into the inferior part of the frontal bone in between the lateral tables.

But according to Stammberger development of frontal sinus is from frontal recess which is embryologically the continuaion of groove present in between first and second ethmoturbinal. At birth, it is blind pouch which often cannot be distinguished from anterior ethmoid cells. Pneumatisation starts at 2 years, significant in adolescence and gets completed in late teens. The left and right frontal sinuses are asymmetrical and develops independently. Sometimes it is common to find one frontal sinus, or the frontal sinus may be aplastic, hypoplastic, or rarely aplastic bilaterally. The fontal sinus llies between the anterior thick and posterior thin tables of the frontal bone which separates the sinus from the posteriorly situated frontal lobe. It is described pyramidal in shape with the boundaries of a bony septum medially, intersinus cell formed by intersinus septum which is pneumatised sometimes, and the floor by the roof of the orbit. The pathway for the drainage of frontal sinus is in an hourglass shape which opens in the level of frontal recess. Narrowest point in the tract is known as ostium or the frontal infundibululm. It is located at the inferomedial aspect. The boundaries of frontal ostium are formed by,

Anteroinerior part is formed by roof of agger nasi, posterior part is formed by roof of bulla ethmoidalis, lateral part by lamina papyracea and anteriorly by middle turbinate. Different groups of anterior ethmoid cells are related to rontal inundibulum. Others which originate from frontal recess are known as frontal infundibular cells.

Frontal cells are classified into types by **Bent** and **Kahn**

Type I – When single air cell lies above agger nasi.

Type II – When group of cells are present above agger nasi and below the roof of the orbit.

Type III – when a single cell extends into frontal sinus from agger nasi.

Type IV – When a cell is present in isolation inside the frontal sinus which is noncontagious with agger nasi.

Frontal sinus infundibulum is the most difficult area to be accessible in FESS surgeries, due to their smaller diameter, anterior most locataion and orientation inside the frontal bone. Its anatomy related to the orbit, the bone of the skull and presence of various groups of cells makes the anatomy most difficult to understand during endoscopy. For a sae and successful visualisation the keys followed during FESS are opening of agger nasi cells, identification of posterior wall by palpating with probe.

Down fracturing the agger nasi and suprabulbar roof and carefully removing for better visualisation of the infundibulum. Track of entry into frontal infundibulum is via the direction of a parallel line drawn to the lacrimal bone at its maximum convexity, behind the middle turbinate, starting at the maxillary sinus in the coronal plane.

Blood supply of the nose:

I. External nose

1). External carotid artery:

Facial artery –

- Angular branch,
- Alar branch,
- Septal branch,
- External nasal branch.

2). Internal carotid artery:

Ophthalmic artery –

- Dorsal nasal branch.

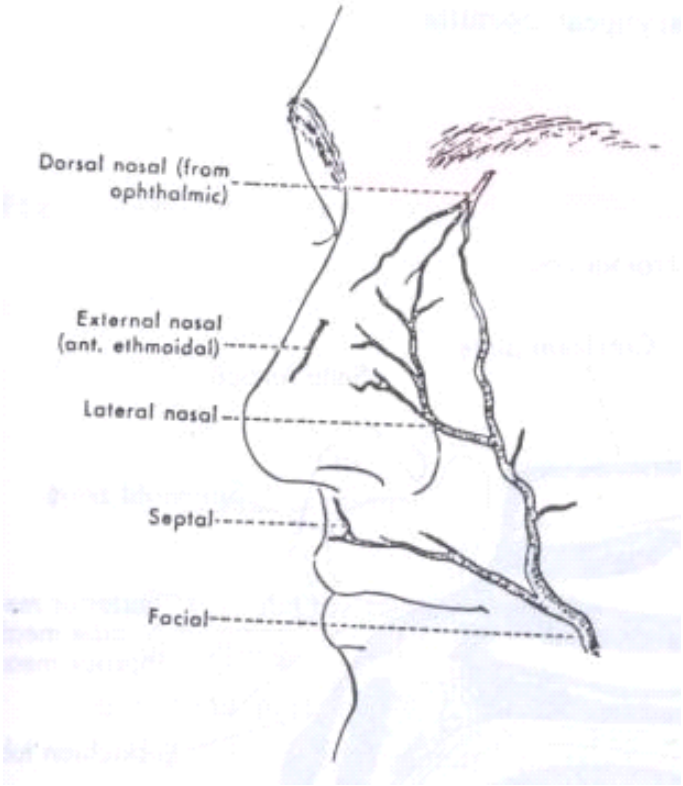


Fig. Blood supply to the external nose

II. Nasal septum

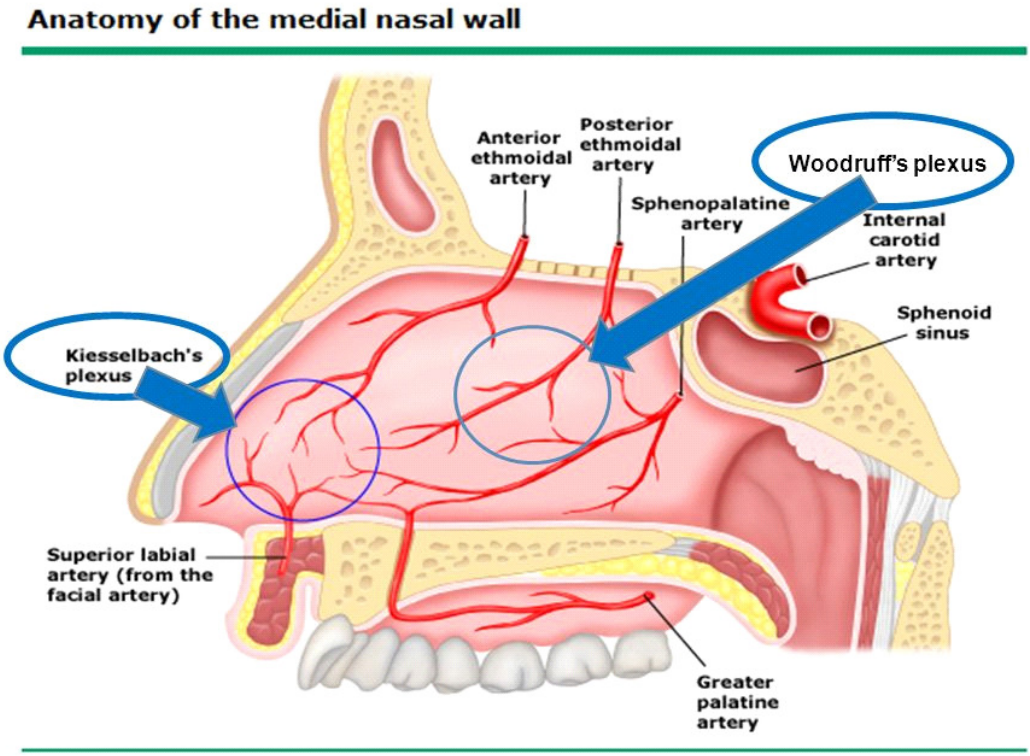


Fig. 1: Anatomie nasale. Source: [2]

III. Lateral wall of nose and turbinates :

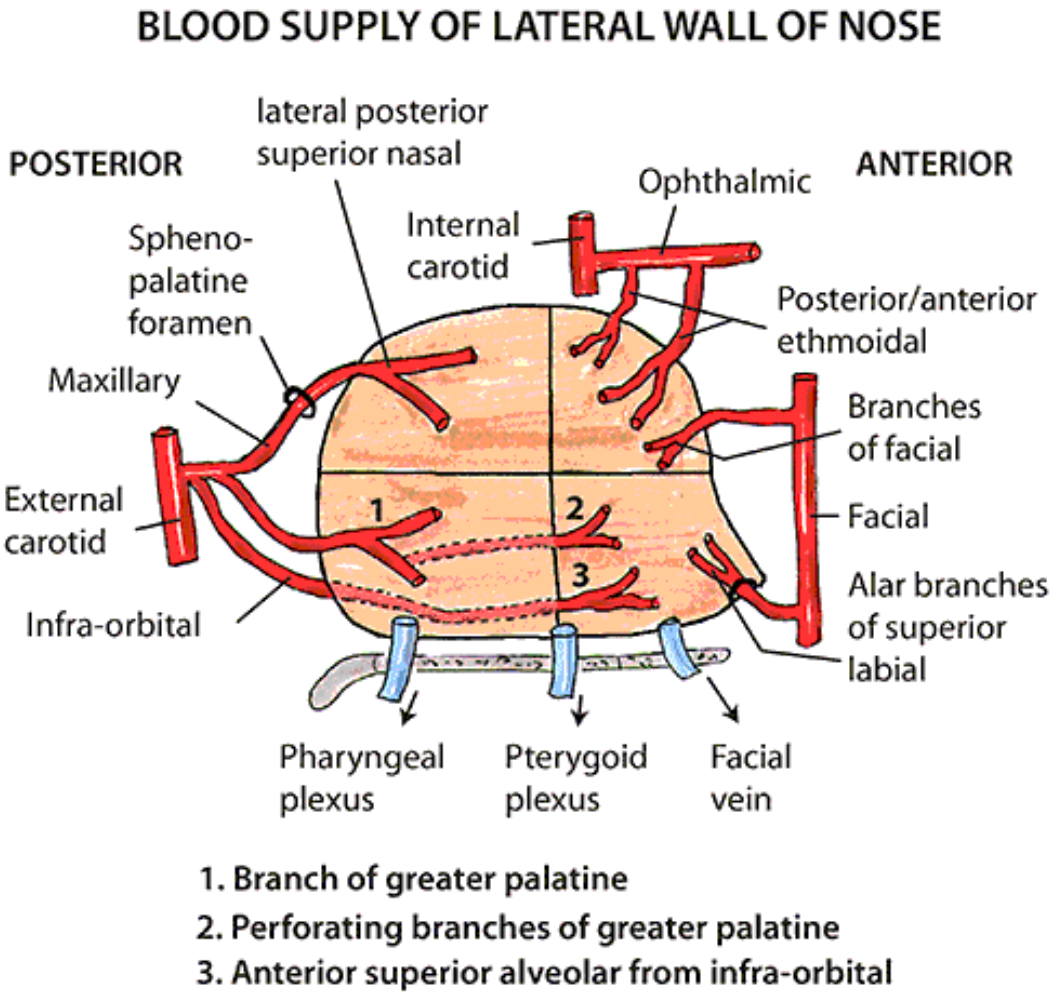


Fig. Arterial network of the lateral wall on nose

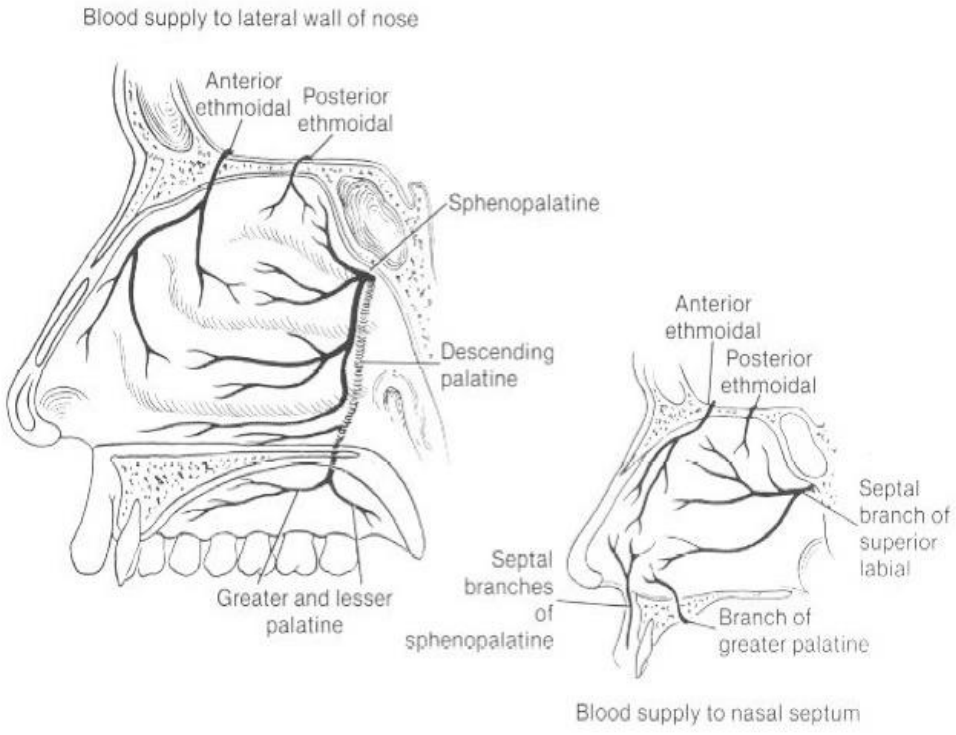


Fig.Blood supply to the lateral wall on nose

Internal carotid:

Ophthalmic artery

- Anterior ethmoid artery to Anterior 1/3 of lateral wall and septum
- Anterior lateral branch
- External nasal branch
- Anterior setal branch
- Posterior ethmoid artery to superior concha

External carotid:

Maxillary artery -

- Sphenopalatine artery.

Posterior lateral nasal branch to run along MT & IT

Posterior septum branch

- Facial artery -

  Superior labial artery to Nasal septal branch

  Lateral nasal branch to Alar branch

- Infraorbital artery
- Descendig palatine artery to Greater palatine artery.

  Superior alveolar artery

Venous drainage

- Roof
  - Ethmoidal vein to Ophthalmic vein
- Posterior
  - Sphenopalatine vein to pterygopalatine fossa to pterygoid venous plexus
- Anterior
  - Anterior facial vein to External or Internal jugular vein

Nerve supply of nose:

Nose is mainly supplied by the following :

- General sensory fibers (CN V1,CN V2)
- Parasympathetic fibers : secretomotor fibers
- Sympathetic fibers : vasomotor fibers

HISTORY OF INDUCED HYPOTENSION

Definition

Controlled hypotension is defined as producing a predictable decrease in the blood pressure but at the same time limited by safety. It was taken from the very early studies done by **ECKENHOFF** and **RICH** in 1960's.The lowest limit of blood pressure should not be determined before the start of the surgical procedure but rather should be provided till the desired level that is the bloodless field is achieved but within the safety limits without compromising the cerebral or the coronary blood flows. However the safety limit has to be individualised.

In general, MAP as low as 50 mmHg or a 30% fall in MAP is considered safe for a ASA 1 subjects. However this might not be considered as a safe limit for a chronic hypertensive patient who will not tolerate a fall in MAP more than 25%.Again this cannot be appropriate level for a patient with cerebrovascular disease as they cannot tolerate any sort of decrease in MAP.

Evolution of Induced hypotension.

It was during **1917**, induced hypotension first introduced into practice so as to provide a bloodless field for neurosurgery.

In the year **1946**, arteriotomy as a technique to produce a bloodless field was introduced.

Regional anesthesia had also been used in inducing hypotension to create a dry field. In **1948**,high spinal anesthesia and in **1951** high epidural block were also used.

The method of inducing hypotension evolved further and the technique of ganglion blockade using pentamethonium, hexamethonium and trimethaphan were used during anesthesia.

Thereafter deepening the plane of anesthesia with the help of volatile inhalational agents was a favourite choice by many anesthesia practitioners.

For the first time in **1962**,sodium nitroprusside was used to induce the hypotension during anesthesia.

Since then many drugs have evolved for the purpose of inducing hypotension .Nitroglycerine, calcium channel blockers, beta blockers, purine compounds and prostaglandin E1 have been used for it.

PHYSIOLOGY :

Adequate knowledge and understanding of regulation of blood flow to the vital organs is obsolute necessary to produce induced hypotension for the optimal benefit of the patient. Controlled hypotension rarely produces any damage, nevertheless because blood flow to the vital organs are well maintained due to the wide range of autoregulation.

Blood flow to cerebral, myocardial and renal beds depends on the function of both MAP and auto regulation. Hence the concept of MAP is used in the practice of controlled hypotension rather than systolic blood pressure. It is

of at most importance to determine the weak link among these three vital organs that sets the minimal permissible pressure. So the physiology of these three systems needs to be examined separately.

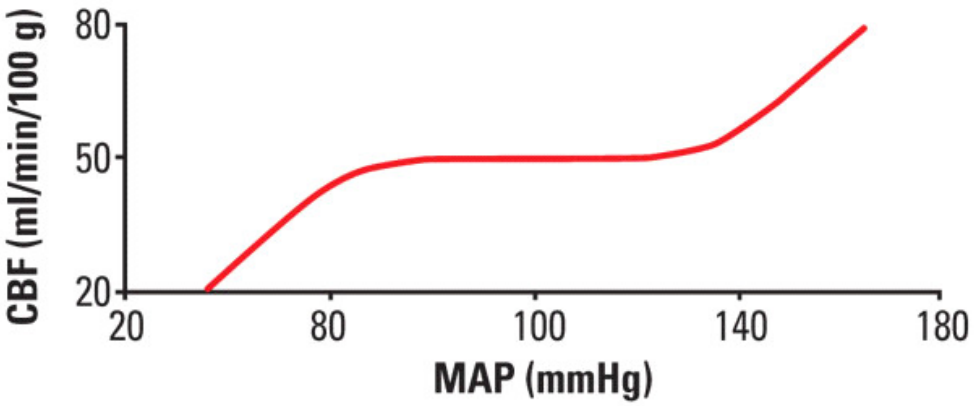
Mechanisms of auto regulation:

1. Myogenic response – response of the vasculature to the altered tension detected in the smooth muscle.
2. Passive response – this happens in an encapsulated organ in which increasing pressure dur to expansion of the organ compresses the thin walled vessels and leads to an increased vascular resistance.
3. Metabolic response – changes in the blood pressure produces vasoactive substances.

The organs capable of autoregulating their blood flow are able to maintain the perfusion over a wide range of blood pressure changes. Only when the blood pressure reduces to a relatively low level they cannot maintain their perfusion. This is called critical blood pressure and it varies from organ to organ, vessel to vessel and probably from patient to patient.

CEREBRAL CIRCULATION

FIGURE 4.
CBF autoregulation curve



CBF becomes pressure passive above a MAP of 140 mmHg and <60 mmHg as the arterioles cannot constrict or vasodilate any further to maintain consistent flow.

CBF=cerebral blood flow; MAP=mean arterial pressure.

Gardner CJ, Lee K. *CNS Spectr.* Vol 12, No 1. 2007.

It is a common belief that it is the cerebral perfusion pressure that is critical in deciding the lower limit of MAP. This is probably because even a minimal derangement in the perfusion pressure of the cerebral circulation produces an unacceptable postoperative dysfunction of the organ. By the way of autoregulation, cerebral blood flow is normally maintained at 45 – 50 ml/100gms/min. This is achieved through a MAP ranging from 50 -150 mmHg.

The absolute value of cerebral blood flow below which the cerebral ischemia occurs is nor clearly understood. But there are several studies reporting an estimate can be made. Sundt et al used xenon to measure the cerebral blood flow and he simultaneously recorded EEG during carotid

endarterectomy during anesthesia with volatile agents like Halothane and with normocapnia.

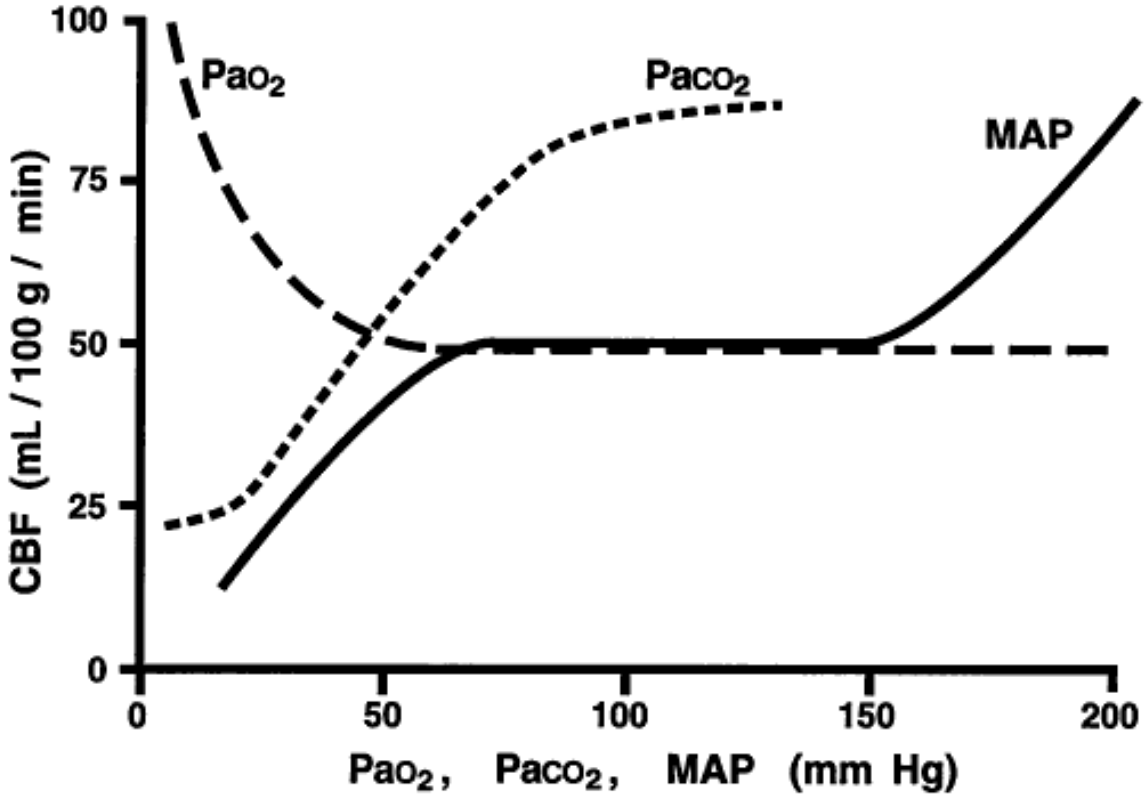
In that study they had found that there were no changes indicative of cerebral ischemia if cerebral blood flow was above 25 mls/100gms/min. Considering this as the critical flow limit, it is possible to estimate a critical cerebral perfusion pressure below which cerebral ischemia might occur.

Never the less, there are several factors that can modify the circulation under the control of anesthesiologist.

1.$PaCO_2$

Arterial PCO2 is the most important determinant of cerebral blood flow within the range of autoregulation.Cerebral blood flow increase by 1 ml/100 gms/min for every 1 mmHg increase in the arterial PCO2 and vice versa.

This is relevant in the clinical situation as hypocapnia is a part of the induced hypotensive technique.The cerebral function could be compromised if both hypotension and the vasoconstrictive effects of the low PCO2 on cerebral vessels are combined.



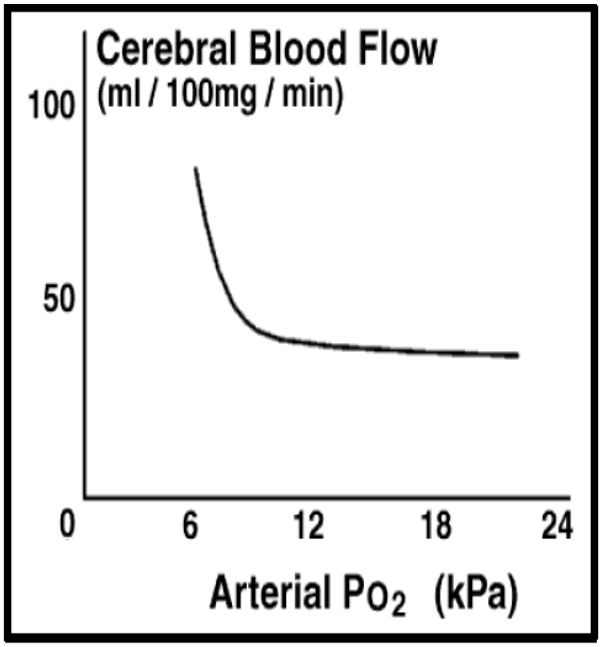
2.PaO2

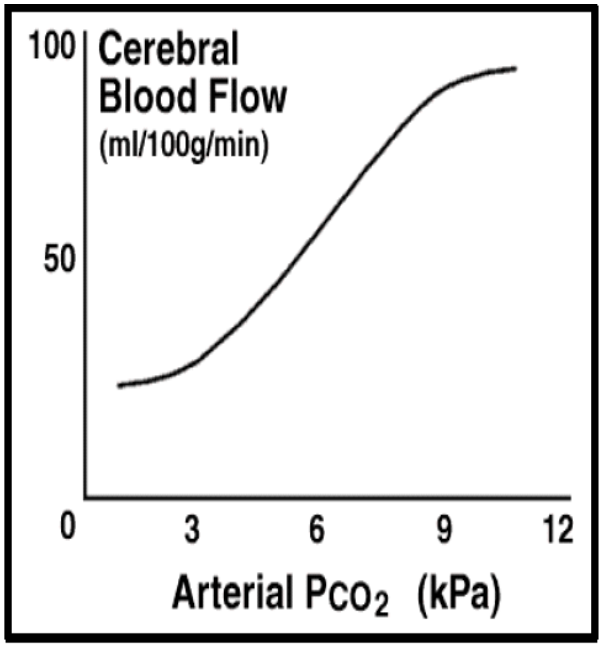
Changes in the arterial oxygen tension also affect the cerebral blood flow. The brain protects itself by vasoconstriction when exposed to very high oxygen tensions like in the hyperbaric range which can induce toxic effects on the cerebral circulation.

This is demonstrated by a reduction of cerebral blood flow by 1/5 th whenever there is an exposure to 100% oxygen.

On the other hand if arterial oxygen tension is decreased below the normal level, the cerebral blood flow increases due to vasodilatation. Though administering high concentration of oxygen during induced hypotension may

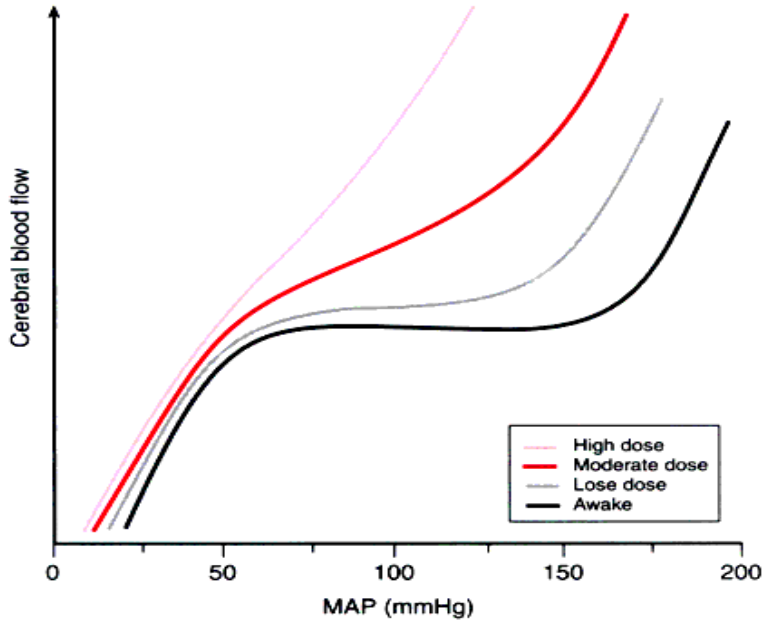
not be beneficial as far as the cerebral blood flow is concerned, it may be necessary to offset the effects of hypotension on the pulmonary gas exchange.





3.Volatile agents :

The effect of volatile liquid agents is to attenuate the autoregulation in a dose dependant manner. This differs from agent to agent and is in the following order.Halothane > Enflurane > Isoflurane.



4. Temperature

There is a linear relationship between temperature and cerebral blood flow .Hypothermia induces cerebral vasoconstriction whereas hyperthermia causes cerebral vasodilatation. For every degree celcius change in the body temperature cerebral blood flow changes by 5 – 7%.

5.Vasodilators

Drugs like Sodiumnitroprusside and Nitroglycerine attenuate the autoregulation of cerebral blood flow same as the volatile liquid agents does.

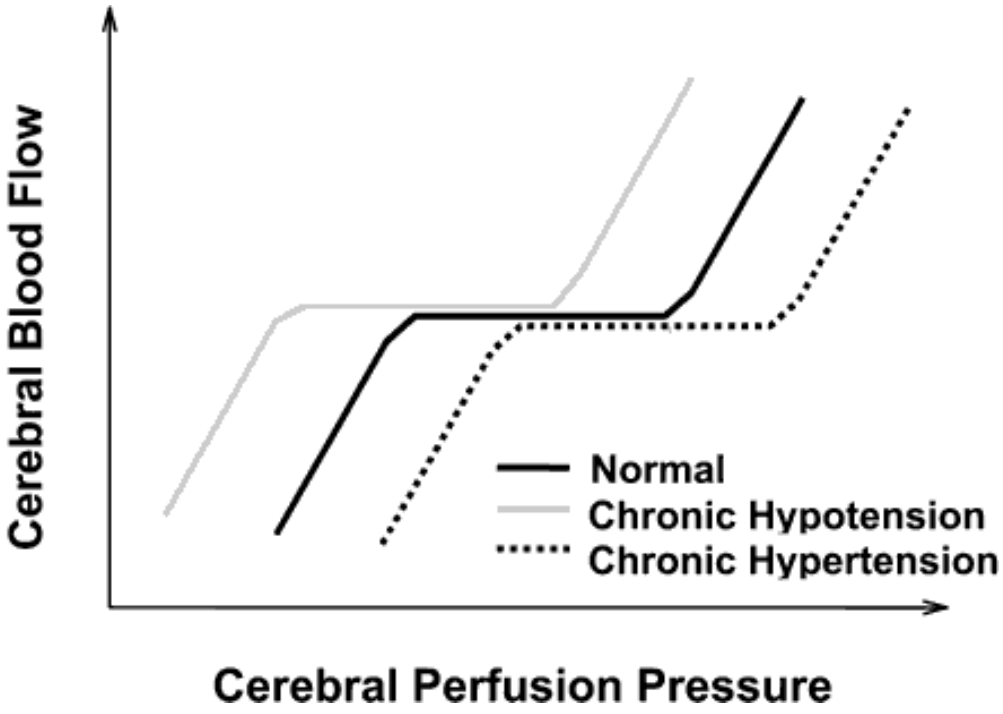
When overall cerebral blood flow is contrasted with the regional blood flow difficulty in interpretation occurs. This is because in the region of marginal blood flow factors such as hypoxia and local acidosis predominate, which may cause maximal dilatation of cerebral vessels in that area.

As there is a limitation of the volume of blood that can be accommodated within the skull vault, events that can cause increase in the blood flow to the areas of perfusion may displace the blood flow to the areas of marginal perfusion.

Because of this unequality and uncertainity of regional blood flow distribution , a safety limit has to be determined as far as the MAP is concerned. It has been found in this way that it should be safe to lower the MAP to 50 mmHg without any significant decrease in the cerebral blood flow.

In case of chronically hypertensive patients ,they have their cerebral autoregulation curve shifted to higher side on both the ends.For them the safest

lower limit of MAP can be calculated based on this curve shift.Even the elevated MAP of these patients are taken into account,they pose an increased risk.Therfore chronically hypertensive patients are relatively contraindicated for the induced hypotension technique.

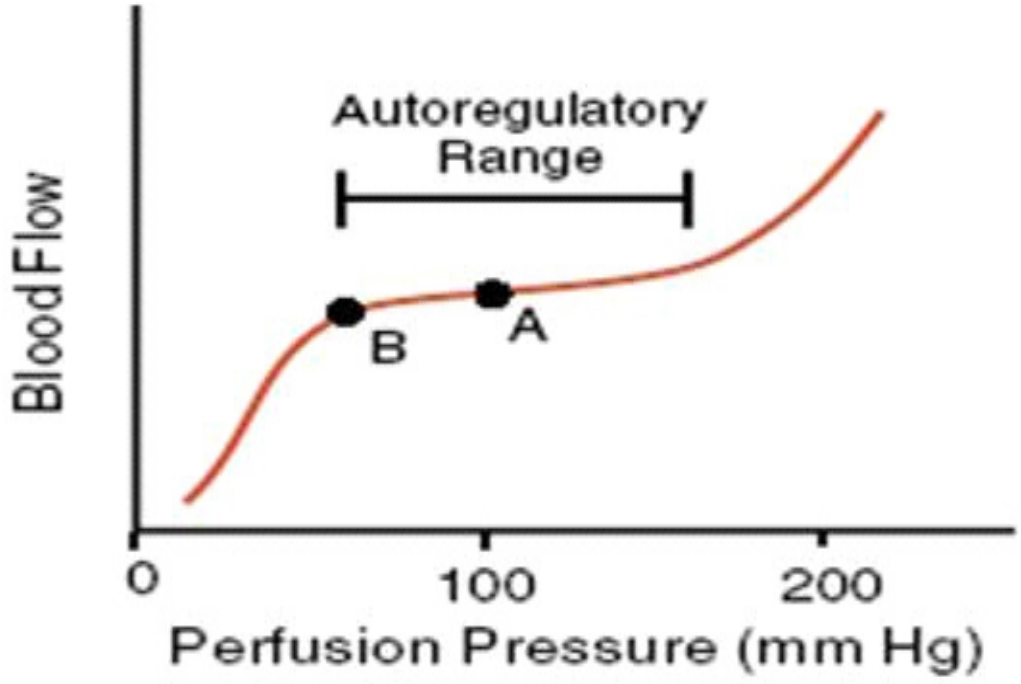


Elevated position of the head during induced hypotension anesthesia can decrease the cerebral perfusion pressure further. For every 2.5 cm raise in the head position above the point of monitoring the cerebral perfusion pressure decreases by 2 mmHg.

CORONARY CIRCULATION

The coronary blood flow depends on the aortic diastolic pressure and the coronary vascular resistance. The autoregulation of coronary blood flow is predominantly determined by the coronary vascular resistance that is made to meet the myocardial oxygen demand.

Obviously hypotension decreases the coronary blood flow but however it simultaneously decreases the myocardial oxygen demand due to reduction in the after load and/or preload. **Rollason** et al in 1959 reported that there is a poor correlation between the lowest value of hypotension and the development oh ischemic changes in ECG during hypotensive anesthesia.

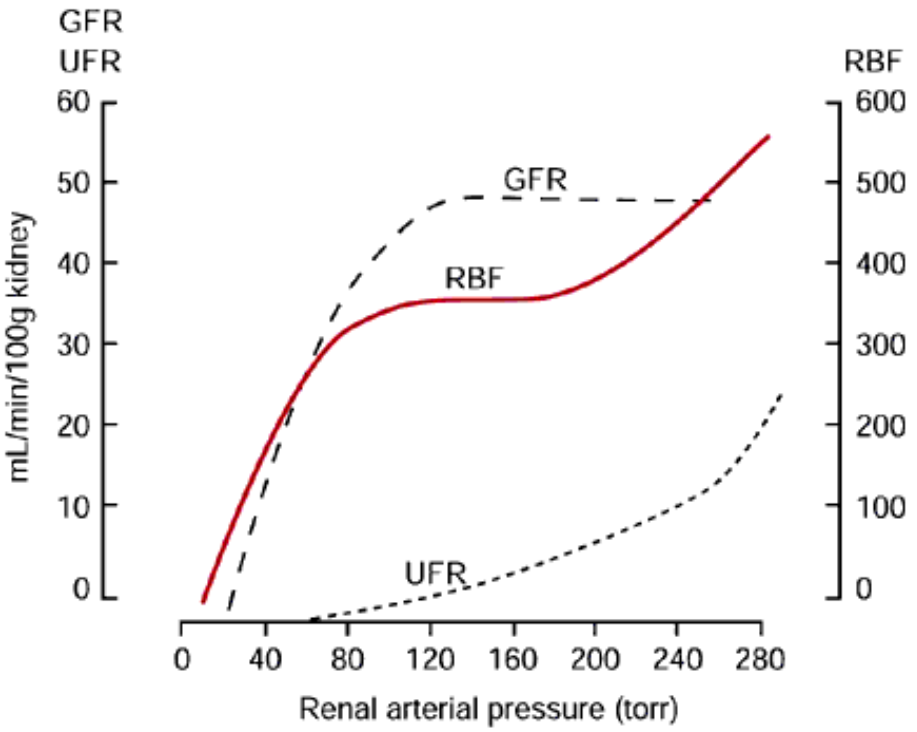


In patients with coronary artery disease,some area of myocardium are entirely dependant upon the pressure to have an adequate blood flow.Usage of vasodilators in these patients readily produces a steel phenomenon which compromises the blood flow to the ischemic areas further.Hence the technique of induced hypotension is accompanied by significant intraoperative risk of myocardial infarction in these patients.

In a study done by **Rollason** & **Hough**,in 1959,induced hypotension with the use of ganglion blocking agents,they had found that although 40% of cases

had evidence of transient myocardial ischemia ,none had ECG changes suggestive of myocardial ischemia. They observed that these changes occurred in elderly patients or patients with a history of pre-existing chronic hypertension of their study group, when the systolic blood pressure fell below 60 mmHg. They concluded that a MAP limit of atleast 80 mmHg should be maintained at all times in these patients whenever hypotensive anesthesia is contemplated.

RENAL CIRCULATION



Renal blood flow is regulated in two ways.

1.Extrinsic autoregulation

Autonomic response

Hormonal response

2.Intrinsic autoregulation

In 1954,**Miller, De Wardener** and **Venton** showed that the renal blood flow autoregulation ranged over 80 -180 mmHg. This renal blood flow autoregulation gets attenuated during general anesthesia and even a slight reduction in blood pressure reduces the renal blood flow. This occurs when systolic blood pressure is 80 – 90 mmHg as observed by **Larson** et al in 1974.

Further drop in the arterial blood pressure decreases the renal blood flow to a point where the urine formation fails. When MAP is decreased below 75 mmHg the GFR gets reduced.

Drugs like volatile agents and opioids used during hypotensive anesthesia stimulate the secretion of Anti Diuretic Hormone which results in oliguria.

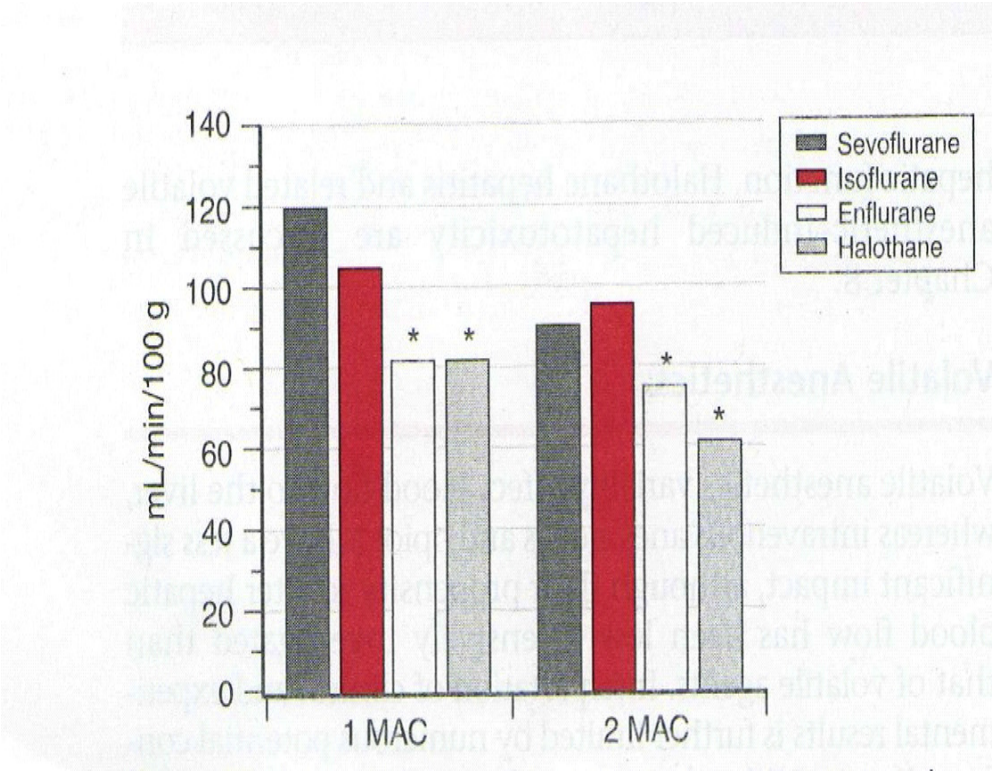
Renal blood flow has also got a critical value as with cerebral circulation, below which acute renal failure occurs. Again the critical value differs from individual to individual and also depends on the pre-existing renal disease. Therefore during induced hypotension, if the reduction in renal blood flow is not below the critical value it is unlikely to have any serious kidney damage. As a matter of fact, it has been shown that the urine formation rapidly returns to normal as soon as the hypotensive anesthesia is terminated.

HEPATIC CIRCULATION

Liver gets in maximum blood flow from portal vein (70%).Remaining 30% is by hepatic artery. The splanchnic circulation has got rich innervations by the sympathetic nervous system unlike the brain and kidney which are autoregulated, the liver is not autoregulated. Therefore any decrease in blood

pressure readily decreases the blood flow to liver. In addition to this, the splanchnic circulation which is highly innervated with sympathetic nervous system responds to any increase in paco2 or any decrease in Paco2 by a catecholamine response and causes decrease in liver blood flow. The decrease in hepatic blood flow by hypercarbia occurring due to hyperventilation during IPPV is due to mechanical effects.

In addition to the hypertension which causes decrease in hepatic blood flow, liver also gets affected by anaesthetic agents like volatiles directly acting on the splanchnic blood flow.



Animal studies have shown that there is a reduction in cardiac output and mean arterial pressure. But the effect is more pronounced in the total hepatic blood flow and Portal blood flow with halothane.

Also animal studies have shown that the hepatic O2 delivery gets reduced maximally by halothane.

When compared with inhalational agents, intravenous anaesthetic agents have shown only a modest decrease in hepatic blood flow and have produced no adverse influence on the post operative hepatic function. However this is based on limited clinical studies and trials.

There are studies in which they have found in fact that propofol had actually increased hepatic blood flow and portal venous blood flow which may be due to its direct vasodilator effects on the splanchnic circulation.

Though the volatile liquid agents have a tendency to decrease the hepatic blood flow, it has been found that deliberate hypotension seems to be well tolerated by the patients. So far there are no reports showing morbidity/mortality resulting from liver hypoperfusion during induced hypertension.

RESPIRATORY SYSTEM

Positioning of the patients during the controlled hypotensive anaesthesia affects the pulmonary function and mechanics by the following ways:

1. Pulmonary blood flow tends to gravitate to the dependent areas of the lung. Therefore there is a ventilation perfusion mismatch as the nondependent areas of the lungs are maximally ventilated. Hence the

amount of dead space increases. This gets exaggerated further in reverse trendelenburg position.

2. The drugs causing hypotension (mainly vasodilators) for the controlled hypotensive anaesthesia inhibits the hypoxic pulmonary vasoconstriction response and causes an increase in the intrapulmonary shunt function.
3. The result of these two mechanism is an increase in end total CO2 and hypoxaemia. This necessiatates the continuous monitorin of Paco2 during controlled hypotensive technique. Addition of higher Fio2 may be beneficial in this situation.

TARGET BLOOD PRESSURE

The objective of the controlled hypotensive anaesthesia is to produce a bloodless field by reducing the blood loss. However the degree of hypotension depends on the individual. If the bleeding appears to be minimal and the vital organ perfusion is found to be adequate then the level of that hypotension can be considered satisfactory. Research have shown that if mean arterial pressure is kept alone the sum of colloid osmotic pressure and central venous pressure, blood flow to the organ shall be adequate the tissue needs.

Theoretically 32mmHg of mean arterial pressure is considered to serve this purpose but this is found to be below the safe limit propably because of the specific blood flow requirements of various organs and other diseases that had caused alteration in the circulation.

The level of hypotension induced by hypotensive anaesthesia should be limited in such a way that it should reduce the bleeding in the operative field and in duration of the procedure seems to get benefited from it as long as the perfusion of various organs are adequate.

From the above studies and references, it has been suggested that controlling the hypotension to a level of 30% reduction of mean arterial pressure is considered safe. For ASA grade I patients it has been found that minimum of 50mmHg mean arterial pressure and in elderly a mean arterial pressure of 80mmHg is considered clinically acceptable.

CONTRAINDICATIONS

- Technique related
    - Lack of understanding
    - Limited experience
    - Lack of adequate patients monitoring
- Patient related
    - Heart diseases
    - Diabetes mellitus
    - Anemia,polycythemia
    - Hemoglobinopathies
    - Hepatic diseases
    - CVA

- Kidney diseases
- Systemic hypertension
- Drug inolerence.

RISKS OF CONTROLLED HYPOTENSION

The morbidity and mortality associated with hypotensive anaesthesia were as little as 1 in 31 and 1 in 291 respectively in a retrospective study done by Little et all in about 39000 cases . Compromise of the vital organ circulation is by far the commonest cause of mortality associated with hypotensive anaesthesia. Mortality may also be due to rebound hemorrhage, high spinal, effect of over heparinisation, arterial air embolism, pulmonary edema and pulmonary infarcts.

Many of the mortalities in the above study would have been probably due to the level of hypotension where the procedure was performed with a systolic blood pressure of <80mmHg.

In 1966 **Eckenoff**and in 1987 **Madson** have shown in their studies that the induced hypotensive anaesthesia technique can be considered safe if the limits are adhered to.

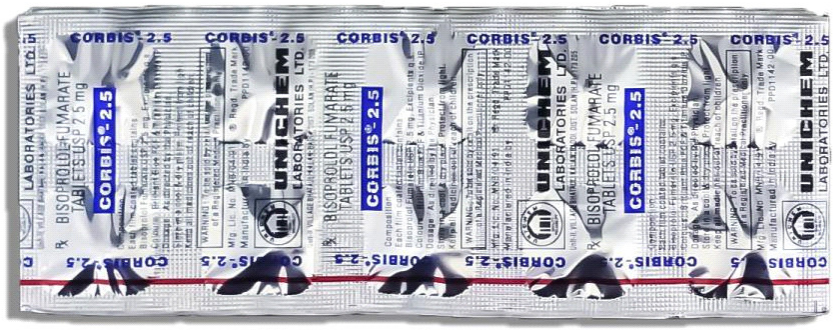
LITERARY EVIDENCE FOR HYPOTENSIVE ANAESTHESIA:

Though unacceptable, mortality and morbidity have occurred in the study conducted by **Little** et al in 1954, it was found that it is the target systolic pressure which was kept below 80mmHg had caused that. Since then 50mmHg of target mean arterial pressure or higher set for ASA grade I patients.

This new target has shown the advantages of the controlled hypotensive technique on the blood loss and the dry surgical field and ultimately the amount of transfusion requirements, with their target mean arterial pressure there were no significant difference in mortality/morbidity between hypertensive and normotensive patients.

Gale Thompson et al in 1978 did a study and showed that the controlled hypotensive anaesthesia had significantly reduced the intraoperative blood loss and overall duration of the surgical procedure on patients scheduled for total hip arthoplasty.

BISOPROLOL



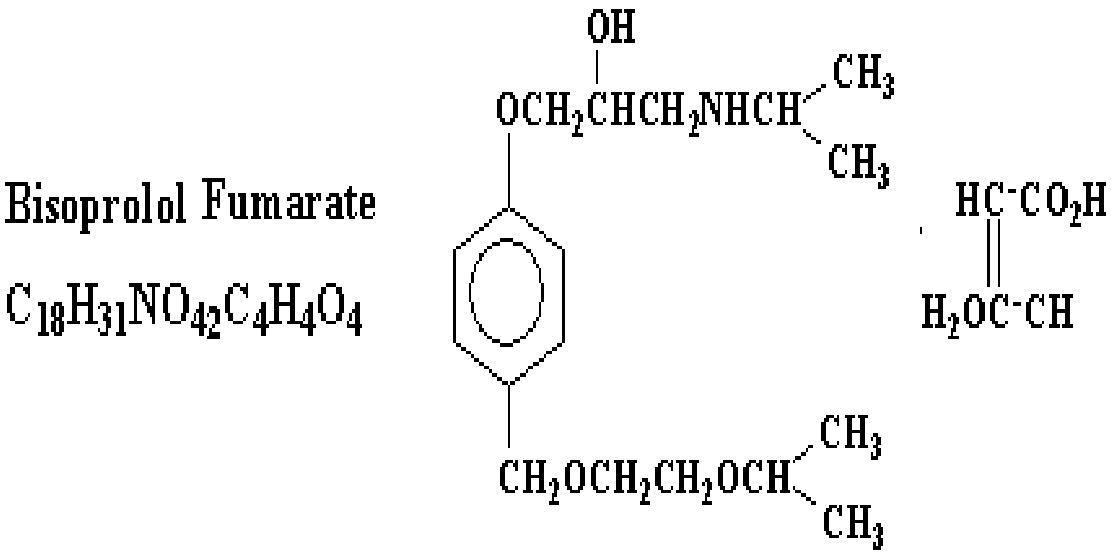
Introduction

In 1962,it was **Sir James Black** who first developed beta blockers at the Imperial Chemical Industries in the United Kingdom.

Beta blockers are one among the four oral medications that has been proven in the clinical studies and trials to have decreased the cardiovascular morbidity and mortality.The life saving potential of beta blockers has been estimated to be around 33%.

Chemistry

Bisoprolol fumerate is a derivative of phenoxyaminopropanol.



It is a white crystalline substance which melts at a temperature of 101 degree celcius. It is freely soluble in ethanol, water and methanol. Bisoprolol is less lipophilic than Propranolol but more than Atenolol.

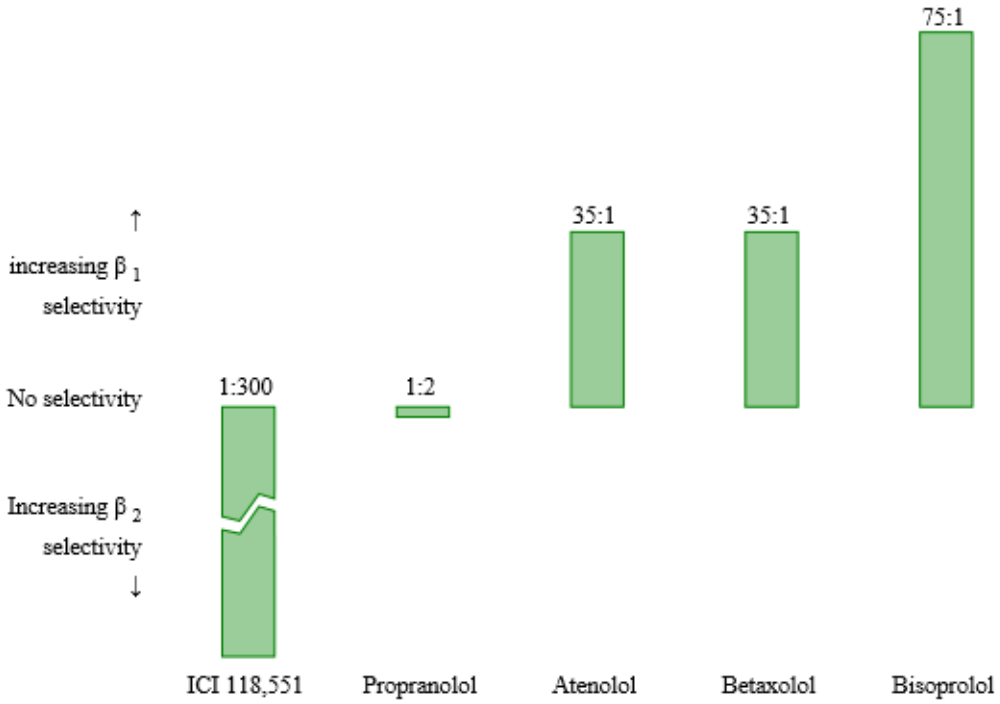
pKa of Bisoprolol base is 9.5

Bisoprolol is available as 1.25 mg, 2.5 mg, 5 mg, and 10 mg tablets.

Pharmacology and Biochemistry:

Beta 1 selectivity

Bisoprolol has been proved to have a higher beta 1 selectivity when compared with Atenolol, Metaprolol and Betaxolol but less than that of Nebivolol. Bisoprolol has displayed 19 fold increased affinity for beta 1 receptor versus beta 2 receptors which has been demonstrated in cloned human beta receptors.



Intrinsic sympathomimetic activity

Bisoprolol has got no intrinsic sympathomimetic activity as shown from the experiment in guinea pigs whose left atrium of their heart is pretreated with Reserpine and contractility measurements after electrical stimulation showed no evidence of ISA.

Cardioprotective property of Bisoprolol has also been demonstrated by an increase in the coronary perfusion pressure in anesthetized pigs.

Membrane stabilizing activity

Bisoprolol has a local anesthetic like action on the cornea of the rabbit and in the skin of guinea pigs but in a concentration several times higher than that required for blockade of beta receptors.

Antihypertensive effect

Antihypertensive effects of Bisoprolol in conscious dogs with renal hypertension has been demonstrated with only a slight decrease in heart rate.Also it clearly reduced the development of high blood pressure with chronic treatment in rats with spontaneous hypertension.

Cardioprotection

In anesthetized open chest dogs, myocardial ischemia was induced by coronary occlusion and it was found that a dose of 4 µg/kg Bisoprolol intravenous reduced the ST segment elevation induced by coronary occlusion by 60 %.This effect lasts for 40 mins after intravenous injection.

Renin – Angiotensin system

Bisoprolol inhibits renin secretion stimulated by Isoprenaline. The release of renin was inhibited by about 65%.In addition to that Bisoprolol reduced the basal activity of renin.

Duration of action

Bisoprolol has a long duration of action which is demonstrated in anesthetized guinea pigs .After intravenous Bisoprolol and Propranolol the inhibition of Isoprenaline induced tachycardia was measured at various times.

Drop in action duration curve is flatter for Bisoprolol than Propranolol.

Side effects

Bisoprolol has no serious or unexpected side effects.sedative effects of Bisoprolol even after high single oral dose (30 mg and 100 mg/kg) is less marked.This has been demonstrated in rats.Bisoprolol only slightly decreases the glucose tolerance in rats.This is observed at very high doses of Bisoprolol.

On repeated administration of Bisoprolol in adult normolipaemic rats absence of changes in lipid metabolism has been demonstrated.

No quantitative change in serum lipid is seen in young hyperlipaemic rats.

Toxic effects

Bisoprolol is not cytotoxic or mutagenic. In higher doses embryotoxicity is demonstrated in animal studies.In a prolonged long term study conducted in dogs with Bisoprolol in a dose of 30 mg/kg, a safety factor of 210 and a safety factor of 525 is calculated in rats corresponding to the dose of 75 mg/kg.

Acute toxicity

Lethal dose (LD50) of 1116 mg/kg for rats and 734 mg/kg for mouse has been demonstrated on oral administration. On intravenous administration values are found to be 24 mg/kg for dogs,127 mg/kg for mouse and 53 mg/kg for rats.

Short term toxicity

0.2,1.0 and 5 mg/kg were tolerated by rats.1.0,3.0 and 10 mg/kg were tolerated by dogs.For four weeks on daily intravenous administration, no signs of toxicological changes were found.

Chronic toxicity

Daily doses of 15, 50 and 150 mg/kg for 6 months in rats has shown to have no toxic effects on oral administration. Slight reduction in body weight has been noted with a dose of 75 mg/kg in a study conducted in rats.

Specific toxic effects

In rabbits Bisoprolol administered in doses of 1.0,2.5 and 6.25 mg/kg and in rats given in doses of 15 and 40 mg/kg has been found to be safe. No teratogenicity or embryotoxicity is demonstrated .

In higher doses non beta blockers embryotoxicity must be taken into consideration. As per the study done on the rats and rabbits.

Safety of Bisoprolol has been demonstrated with studies conducted on pregnant rats and rabbits which showed no influence in the postpartum period or partiurition,rearing,lactation and on the behavior of the offsprings.

Mutagenic potential

In Chinese striped hamsters subjected to chromosome aberration tests in fibroblasts proved to be safe. No mutagenicity was found either with mutagenicity tests with bacteria or micronucleus tests in mouse.

In a long term study conducted in animals with Bisoprolol has showed no carcinogenicity.

Contraindications

Bisoprolol is contra-indicated in patients with:

1.acute heart failure, episodes of heart failure decompensation requiring IV inotropic therapy,cardiogenic shock;

2. second or third degree AV block (without a pacemaker);

3. sick sinus syndrome or sinoatrial block;

4.bradycardia with less than 60 beats/minute before the start of therapy;

5. hypotension (systolic blood pressure less than 100mmHg);

6.severe bronchial asthma or severe chronic obstructive pulmonary disease;

7.late stages or peripheral arterial occlusive disease;

8.Raynaud's syndrome;

9.Untreated phaeochromocytoma

10.Metabolic acidosis;

11.Hypersensitivity to bisoprolol or to any of the excipients included in the tablets.

PHARMACOKINETICS

The middle position of the Bisoprolol gives the pharmacokinetic property that has the features of lipophilicity (which favours high absorption),hydrophilicity (longer elimination half life and less first pass effect)

PHARMACOKINETICS DATA	
Absorption	>90%
Firstpass effect	<10%
Bioavailability	90%
Cmax	~50ng/ml
Tmax	2 – 3 hrs
Elimination t ½	10 – 12 hrs
Clearance	50% unchanged
	50% metabolized
Excretion	95% renal
	2% faecal
Renal clearance	140 ml/min
Distribution	3.2 l/kg
Plasma protein binding	~30%
Placental transfer	Yes

Pharmacokinetics of Bisoprolol is independent of age and sex.

Biotransformation is not accelerated even in hyperthyroidism.

BIOAVAILABILITY

More than 90 % of the drug is absorbed after oral administration.10 % of the drug undergoes first pass metabolism. So bioavailability of Bisoprolol is very high (90 %).

DISTRIBUTION

Plasma protein binding of Bisoprolol is around 30 %.

Pathophysiological changes in plasma proteins (e.g increase in alpha 1 glycoprotein) do not influence the pharmacokinetics of Bisoprolol. Since it is moderately lipophilic volume of distribution is medium and less protein binding capacity.

METABOLISM & ELIMINATION

Two routes of clearance effective in Bisoprolol is by

1.Metabolism in the liver to inactive metabolites

2.Excretion of unchanged substances via kidneys.

This balanced clearance enables the half life of Bisoprolol only to double, even in case of complete failure of either liver or kidney. So generally there is no need for adjustment of dose in mild to moderate liver or kidney impairments. However in chronic severe insufficiency of either of the two organs, daily dose of Bisoprolol should not exceed 10 mg.

With single daily dose of Bisoprolol for one week accumulation factor is 1.2.Average first pass effect is 10 %.So accumulation and first pass effect is counteracted with single daily dose.

Elimination half life investigated in young healthy human volunteers (26 – 63 yrs) and in elderly hypertensives (69 – 80 yrs) was always in the range of 10 – 12 hours. Peak plasma levels are noted after 1 – 3 hours of administration.So once daily dose regimen is very effective with Bisoprolol.

Interactions

The effect of use of enzyme inducers/enzyme inhibitors on the half life of Bisoprolol is negligible. Half life is decreased by 35 % on rifampicin administration (potent enzyme inducer).Dose of Bisoprolol need not to be adjusted. Pharmacokinetics of Theophylline and Warfarin is not altered by Bisoprolol. Combining Bisoprolol with Procainaminde in patients with ventricular tachycardia prolongs the ventricular refractory period.So ventricular tachycardia treatment with this combination is proved to be effective.

PHARMACOLOGY

Hemodynamics

Several hemodynamic studies have demonstrated that Bisoprolol to have less inotropic effect on heart. Two hours after 5 mg and 20 mg of oral Bisoprolol in coronary patients the hemodynamics were studied using radionuclide ventriculography and flow directed catheter in right ventricle. During rest and exercise there is decrease in heart rate, cardiac index and rate

pressure product after 5 mg of Bisoprolol. The results were slightly different quantitatively after 20 mg of Bisoprolol. No significant effect in pulmonary capillary pressure or ejection fraction following two doses of Bisoprolol during rest and exercise.

Electrophysiology

Adrenergic stimulation is inhibited by electrophysiological effects of beta blockers. Frequency of primary and secondary pacemaker centers is decreased. Delaying of AV conduction and prolongation of refractory period of AV node is noted. Ten patients with paroxysmal supraventricular tachycardia were investigated for electrophysiological process of Bisoprolol after 10 mg of Bisoprolol administered intravenously as a single dose.Surface ECG potentials from right atrium and ventricle,Bundle of His are recorded before and after intravenous Bisoprolol. After intravenous Bisoprolol sinus node frequency is significantly decreased. Sinus node recovery time is significantly increased. AV node refractory period was prolonged. Frequency corrected QT time is slightly decreased ,which is suggestive of antiarrythmic effect in acute myocardial infarction.

Receptor occupancy

In volunteers or patients treated with beta blockers, percentage of beta 1 receptor occupied is correlated directly with decrease in heart rate induced by exercise.

In a double blind placebo controlled study groups, six patients were administered 200 mg of Atenolol and 100 mg Bisoprolol as a single oral dose. Percentage of beta 1 and beta 2 blockade was studied by ex vivo/invitro assays.80 % of beta 1 receptors and 25 % of beta 2 receptors were occupied with Atenolol group. With Bisoprolol group no beta 2 receptors were occupied. Thus higher beta 1 selectivity is demonstrated.

Lung function

Even at peak plasma levels Bisoprolol has no clinically significant beta 2 receptor occupancy. Bronchial muscle dilatation is mediated by beta 2 receptors. Nonselective beta blockers poses risk in patients with COPD and asthma. Already existing increase in airway resistance is worsened and FEV1 is reduced.Ina controlled study done in COPD patients with Bisoprolol (30 and 40 mg) doeses outside the therapeutic range, minimal increase in airway resistance and decrease in FEV1 was measured. Within the therapeutic range (2.5 mg – 20 mg) beta 1 selectivity of Bisoprolol has been proved.

Another study comparing placebo, Atenolol and Bisoprolol in coronary artery disease patients with COPD airway resistance was measured. Airway resistance remained unchanged with placebo and Bisoprolol group. Slight increase in airway resistance was noted in Atenolol group.

Peripheral circulation

Influence of beta blockers on isoprenaline induced increased blood flow and decreased diastolic blood pressure was studied as a measure of receptor

selectivity (bela 1).Non selective beta blockers significantly reduces these isoprenaline effects .But very negligently by Bisoprolol. In a study with 16 healthy volunteers dose response curves for isoprenaline were derived for fall in diastolic blood pressure prior to and after intravenous beta 1selective drugs (Bisoprolol, Metaprolol),beta 1 selectivity with intrinsic sympathomimetic activity (Acebutalol),non selective drugs with intrinsic sympathomimetic drugs (Penbutalol) and non selective beta blocker (Propranolol). All the beta blockers reduces the heart rate during exercice to almost an equal extent. Shift to right of the dose response curve determines the highselectivity (beta 1) which is noted with Bisoprolol, Metaprolol and Acebutalol.

Lipid metabolism

Non selective beta blockers have adverse effects on lipid metabolism. They increase the total and LDL cholesterol levels and decreases the HDL levels (protective against atheroma).In long standing treatment with Bisoprolol has no change in either of the cholesterol levels. In a double blind placebo controlled study done in patients with hypertension and type II diabetes mellitus , serum levels of cholesterols and triglycerides were measured. No significant change in lipid levels were observed with Bisoprolol (10 mg) when compared with placebo. Results of the study done with long term treatment of Bisoprolol shows no significant change in lipid parameters.

Also studies on lipolysis, after treatment with terbutaline (beta 2 agonist) Bisoprolol showed no effect on free fatty acid levels. Bisoprolol at a dose of 5

mg showed no action on beta 2 receptors. These results are confirmed by studies done over 5 years.

Carbohydrate metabolism

Bisoprolol due to its high beta 1 selectivity does not affect the carbohydrate metabolism. In diabetic patients treated with Bisoprolol dose adjustments of oral hypoglycemic or additional blood sugar monitoring is not needed.In a study, healthy volunteers were administered various beta blockers orally and followed by insulin after 3 hours.No change in duration of hypoglycemia ,serum lactate concentration was observed with 10 mg Bisoprolol when compared with the control group.

Insulin sensitivity

Beta blockers adversely affect the glucose levels and increases the insulin resistance. Tests which measures glucose uptake is taken as a measure of insulin sensitivity. Such tests showed no adverse effect on sensitivity of insulin with Bisoprolol.

In a double blind study done in 22 healthy volunteers who were administered either ACE inhibitors (Lisinopril) or selective beta 1 blocker (Bisoprolol) for four weeks. Serum insulin concentration and glucose infusion rate were measured. No significant change is noted in either group.

In conclusion neither group had influenced the insulin sensitivity in normotensive patients.

Fibrinolytic system

Circadian variability is noted in sympathetic activity and fibrinolytic system components. This explains the highest risk of coronary occlusion in the morning when the activity of tissue plasminogen activator and plasminogen activator inhibitor 1 is at its peak and produce a prothrombotic state. In patients treated with beta blockers attenuation of the circadian rhythm is noted in patients with myocardial infarction. In a study conducted in 20 coronary artery disease patients whose disease was in a stable state (stable plaque) were administered placebo, Bisoprolol (10 mg/day and increased to 20 mg/day if basal heart rate is more than 60 per min), Quinapril (10 mg/day and increased to 20 mg/day if basal heart rate is more than 60 per min) each for 4 weeks consecutively. After every 4 weeks period 6 hourly blood samples,24 hours Holter monitoring were done. Heart rate variability was significantly increased with Bisoprolol. Peak plasminogen activator inhibitor 1 activity which is seen in the morning is decreased by Bisoprolol though not statistically significant. Quinapril had no effect in either of the parameter.

REVIEW OF LITERATURE

Various studies have evaluated the efficacy of Bisoprolol in the management of hypertension and heart failure and many studies have demonstrated the importance of bloodless surgical field using various drugs and combinations.

In a study by Matsuoka H,Kuwajima I and Shimada K, they have compared the efficacy and safety of Bisoprolol transdermal patch and oral formulation in controlling the grade I or II essential hypertension.They included both sexes with age ranging from 20-80yrs with grade I or II essential hypertension in their study.They concluded that both transdermal patch as well as the oral formulation of Bisoprolol are superior to Placebo in controlling blood pressure.

In a study by Andre P.Boezaart and Johan Van der Merwe,they compared the efficacy of Sodium Nitroprusside and Esmolol in providing an optimal surgical field and better control of the blood pressure intraoperatively done in 20 consenting ASA I & II patients.They concluded that Esmolol provided optimal surgical field than SNP stating that hypotension caused by cardioselective beta blockers resulted in increased sympathetic tone of the mucous membrane arterioles that exerted unopposed alpha-adrenergic effects on the mucous membrane vasculature, causing capillary vasoconstriction.On the

other hand SNP produced arteriolar vasodilatation which may explain the poor surgical condition produced by it.

In an another study, Goran Kekovic and Branislav Milovanovic have compared the effect of Bisoprolol and Losartan in the treatment of essential hypertension.In their study they included both sexes age ranging from 26-75 yrs with essential hypertension and evaluated and compared the efficacy of Bisoprolol and Losartan in a oral dose of 5mg and 50mg respectively. They concluded that both the drugs effectively regulated the blood pressure.

In a study done by Nitu Puthenveettil and Sunil Rajan, they have evaluated the hemodynamic changes and surgical conditions by comparing oral premedication with Clonidine and Metoprolol. In their study they had given the drugs 2 hrs before surgery and evaluated the heart rate and blood pressure every 15 mins till the end of surgery. And also they estimated the quality of surgical field with a pre-defined category scale with scores 1 – 5 .

In an another study by Tarek Shams and Nahla S El Bahnasawe,they compared and evaluated the efficacy of Dexmeditomidine and Esmolol in FEES.The study was done on 40 ASA I & II patients scheduled for FESS receiving either Dexmeditomidine or Esmolol.The surgical field was assessed using Average Category Scale and the parameters observed were HR,MAP and intraoperative Fentanyl consumption. They concluded that both Dexmeditomidine and Esmolol can be safely used in FESS to provide a better surgical field and better control of blood pressure.

METHODOLOGY

This study was a randomized, prospective double blinded clinical trial conducted over a period of 1 year in the Department of Anesthesiology at Madurai Medical College, Madurai.

Inclusion criteria :

1.Functional Endoscopic Sinus Surgeries

2.Both sexes.

3.Age between 15 – 65 years

4.ASA Grade I & II

Exclusion criteria :

1.Patients with history of Hypertension

2.Patients with history of Asthma

3.Patients with history of Heart blocks

4.Patients with history of Bleeding disorders

5.Patients taking Antiplatelet drugs or Antihypertensive drugs

6.Patients with known Allergy or hypertensive reactions to medications

METHODS

After getting consent from each patients and Institutional Ethical Committee approval, 60 patients of age between 15 – 65 years belonging to ASA Grade I & II who are posted for Functional Endoscopic Sinus Surgery were randomized into one of the two groups. Group A (receiving placebo) and group B (receiving bisoprolol) of 30 each for induction and maintenance of anesthesia (sample size was taken in accordance with the similar type of studies done in the past).

All patients underwent a thorough pre – anesthetic assessment on the evening before the day of surgery. A thorough medical and surgical history was taken and all the required investigations were reviewed. detailed and valid informed consent was obtained from each patient after explain the procedure.

In the morning of surgery all patients received Inj.Glycopyrollate 0.2 mg and Inj.Midazolam 1 mg as premedication. All patients were fasting for atleast 8 hours before the start of the surgery. Group B patients were given Bisoprolol 2.5 mg orally with a sip of water 90mins before the surgery by an assistant as the anesthesiologist was blinded to the randomization.

After the patients were wheeled inside the operating room, a large bore intravenous canula (18G) was inserted on the left upper limb. All patients received crystalloid infusion as standard. Monitoring include ECG,Pulseoximetry, ETCo2 and non invasive blood pressure .

Anesthetic management of all patients were similar. Before inductionpatients were preoxygenated with 100 % oxygen for a period of 3mins followed by induction with Inj.Thiopentone in a dose of 5 mg/kg, Inj.Fentanyl in a dose of 2µg/kg and Inj.Atracurium 0.5 mg/kg. Patients were intubated with a suitable sized cuffed endotracheal tubes. Throat was packed with tape gauze to prevent microaspirations. All patients received crystalloid infusion at a rate of 4 ml/kg/hr. Patients were positioned supine with about 30 degree head elevation.

The surgeons used 2% Lignocaine with Adrenaline in the concentration of 1in 2,00,000 dilution for the nasal mucosa infiltration. Maintainance was with O_2 and N_2O in the percentage of 40 and 60 respectively and Sevoflurane.

The target MAP was around 60 – 70 mmHg during the surgery and was left to the anesthesiologist who is conducting anesthesia to judge the clinical situation and to adjust the concentration of Sevoflurane and the additional doses of Fentanyl. All patients received Inj.Dexamethasone 4 mg and Inj.Ondansetron 4 mg after the start of the procedure.

After the surgery is over,patients were reversed with Inj.Neostigmine 0.05 mg/kg dose and Inj. Atropine 0.02 mg/kg dose. Patients were shifted to the PACU and were observed for an hour and then shifted to the respective wards. Postoperative hemoglobin estimation was done on the evening of the day of surgery.

During the surgery, Sevoflurane volume percentage, MAP and HR were recorded every 10mins.The blood loss was estimated from the number of soaked cotton strips and the volume of blood lost in the suctioning apparatus which was kept empty before the start of the surgery.

A fully soaked cotton strip was estimated to contain 5 ml of blood and a partially soaked cotton strip was estimated to contain 2.5 ml of blood.

After the procedure was over, surgeons who performed the surgery were asked about the condition of the operating field and to grade it using the FROMME BOEZAART Scale.

FROMME – BOEZAART GRADING

Grade 0	No bleeding
Grade 1	Slight bleeding. No suctioning required
Grade 2	Slight bleeding. Occasional suctioning required. Bleeding does not threaten surgical field
Grade 3	Slight bleeding. Frequent suctioning required. Bleeding threatens surgical field for a few seconds after removal of suction
Grade 4	Moderate bleeding. Frequent suctioning required. Bleeding threatens surgical field immediately after removal of suction
Grade 5	Severe bleeding Constant suctioning required Bleeding appears faster than can be removed by suction Surgical field threatened and surgery not possible

OBSERVATION AND RESULTS

STUDY DESIGN

In the present study,60 patients with age between 15 – 65 years belonging to ASA Grade I & II were randomly allocated into two groups each consisting of 30 patients.

Group A – patients receiving placebo

Group B – patients receiving Bisoprolol.

The age , sex, preoperative hemoglobin of all patients were comparable between the two groups.

STATISTICAL TOOLS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using statistical package for the social sciences (**SPSS** software **version 16**).

Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chisquare test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

SEVOFLURANE CONSUMPTION CALCULATION

The **density**of Sevoflurane is 1.520.That is 1 ml of sevoflurane weighs 1.520 grams.

Sevoflurane **molecular weight** is 200 grams which is the weight of 1 mole of Sevoflurane.

So if 200 grams of Sevoflurane has 1 mole then 1.520 grams (1 ml) will have 0.0076 moles.(1.520/200).

According to the universal gas equation 1 mole of an ideal gas will liberate 22.4 liters of vapour at STP.

So 1 ml of Sevoflurane which has got 0.0076 moles will convert to 170.24 mls of Sevoflurane vapour.(22400 × 0.0076)

1 mole will liberate 22400 ml of vapour.

1 ml will liberate 170 mls of vapour .(22400 x 0.0076) as 1 ml contains 0.0076 mloes.

Fresh gas flow (L/min) x Dial concentration (%) = ml of vapour/min

To liberate 170 ml of vapour 1 ml is used. So

1/170 x ml of vapour/min = ml of Senoflurane used (or)

1/170 x Fresh Gas Flow(ml/min) x Dial concentration = liquid Sevoflurane in ml. (or)

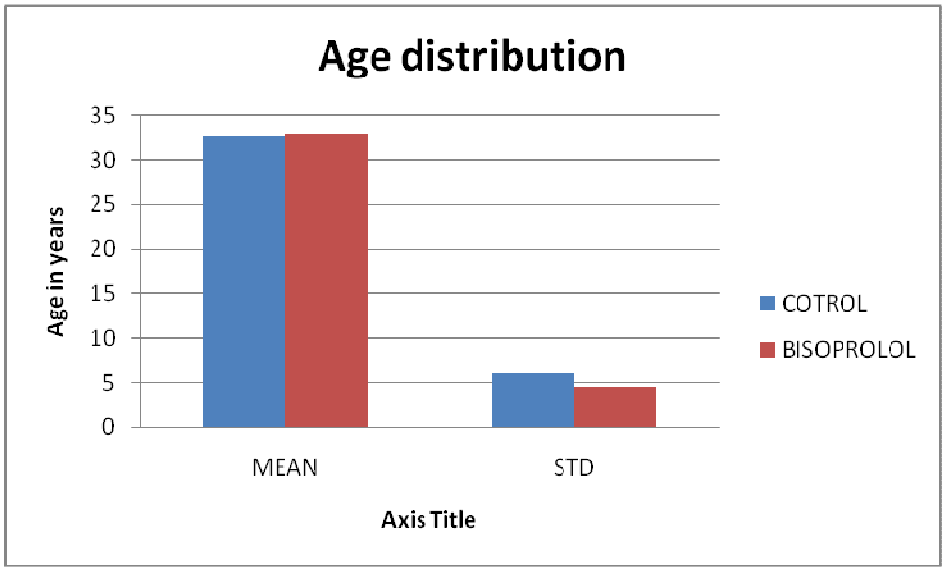
Fresh Gas Flow (L) x Dial Concentration (%) x 10/170 (or)

Fresh Gas Flow (L) x Dial Concentration (%) x 0.06 = ml of Sevoflurane.

Table : AGE DISTRIBUTION

GROUPS	Age	P value
CONTROL	34.96 ± 12.69	
BISOPROLOL	32.73 ± 11.87	
		0.35

In Group A the mean age was 34.96 ± 12.69 and in Group B the mean age was 32.73 ± 11.87.The p value was 0.35 which was not statistically significant.

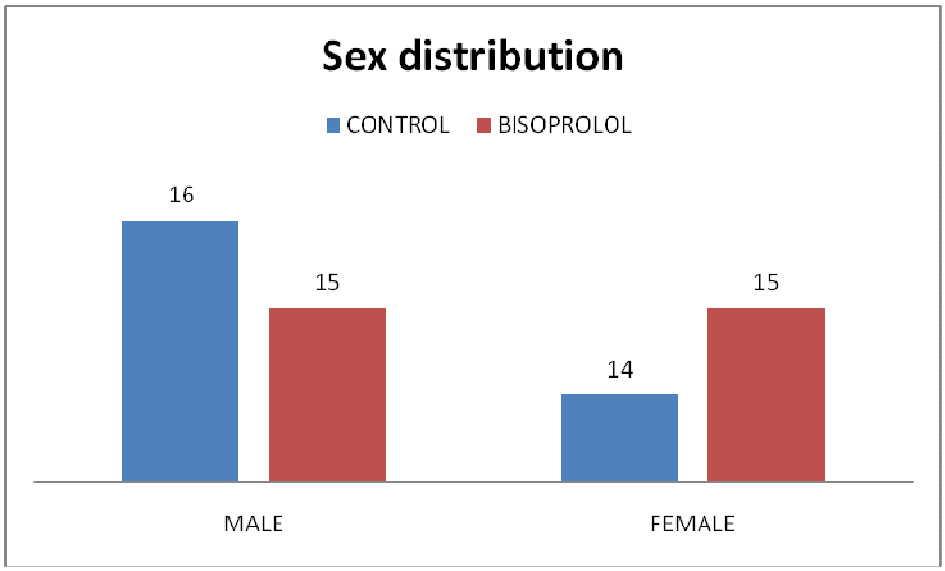


COMPARISON OF AGE DISTRIBUTION BETWEEN THE TWO GROUPS

Table 2: SEX DISTRIBUTION

GROUPS	MALE	FEMALE	TOTAL	P Value
CONTROL	16	14	30	
BISOPROLOL	18	12	30	
TOTAL	34	26	60	.602

Nearly 56.66 % of the study were males and 43.33 % were females among the study population. Sex composition of both the groups were similar in both the groups. p value is 0.602 which was not significant.

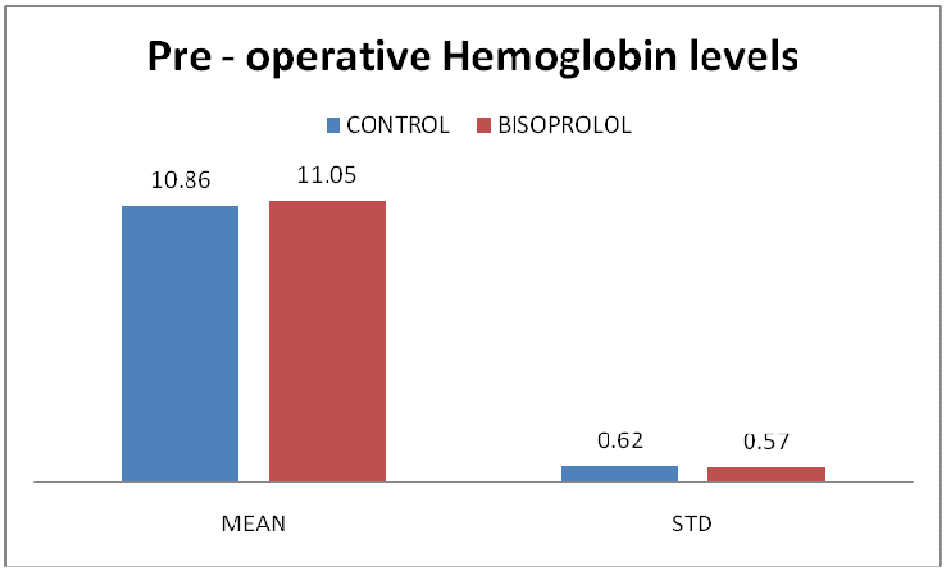


COMPARISON OF SEX DISTRIBUTION BETWEEN THE TWO GROUPS

Table 3 :PREOPERATIVE HAEMOGLOBIN

GROUPS	Mean	Std. Deviation	P Value
CONTROL	10.86	0.563	
BISOPROLOL	11.05	0.635	
			0.12

In Group A the mean preoperative hemoglobin was 10.86 ± 0.563 and in Group B it was 11.05 ± 0.635.The p value is 0.12 which is not significant.



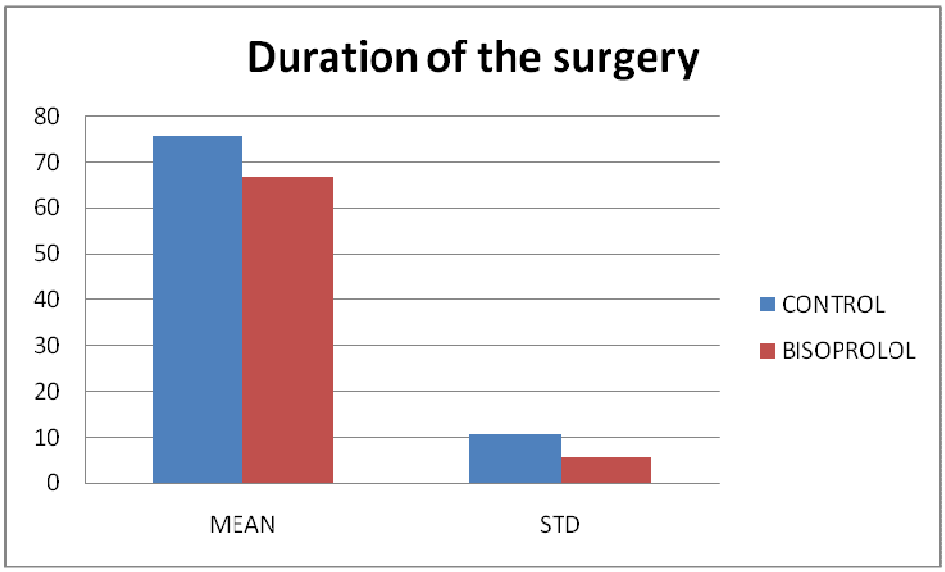
COMPARISON OF PREOPERATIVE HEMOGLOBIN

BETWEEN THE TWO GROUPS

Table 4:DURATION OF SURGERY

GROUPS	Mean	Std. Deviation	P Value
CONTROL	75.66	10.48	
BISOPROLOL	67.0	5.81	
			< 0.0001

The mean duration of surgery in Group A was 75.66 ± 10.48 and in Group B it was 67.0 ± 5.81.The p value is < 0.0001 which is statistically significant.



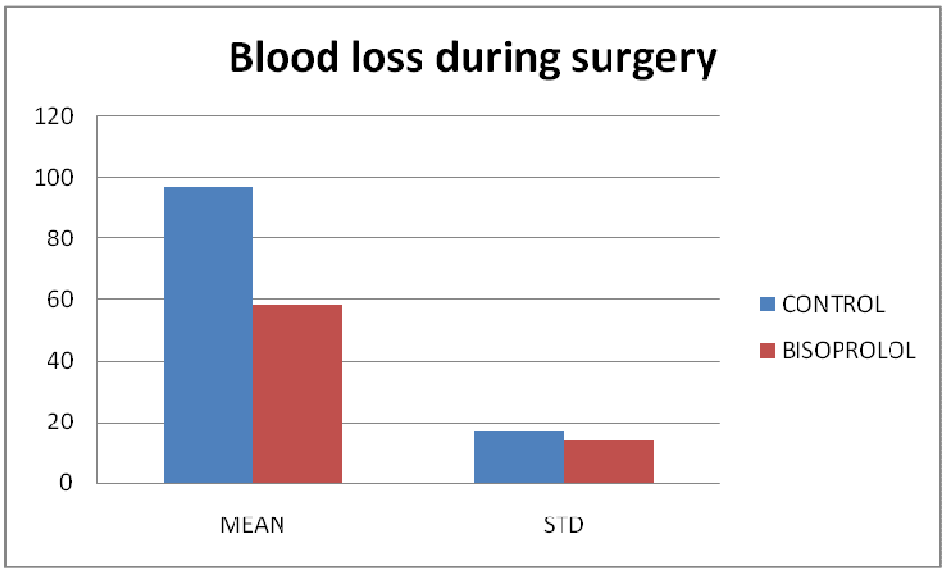
COMPARISON OF DURATION OF SURGERY

BETWEEN THE TWO GROUPS

Table 5 :BLOOD LOSS DURING THE SURGERY

GROUPS	Mean	Std. Deviation	P Value
CONTROL	97	16.75	
BISOPROLOL	58.3	13.9	
			< 0.0001

In Group A the mean blood loss during the surgery was 97 ± 16.75 and in Group B the mean blood loss was 58.3 ± 13.9.The p value is < 0.0001 which is statistically significant.



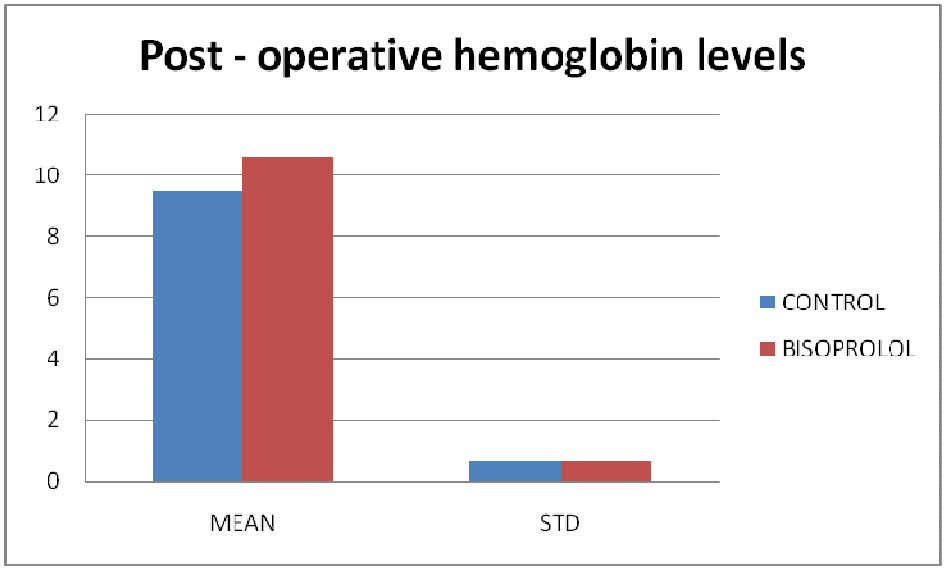
COMPARISON OF BLOOD LOSS DURING THE SURGERY

BETWEEN THE TWO GROUPS

Table 6: POST OPERATIVE HEMOGLOBIN

GROUPS	Mean	Std. Deviation	P Value
CONTROL	9.5	0.65	
BISOPROLOL	10.63	0.65	
			< 0.0001

The mean post operative hemoglobin in Group A was 9.5 ± 0.65 and in Group B it was 10.63 ± 0.65.The p value is< 0.0001 which is statistically significant.



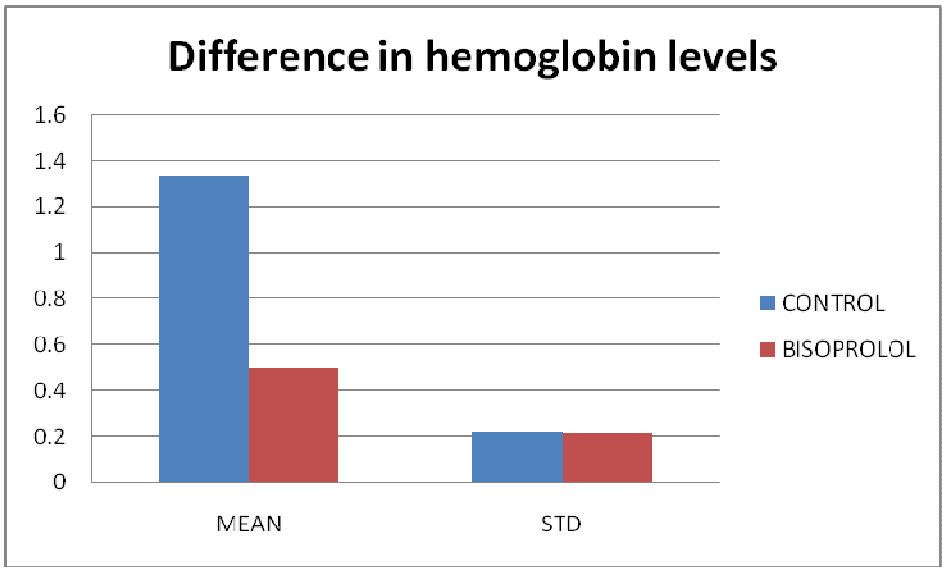
COMPARISON POSTOPERATIVE HEMOGLOBIN

BETWEEN THE TWO GROUPS

Table 7: DIFFERENCE IN HEMOGLOBIN

GROUPS	Mean	Std. Deviation	P Value
CONTROL	1.04	0.22	
BISOPROLOL	0.5	0.21	
			< 0.0001

The mean difference in haemoglobin in Group A was 1.04 ± 0.22 and in Group B was 0.5 ± 0.21.The p value is < 0.0001 and is statistically significant.



COMPARISON OF DIFFERENCE IN HEMOGLOBIN

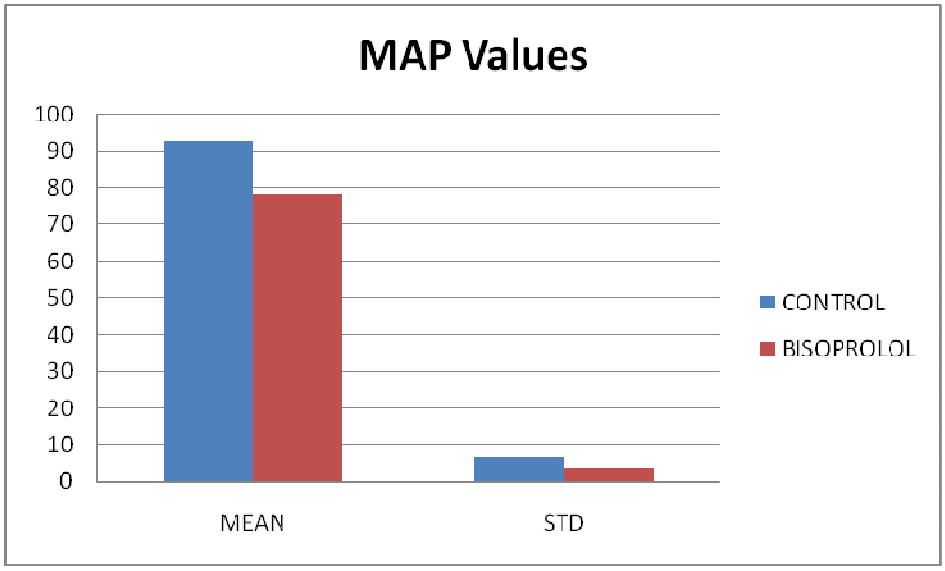
BETWEEN THE TWO GROUPS

Table 8

COMPARISON OF MAP VALUE BETWEEN TWO GROUPS

GROUPS	Mean	Std. Deviation	p Value
CONTROL	92.87	6.39	
BISOPROLOL	78.25	3.5	
			< 0.0001

In Group A the mean MAP value was 92.87 ± 6.39 and in Group B it was 78.25 ± 3.5.The p value is < 0.0001 which is statistically significant.



COMPARISON OF MAP VALUES BETWEEN THE TWO GROUPS

	Groups	n	Mean	Std. Deviation	Std. Error Mean	P VALUE
MAP PRE OP	Bisoprolol	30	73.3000	6.67548	1.21877	0.000
	Control	30	86.2667	6.32964	1.15563	
MAP 10 MINS	Bisoprolol	30	74.3000	5.25324	.95911	0.000
	Control	30	87.9000	5.39700	.98535	
MAP20 MINS	Bisoprolol	30	74.2667	6.23634	1.13859	0.000
	Control	30	86.2667	5.83647	1.06559	
MAP30 MINS	Bisoprolol	30	73.4000	5.58076	1.01890	0.000
	Control	30	88.7333	6.41622	1.17144	
MAP 40 MINS	Bisoprolol	30	74.0667	4.89851	.89434	0.000
	Control	30	89.2000	5.73194	1.04650	
MAP 50 MINS	Bisoprolol	30	74.2000	4.56675	.83377	0.000
	Control	30	86.9333	4.82760	.88140	
MAP 60 MINS	Bisoprolol	30	72.9000	4.61146	.84193	0.000
	Control	30	91.0333	5.17609	.94502	
MAP 70 MINS	Bisoprolol	15	72.4000	5.15198	1.33023	0.000
	Control	20	89.0500	5.88911	1.31684	

Group Statistics showing MAP variation between the two groups.

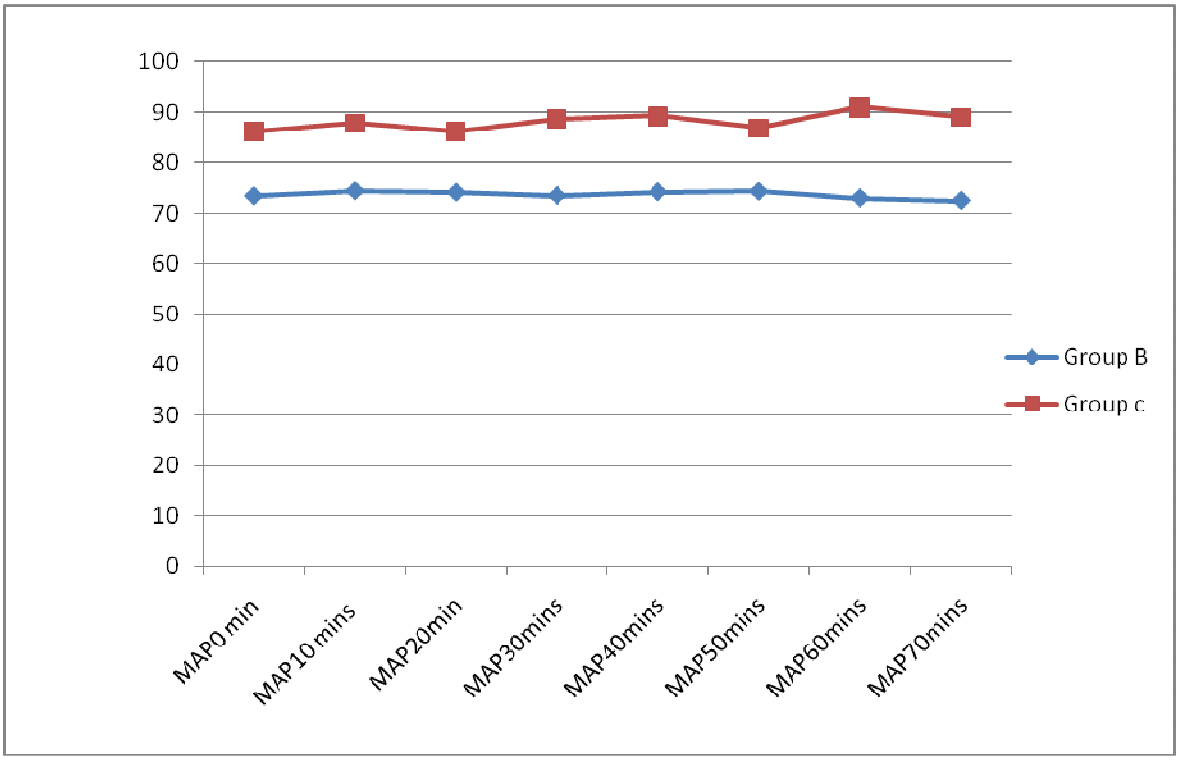
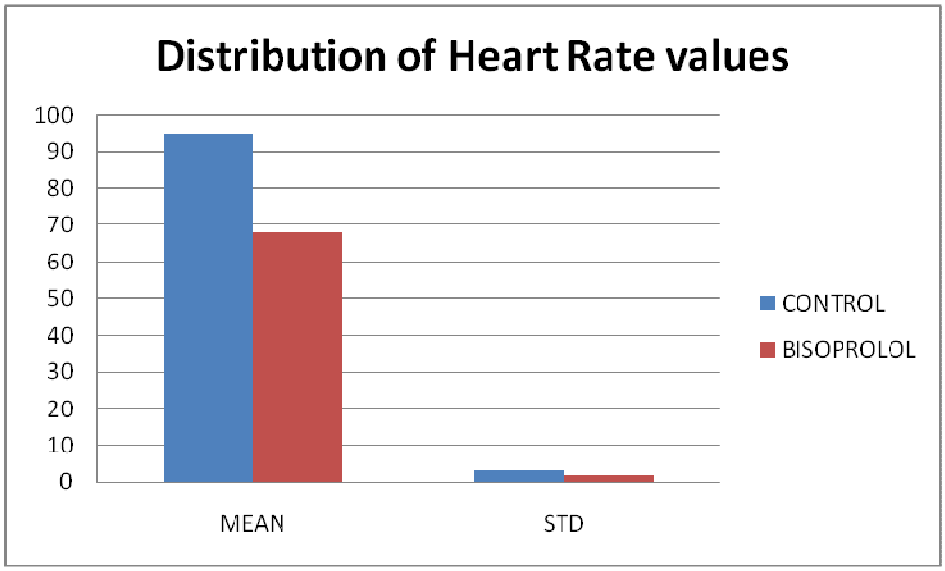

100
90
80
70
60
50
40
30
20
10
0
MAP0 min
MAP10 mins
MAP20min
MAP30mins
MAP40mins
MAP50mins
MAP60mins
MAP70mins
Group B
Group c

Table 9: COMPARISON OF HEART RATE

BETWEEN THE TWO GROUPS.

GROUPS	Mean	Std. Deviation	P Value
CONTROL	94.75	3.14	
BISOPROLOL	67.97	1.84	
			< 0.0001

In Group A the mean HR was 94.75 ± 3.14 and in Group B the mean HR was 67.97 ± 1.84.The p value is < 0.0001 and it is statistically significant.



COMPARISON OF HEART RATE VARIATION

BETWEEN THE TWO GROUPS

	Study Groups	N	Mean	Std. Deviation	Std. Error Mean	p VALUE
HR PRE OP	Bisoprolol	30	70.8000	4.72265	.86223	.000
	Control	30	94.1333	6.84676	1.25004	
HR 10 MINS	Bisoprolol	30	69.3667	5.26199	.96070	.000
	Control	30	95.8333	5.79586	1.05817	
HR 20 MINS	Bisoprolol	30	67.3667	4.00416	.73106	.000
	Control	30	95.1000	5.39060	.98419	
HR 30 MINS	Bisoprolol	30	68.5333	5.11747	.93432	.000
	Control	30	95.7000	4.94208	.90230	
HR 40 MINS	Bisoprolol	30	67.9000	5.07428	.92643	.000
	Control	30	93.0000	6.05720	1.10589	
HR 50 MINS	Bisoprolol	30	66.5000	5.60018	1.02245	.000
	Control	30	95.1667	5.47145	.99895	
HR 60 MINS	Bisoprolol	30	66.7333	4.80613	.87747	.000
	Control	30	95.2000	5.83332	1.06501	
HR 70 MINS	Bisoprolol	16	65.6875	3.47791	.86948	.000
	Control	21	93.1905	4.68635	1.02265	

Group Statistics showing Heart Rate variation between two groups

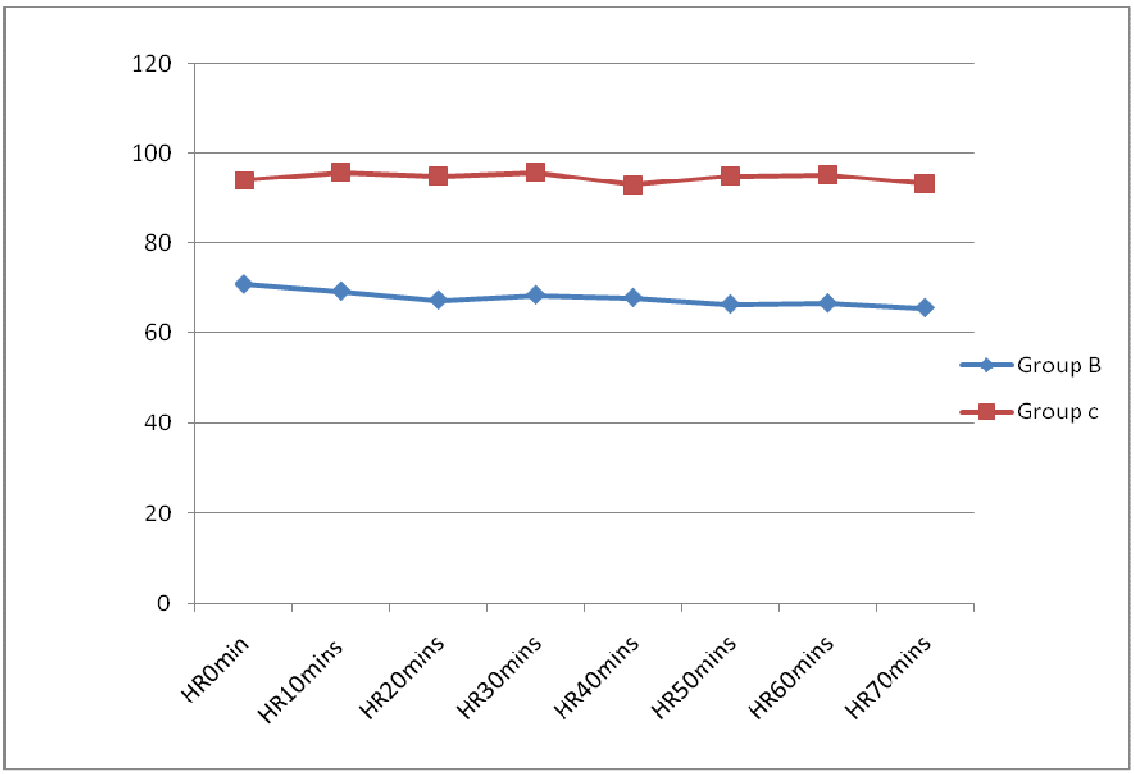

120
100
80
60
40
20
0
HR0min
HR10mins
HR20mins
HR30mins
HR40mins
HR50mins
HR60mins
HR70mins
Group B
Group c

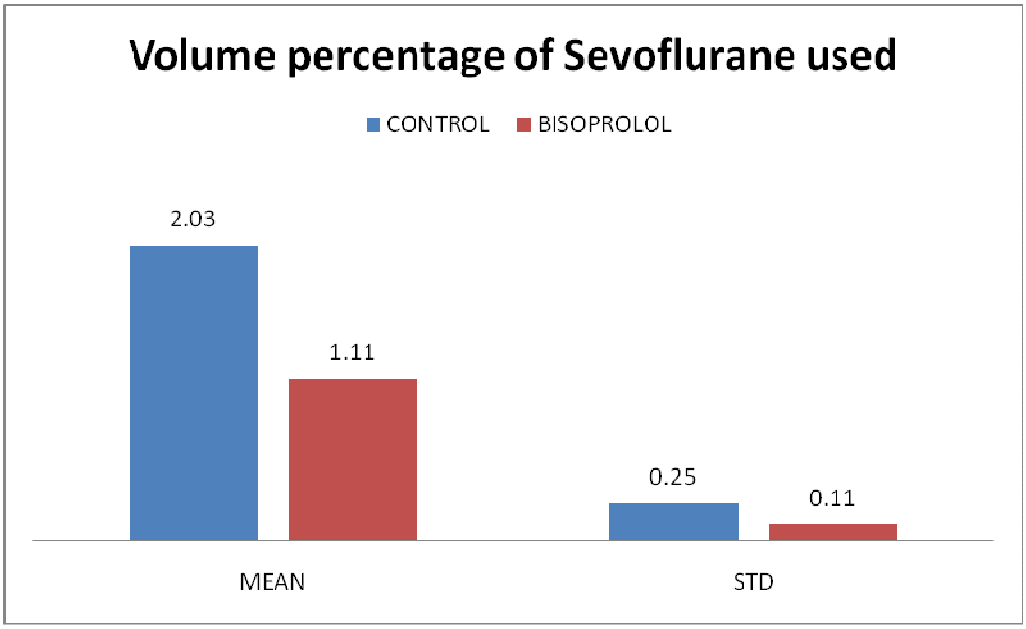
Table 10

COMPARISON OF SEVOFLURANE VOLUME % USED

BETWEEN TWO GROUPS

GROUPS	Mean	Std. Deviation	P Value
CONTROL	2.03	0.25	
BISOPROLOL	1.11	0.11	
			< 0.02

In Group A the mean sevoflurane volume percentage used was 2.03 ± 0.25 and in Group B the mean value was 1.11 ± 0.11.The p value is < 0.02 and it is statistically significant.

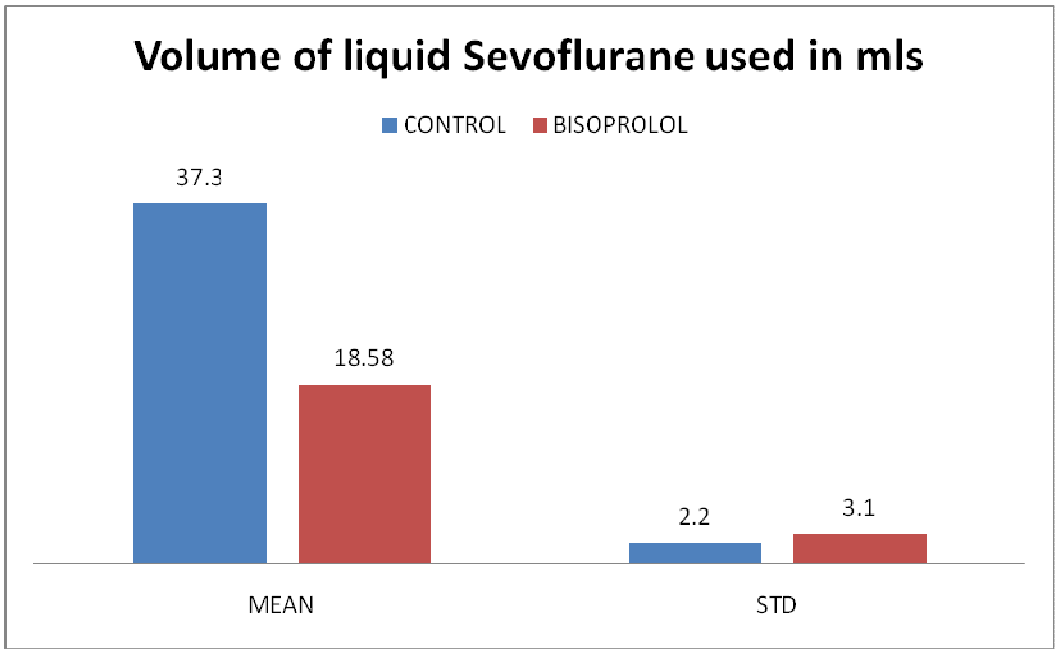


COMPARISON OF VOLUME PERCENTAGE OF SEVOFLURANE USED BETWEEN THE TWO GROUPS

Table 11: **COMPARISON OF LIQUID SEVOFLURANE USED BETWEEN THE TWO GROUPS**

GROUPS	Mean	Std. Deviation	P Value
CONTROL	37.3	2.2	
BISOPROLOL	18.58	3.1	
			< 0.0001

The mean volume of liquid sevoflurane used in Group A is 37.3 ± 2.2 ml and in group B it is 18.58 ± 3.1.The p value is < 0.0001 which is statistically significant.

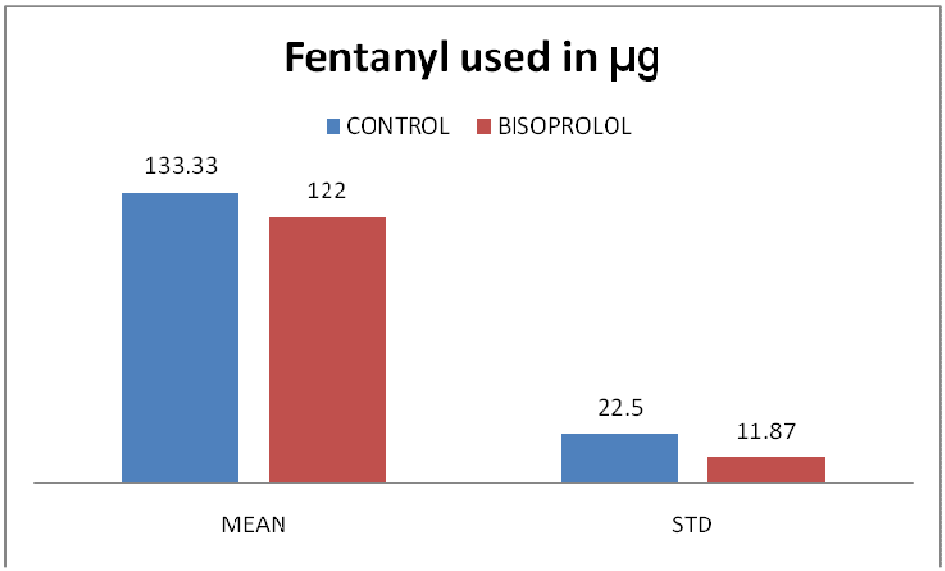


COMPARISON OF VOLUME OF LIQUID SEVOFLURANE USED BETWEEN THE TWO GROUPS

Table 12: **COMPARISON OF FENTANYL REQUIREMENT BETWEEN THE TWO GROUPS**

GROUPS	Mean	Std. Deviation	P Value
CONTROL	133.33	22.5	
BISOPROLOL	122	11.87	
			< 0.02

In Group A the mean value of Fentanyl used was 133.33 ± 22.5 and in Group B it was 122 ± 11.87.The p value is < 0.02 which is statistically significant.

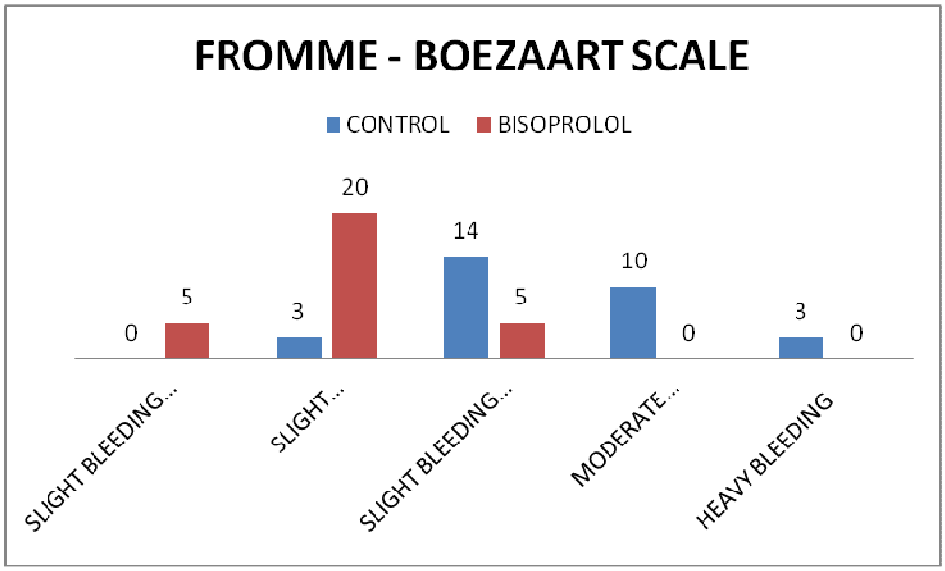


COMPARISON OF FENTANYL USED BETWEEN THE TWO GROUPS

Table 13: **COMPARISON OF FROMME – BOEZAART SCALE BETWEEN THE TWO GROUPS.**

Formme Boezaart Score				
	FB Score	Study Groups		Total
		Bisoprolol	**Control**	
	Slight Bleeding No suctioning	5	0	5
	Slight Bleeding , suctioning+, No obliteration of operative feild	20	3	23
	Slight Bleeding Frequent suctioning	5	14	19
	Moderate bleeding	0	10	10
	Heavy bleeding	0	3	3
Total		30	30	60

In Bisoprolol group 5 patients had slight bleeding with no need for suctioning , 20 patients had slight bleeding which required occasional suctioning , 5 patients had slight bleeding which required frequent suctioning and none had moderate to severe bleeding. In Group A 10 and 3 patients had moderate and severe bleeding respectively. The p value is < 0.0001 and is statistically significant.



COMPARISON OF FROMME BOEZAART SCALE

BETWEEN THE TWO GROUPS

DISCUSSION

FESS is one of the well accepted treatment modalities (rhinosurgeries) for the chronic inflammatory sinus diseases. FESS is done by introducing a high definition telescope into the nasal cavity through the anterior nares. As the nasal cavity is a very sensitive one ,any surgical manipulation of the area can result in severe sympathetic stimulation which would cause tachycardia and hypertension. In addition to that the nasal mucosa has got a very rich network of blood supply and very delicate to touch in nature it would bleed easily which severely compromises the visualization of the operating field. This becomes even more difficult with the use of endoscopes. As a result of this there could be an inadvertent tissue injury which leads to postoperative adhesions and even scarring. At the worst it can lead to severe complications such as orbital or brain injury.

This necessitates a blood less field for the surgeon to operate upon easily so as to minimize the complications.

Various techniques have been used during FESS to achieve a bloodless field and an acceptable operating condition, including local anesthesia, TIVA and inhalational anesthesia. Many of these techniques are not without complications. Adrenaline used along with local anesthesia for the infiltration of

the nasal mucosa causes local vasoconstriction and reduces bleeding for a short period of time but at the cost of transient hypertension and tachycardia.

Reducing the inflammatory process of the disease by using steroids for several preoperative days can also reduce the bleeding during surgery. Other drugs like Propofol, Dexmeditomidine and Remifentanil have also been used to reduce the bleeding which provides an optimal surgical field However the expenditure and the availability of these drugs could be a factor to be considered.

To minimize the intraoperative bleeding at the surgical field reduction of the arterial blood pressure is required. This is achieved by either increasing the concentration of the volatile anesthetic agent or with the use of vasodilator drugs like Sodium nitroprusside. But with these techniques reflex tachycardia is a common side effect which increases the venous oozing in the surgical field. This is because the extent of bleeding in the operative field not only depends on the MAP but also on the venous pressure and capillary blood flow.

Studies have suggested that if the heart rate is decreased it increases the diastolic filling time and lowers the venous pressure and causes reduced venous oozing at the surgical field.

In this study the MAP values during the surgery were 92.87 ± 6.39 and 78.25 ± 3.5 in Group A and Group B respectively. This is statistically significant. Heart rate of the patients were 67.97 ± 1.84 and 94.75 ± 3.14 in

Bisoprolol group and Control group respectively which is also statistically significant.

From this observation, it seems likely that the blood loss can be directly correlated with the heart rate.

Also the anesthetic requirements such as Sevoflurane and Fentanyl are found to be higher in the control group.

The usage of beta blocker to lower the heart rate and blood pressure reduces the bleeding and improves the visualization of the surgical field. Metaprolol and Esmolol have been used for this purpose and did reduce the bleeding. However the effect lasted for a short period of time as these drugs belong to the short acting beta blockers. Also these drugs caused a rebound bleeding due to increased heart rate and venous pressure after the effect wore off. Continuous infusion of Esmolol can also be used to produce same effect throughout t the surgery but a more simpler, easier and single dose orally would be considered both prudent and cost effective.

This clinical trial was done to study the effect of Bisoprolol a long acting beta blocker, orally in reducing the bleeding and improvement in the surgical field during FESS.

The blood loss during surgery was lower with Bisoprolol group as compared with control group which is statistically significant. The reason for this could be:

1. Due to the negative chronotropic action of Bisoprolol which reduces the frequency of arterial pulsations and thereby causing less exudation of blood per unit time from the injured vessels.
2. The resultant reduction in the heart rate increases the diastolic filling time leading to reduced venous pressure and thus the venous oozing.

In this study the dose of Bisoprolol was only 2.5 mg orally which should not cause any untoward serious side effects.

The patients in Bisoprolol group needed lower doses of both liquid Sevoflurane as well as Fentanyl which was statistically significant and provided a clinical and financial benefit.The volume of liquid Sevoflurane used were 37.3 ± 2.2 ml and 18.58 ± 3.1in control group and Bisoprolol group respectively which is statistically significant.

Opinion was obtained from the operating surgeon at the end of the surgery about the surgical field and this was graded according to the FROMME-BOEZAART Scale. A direct real time correlation between the hemodynamic parameters like MAP, heart rate and the surgical field was not made in this study as it would distract the surgeon concentration. The overall operatong time was reduced because of the reduced bleeding and better view of the field.

SUMMARY

This is prospective, randomized double blided controlled study involving 60 cases posted for Functional Endoscopic Sinus Surgeries under general anesthesia. They were divided into two groups, Group A receiving Placebo and Group B receiving Bisoprolol 2.5 mg orally. Bisoprolol was given by an assistant 90 mins before surgery with sip of water. The following parameters were noted during the study period. The anesthetic requirements of Sevoflurane and Fentanyl, grading of the surgical field by the surgeons, volume of blood lost and difference in the preoperative and postoperative hemoglobin. The hemodynamic parameters noted are MAP and heart rate, oxygen saturation with pulseoximeter.

According to the present study ,it was noted that the anesthetic requirement of both Sevoflurane and Fentanyl were lower in the Bisoprolol group. There was reduced bleeding in the surgical field in the Bisoprolol group. And also the surgical field was found to be optimal in the Bisoprolol group as stated by the operating surgeons. This was reflected in the difference between the preoperative and postoperative hemoglobin. There was a significant reduction in the MAP and HR with the Bisoprolol group.

Therefore this clinical study has demonstrated that the use of a single preoperative oral dose of Bisoprolol 2.5 mg can reduce the intraoperative bleeding during FESS significantly and also improves the visualization of the surgical field. Also it lowers the anesthetic requirements of Sevoflurane and Fentanyl.

CONCLUSION

In conclusion ,the data obtained and statistical analysis suggest that the bleeding is significantly less with Bisoprolol when compared with placebo.Improvement in the surgical field is significantly better with Bisoprolol.The hemodynamic variables like MAP and heart rate were significantly low when compared with placebo.There is a significant reduction in the anesthetic requirement of Sevoflurane and Fentanyl with Bisoprolol. Bisoprolol can be used as an alternative drug in controlled hypotension by which the patients are benefitted clinically and financially.

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PROFORMA

NAME : **I.P.NO :**

ASA :

AGE & SEX :

WEIGHT :

DATE & TIME OF ADMISSION:

DATE & TIME OF DISCHARGE:

DIAGNOSIS:

PROCEDURE:

HISTORY:

Allergy to drugs,

Bleeding disorders,

H/o Hypertension,Asthma,Heart blocks.

CLINICAL EXAMINATION:

PR, BP, SPO2,

RS, CVS

BASIC INVESTIGATIONS:

Haemoglobin, PCV

Renal parameters &Serum electrolytes,

ECG

ANAESTHETIC TECHNIQUE:

All patients are induced with Inj.Thiopentone 5mg/kg and Inj.Atracurium 0.5mg/kg after preoxygenation with O2 5L/min for 5mins.Anesthesia was maintained with 66% N2O and 33% O2.All patients received Inj.Fentanyl 2 µg/kg initially.

MONITORING OF VITALS EVERY 15 MINS TILL THE END OF SURGERY:

DURATION OF SURGERY:

ADDITIONAL INJ.FENTANYL NEEDED:

DIAL CONCENTRATION OF SEVOFLURANE EVERY 15 MINS:

FRESH GAS FLOW:

CONTROL GROUP

S.No	Name	Age	Sex	IP No	Pre-op Hb	Post-op Hb	Diff	Duration	Blood loss	FB Scale	Sevo Vol%	Liquid Sevo	Fentanyl
1	MURUGAN	18	M	45345	10.2	9.2	1	100	90	3	1.2	27	160
2	SELVI	18	F	5452	10.6	9.6	1	70	85	3	1	26.4	160
3	JEGAN	20	M	4575	9.8	9	0.8	65	80	2	0.8	21	140
4	SURESH	24	M	2452	10	9.2	0.8	90	110	4	0.75	20.5	160
5	ALAGAN	45	M	12452	11.2	9.8	1.4	85	120	4	1.5	30	160
6	SAMI	45	M	4242	10	8.8	1.2	90	110	4	1.2	28	140
7	THOTTICHI	40	F	2422	10.4	9.4	1	95	95	3	1.4	28.4	120
8	KRISHNAN	52	M	45212	10.6	9.7	0.9	70	120	4	0.9	26.4	160
9	RAJESWARI	38	F	24252	9.8	9	0.8	65	100	3	0.86	26	140
10	LAKSHMI	38	F	24524	9.8	8.9	0.9	70	90	3	0.88	26.4	120
11	KANDHI	40	F	68785	10.2	9	1.2	75	80	2	0.75	26	110
12	VIRALI	55	F	8574	11	9.6	1.4	80	120	4	1	28	160
13	MALACHAMY	42	M	47564	11.2	10.2	1	80	80	2	0.8	27.2	110
14	SENTHIL	30	M	75785	10.8	9.8	1	75	75	2	0.78	26.4	110
15	PAKIYAM	39	F	57552	11.4	10.2	1.2	65	120	4	1.2	28.2	160
16	RAJESH	15	M	52752	10.8	9	0.8	85	110	4	1	28	120
17	PALANI	42	M	75755	9.8	9	0.8	80	120	5	1.5	29	160
18	PAECHI	46	F	5752	9.6	8.7	0.9	65	65	2	0.78	26	100
19	SARAVANAN	35	M	75752	10.2	9	1.2	60	75	3	0.76	24.8	110
20	MUTHU	40	M	44242	10.4	9	1.4	70	110	5	1.2	29	160
21	VALLI	43	F	72427	11.8	10.8	1	70	110	4	1	28.6	100
22	KUMARI	18	F	4204	11.6	10.8	0.8	85	75	3	0.82	27.6	140
23	SELVI	19	F	4255	9.8	8.9	0.9	80	100	4	1	28	110
24	PRAKASH	22	M	75275	10.2	9	1.2	70	80	3	0.84	28.2	110
25	VINOTH	42	M	75275	10.4	9	1.4	65	85	3	0.92	28.6	110
26	SELVARAJ	21	M	24525	10.6	9.6	1	60	95	4	0.96	29	120
27	VENI	55	F	524241	11.2	9.8	1.4	75	90	3	0.84	28.2	110
28	ANDAL	57	F	52558	11.4	10.6	0.8	65	120	5	1.5	29.8	160
29	MEENAKSHI	24	F	58545	11.6	10.8	0.8	85	110	4	1.5	30	140
30	PRABHU	26	M	25554	10.4	9.2	1.2	80	100	3	1.2	28.8	140

BISOPROLOL GROUP

S.No	Name	Age	Sex	IP No	Pre-op Hb	Post-op Hb	Diff	Duration	Blood loss	FB Scale	Sevo vol%	Liquid Sevo	Fentanyl
1	SENTHIL	16	M	56335	10.4	9.8	0.6	75	50	2	0.75	20.25	140
2	JOSEPH	18	M	75375	11.2	11	0.2	60	50	2	0.64	8.75	120
3	PRIYA	22	F	53275	10.6	10	0.6	60	60	2	0.7	78.6	120
4	SUGANTHI	33	F	25478	10.2	9.8	0.4	65	60	2	0.78	21	100
5	PRIYA	39	F	24525	11	10.2	0.8	70	65	2	0.8	21.6	120
6	BALA	26	M	25557	11.8	11.2	0.6	75	80	3	0.8	21.6	120
7	VELAN	42	M	75524	12	11.8	0.2	65	85	3	1	25	120
8	KANNAN	50	M	53722	10.8	10.2	0.6	60	105	3	1	25	140
9	SUBASH	48	M	5275	11	10.4	0.6	75	65	2	0.76	15.2	120
10	VELLAITHAI	47	F	5373	11.4	11	0.4	70	60	2	0.68	16.4	120
11	NITHIN	19	M	24537	10.6	10	0.6	60	75	3	0.9	18.2	140
12	THANGARAJ	46	M	53753	10.8	10.6	0.2	65	70	3	0.88	20	140
13	THENDRAL	22	F	2753	11.8	11.6	0.2	60	50	2	0.86	15.8	140
14	SIVAPRIYA	46	F	74537	12	11.2	0.8	75	55	2	1	17.6	120
15	GANESH	33	M	24523	10.6	10.2	0.4	75	40	1	1	20.7	110
16	MALAR	28	F	52375	10.4	9.8	0.6	70	45	1	0.9	19.2	100
17	KAVITHA	27	F	75255	10.6	10.2	0.4	65	55	2	0.75	18.8	120
18	VIJAYAN	52	M	5752	11.4	11.2	0.2	60	50	2	0.74	17.9	120
19	VIMALA	46	F	2535	11.8	11.6	0.2	65	40	1	0.65	16.8	130
20	GANGA	22	F	5237	11	10.6	0.4	75	60	2	0.664	14.8	130
21	JASMINE	21	F	75752	12	11.4	0.6	75	60	2	0.7	19.2	125
22	PETER	15	M	52752	11.8	11.2	0.6	70	55	2	0.8	20	120
23	KUMAR	18	M	52755	10.6	10.2	0.4	70	50	2	0.72	21	110
24	VALLI	46	F	52752	10.4	11.6	0.8	70	45	1	0.68	18.6	100
25	RAMESH	19	M	45275	10.8	10.2	0.6	65	60	2	0.64	17.6	140
26	SURULI	40	F	24527	10.6	10.2	0.4	60	45	1	0.66	15.8	120
27	PANDI	42	M	24524	11.4	11.2	0.2	60	50	2	0.67	16.8	120
28	KALAIVANI	29	F	27522	11.2	10.8	0.4	60	50	2	0.8	17.2	130
29	DURAI	36	M	87852	11	10.2	0.8	70	55	2	0.82	18.6	120
30	MANGALA	34	F	53224	10.4	9.6	0.8	65	60	2	0.65	19.2	110

CONTROL GROUP MAP

S.No	Name	0 min	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	70 mins
1	MURUGAN	88	90	88	83	88	83	99	88
2	SELVI	90	92	86	84	90	83	97	
3	JEGAN	93	97	79	89	97	87	96	
4	SURESH	89	87	86	97	86	86	83	87
5	ALAGAN	93	88	93	85	78	89	89	76
6	SAMI	79	84	92	87	88	85	86	
7	THOTTICHI	88	92	80	80	78	89	97	
8	KRISHNAN	80	80	87	89	95	93	89	89
9	RAJESWARI	93	83	85	86	95	91	80	99
10	LAKSHMI	97	88	70	79	88	89	90	93
11	KANDHI	80	89	79	94	90	85	92	
12	VIRALI	86	93	89	96	97	80	98	97
13	MALACHAMY	79	94	95	98	87	88	86	93
14	SENTHIL	79	92	94	97	89	85	89	86
15	PAKIYAM	83	89	90	89	86	89	86	78
16	RAJESH	79	87	87	97	89	93	88	
17	PALANI	80	79	86	90	97	94	89	
18	PAECHI	83	80	93	93	86	91	99	93
19	SARAVANAN	89	81	97	88	87	88	97	94
20	MUTHU	92	92	89	79	80	79	95	90
21	VALLI	80	91	83	88	89	79	90	88
22	KUMARI	83	90	91	99	93	97	92	
23	SELVI	92	93	87	97	94	88	94	
24	PRAKASH	99	89	80	94	89	93	86	90
25	VINOTH	98	99	89	83	97	85	88	90
26	SELVARAJ	87	87	83	80	93	79	89	79
27	VENI	86	80	79	89	86	79	96	92
28	ANDAL	78	79	84	86	85	84	96	
29	MEENAKSHI	85	89	85	77	80	88	92	91
30	PRABHU	80	83	82	89	99	89	83	88

BISOPROLOL GROUP MAP

S.No	Name	0 min	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	70 mins
1	SENTHIL	78	82	77	72	82	80	79	80
2	JOSEPH	69	73	74	71	81	83	74	78
3	PRIYA	77	78	72	81	79	79	78	
4	SUGANTHI	68	77	73	82	69	70	72	77
5	PRIYA	72	68	66	65	65	77	74	
6	BALA	88	70	64	68	69	75	68	
7	VELAN	75	70	76	73	70	69	69	68
8	KANNAN	74	72	68	65	72	70	73	67
9	SUBASH	81	72	67	80	76	79	80	
10	VELLAITHAI	68	78	88	80	80	81	73	
11	NITHIN	69	74	76	72	83	72	71	72
12	THANGARAJ	72	69	74	78	83	79	66	68
13	THENDRAL	74	68	69	63	69	73	69	66
14	SIVAPRIYA	78	71	77	76	72	69	73	80
15	GANESH	73	78	70	74	75	80	81	64
16	MALAR	69	70	80	81	77	73	80	
17	KAVITHA	78	80	82	79	78	75	69	
18	VIJAYAN	72	81	84	80	72	77	81	77
19	VIMALA	72	82	86	80	71	68	77	
20	GANGA	66	78	77	76	69	77	74	
21	JASMINE	64	88	68	66	68	69	68	72
22	PETER	78	74	64	66	77	77	72	73
23	KUMAR	62	72	75	72	73	72	70	
24	VALLI	61	69	76	71	78	80	79	
25	RAMESH	88	68	72	70	72	68	70	
26	SURULI	83	66	71	76	74	73	71	73
27	PANDI	79	77	69	69	70	70	68	71
28	KALAIVANI	70	78	82	70	76	72	68	
29	DURAI	69	72	73	70	69	68	66	
30	MANGALA	72	74	78	76	73	71	74	

CONTROL GROUP HEART RATE

S.No	Name	0 min	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	70 mins
1	MURUGAN	88	99	92	89	89	88	99	90
2	SELVI	89	90	98	96	87	89	98	
3	JEGAN	86	93	99	97	89	97	95	87
4	SURESH	89	87	89	94	80	90	97	89
5	ALAGAN	84	89	94	102	99	99	93	
6	SAMI	99	90	93	103	97	93	100	
7	THOTTICHI	90	93	100	110	93	98	102	100
8	KRISHNAN	94	97	101	100	103	99	105	99
9	RAJESWARI	98	94	89	99	103	100	100	98
10	LAKSHMI	102	94	94	98	102	103	110	
11	KANDHI	111	99	97	96	98	106	99	97
12	VIRALI	104	103	93	93	99	110	97	93
13	MALACHAMY	98	89	90	89	96	99	95	92
14	SENTHIL	90	90	92	88	89	97	88	89
15	PAKIYAM	99	93	99	97	80	93	79	
16	RAJESH	98	98	92	96	87	89	89	
17	PALANI	94	97	103	98	88	88	89	98
18	PAECHI	97	90	100	88	98	94	90	94
19	SARAVANAN	89	94	104	100	97	95	96	89
20	MUTHU	93	110	99	98	96	95	97	100
21	VALLI	96	110	96	97	94	89	94	101
22	KUMARI	96	103	98	98	89	99	94	
23	SELVI	89	98	80	90	99	93	92	
24	PRAKASH	85	99	89	90	90	90	91	90
25	VINOTH	79	94	85	98	93	94	99	95
26	SELVARAJ	100	96	97	90	93	94	90	88
27	VENI	103	97	96	93	89	88	95	90
28	ANDAL	90	89	100	93	86	93	93	
29	MEENAKSHI	98	100	95	95	93	93	91	88
30	PRABHU	96	100	99	96	94	100	99	90

BISOPROLOL GROUP HEART RATE

S.No	Name	0 min	10 mins	20 mins	30 mins	40 mins	50 mins	60 mins	70 mins
1	SENTHIL	77	66	63	69	72	64	59	66
2	JOSEPH	72	68	66	64	73	72	60	63
3	PRIYA	66	65	67	65	71	68	63	
4	SUGANTHI	68	66	68	67	66	66	68	70
5	PRIYA	67	67	65	68	62	64	67	
6	BALA	69	66	67	64	78	68	63	
7	VELAN	68	77	68	63	61	62	68	63
8	KANNAN	78	71	64	68	65	61	64	67
9	SUBASH	82	73	66	77	69	66	65	
10	VELLAITHAI	73	75	67	72	72	63	61	
11	NITHIN	75	72	68	73	73	77	77	72
12	THANGARAJ	73	78	64	78	65	63	72	66
13	THENDRAL	77	75	67	75	69	62	68	63
14	SIVAPRIYA	76	68	67	78	73	61	67	61
15	GANESH	69	69	65	68	78	67	63	64
16	MALAR	68	76	64	62	61	63	69	70
17	KAVITHA	65	62	67	62	60	62	64	
18	VIJAYAN	64	68	77	68	70	71	65	
19	VIMALA	67	73	73	69	63	66	77	71
20	GANGA	66	66	68	63	72	80	70	
21	JASMINE	68	69	73	67	68	59	64	66
22	PETER	72	73	61	65	63	80	74	61
23	KUMAR	73	77	64	67	72	58	59	
24	VALLI	72	72	77	63	70	63	63	
25	RAMESH	66	77	62	68	70	63	66	
26	SURULI	68	65	73	78	60	67	70	64
27	PANDI	69	62	68	77	63	71	70	64
28	KALAIVANI	64	61	68	66	64	72	74	
29	DURAI	77	60	63	65	65	68	66	
30	MANGALA	75	64	71	67	69	68	66	

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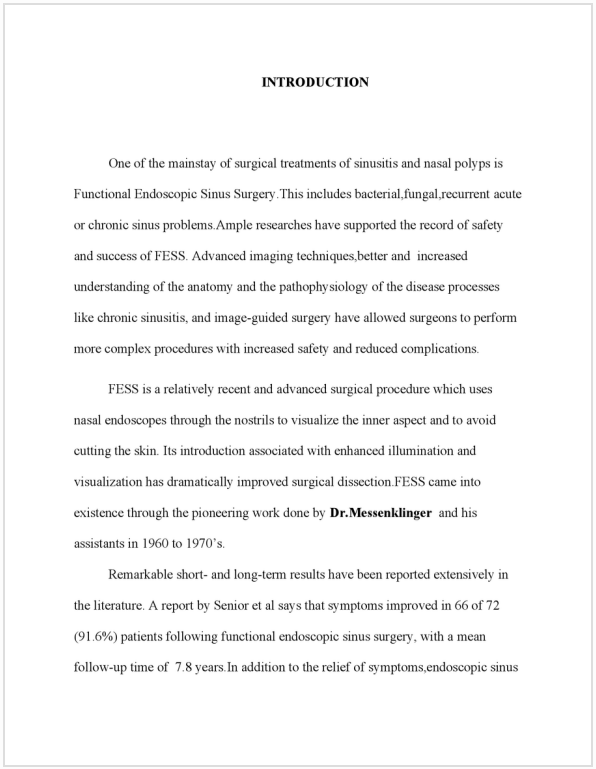

INTRODUCTION

One of the mainstay of surgical treatments of sinusitis and nasal polyps is Functional Endoscopic Sinus Surgery.This includes bacterial,fungal,recurrent acute or chronic sinus problems.Ample researches have supported the record of safety and success of FESS. Advanced imaging techniques,better and increased understanding of the anatomy and the pathophysiology of the disease processes like chronic sinusitis, and image-guided surgery have allowed surgeons to perform more complex procedures with increased safety and reduced complications.

FESS is a relatively recent and advanced surgical procedure which uses nasal endoscopes through the nostrils to visualize the inner aspect and to avoid cutting the skin. Its introduction associated with enhanced illumination and visualization has dramatically improved surgical dissection.FESS came into existence through the pioneering work done by **Dr.Messenklinger** and his assistants in 1960 to 1970's.

Remarkable short- and long-term results have been reported extensively in the literature. A report by Senior et al says that symptoms improved in 66 of 72 (91.6%) patients following functional endoscopic sinus surgery, with a mean follow-up time of 7.8 years.In addition to the relief of symptoms,endoscopic sinus

oral bisoprolol improves surgical field in FESS

BY 201320117 DR.JEYAKKUMAR

INTRODUCTION

One of the mainstay of surgical treatments of sinusitis and nasal polyps is Functional Endoscopic Sinus Surgery.This includes bacterial,fungal,recurrent acute or chronic sinus problems.Ample researches have supported the record of safety and success of FESS. Advanced imaging techniques,better and increased understanding of the anatomy and the pathophysiology of the disease processes like chronic sinusitis, and image-guided surgery have allowed surgeons to perform more complex procedures with increased safety and reduced complications.

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Ref. No1864/E4/2/2014,

Govt. Rajaji Hospital,
Madurai.20. Dated:29.03.2014

Institutional Review Board / Independent Ethics Committee.
Capt. Dr.B. Santhakumar, M.D., (F.M.,) deanmdu@gmail.com
Dean, Madurai Medical College &
Govt Rajaji Hospital, Madurai 625020. **Convenor**

Sub: Establishment-Govt. Rajaji Hospital, Madurai-20-
Ethics committee-Meeting Minutes- for March 2014
Approved list - Regarding.

The Ethics Committee meeting of the Govt. Rajaji Hospital, Madurai was held on 05.03.2014, Wednesday at 10.00 am to 12.00.noon at the Auditorium, Govt. Rajaji Hospital, Madurai. The following members of the committee have attended the meeting.

1.Dr.V. Nagarajan, M.D., D.M (Neuro) Ph: 0452-2629629 Cell.No 9843052029 nag9999@gmail.com	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2. Dr.Mohan Prasad , M.S M.Ch Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology(Retired) D.No.32, West Avani Moola Street, Madurai -1	Member Secretary
3. Dr. Parameswari M.D (Pharmacology) Cell.No.9994026056 drparameswari@yahoo.com	Director of Pharmacology Madurai Medical College	Member
4. Dr.S. Vadivel Murugan, MD., (Gen.Medicine) Cell.No 9566543048 svadivelmurugan_2007@rediffmail.com	Professor& H.O.D of Medicine Madurai Medical College	Member
5. Dr.S. Meenakshi Sundaram, MS (Gen.Surgery) Cell.No 9842138031 drsundarms@gmail.com	Professor & H.O.D of Surgery Madurai Medical College	Member
6. Mrs. Mercy Immaculate Rubalatha, M.A., Med., Cell. No. 9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's quarters, Gandhi Museum Road, Thamukam, Madurai-20	Member
7. Thiru..Pala. .Ramasamy , BA.,B.L., Cell.No 9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72.Palam Station Road, Sellur, Madurai -2	Member
8. Thiru. P.K.M. Chelliah ,B.A Cell.No 9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20	Member

The following Projects was approved by the committee.

Name of P.G.	Course	Name of the Project	Remarks
Dr.R.Jeyakkumar, drjk1976@yahoo.co.in	PG in MD (Anaesthesiology), Madurai Medical College and Government Rajaji Hospital, Madurai	Oral Bisoprolol improves surgical field in functional endoscopic sinus surgery.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.
2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Member Secretary **Chairman**
Ethical Committee

29.3.14
DEAN/Convenor
Govt. Rajaji Hospital,
Madurai- 20.

19/3/14

To
The above Applicant
-thro. Head of the Department concerned

forwarded to Dr. R. Jeyakkumar

DIRECTOR
INSTITUTE OF ANAESTHESIOLOGY
Madurai Medical College &
Govt. Rajaji Hospital
Madurai-625 020