“COMPARATIVESTUDY OF NITROGLYCERIN AND ESMOLOL FOR CONTROLLED HYPOTENSION IN FESS”

By

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IN

ANAESTHESIOLOGY

UNDER THE GUIDANCE OF

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Dr. Rahul S

LIST OF ABBREVIATIONS

ASA	=	American Society of Anaesthesiologists
CBF	=	Cerebral Blood Flow
cGMP	=	Cyclic Guanosine Monophosphate
DBP	=	Diastolic Blood Pressure
FESS	=	Functional Endoscopic Sinus Surgery
GFR	=	Glomerular Filtration Rate
GI	=	Gastrointestinal
HR	=	Heart Rate
i.v.	=	Intravenous
IPPV	=	Intermittent Positive Pressure Ventilation
kg	=	Kilograms
MAC	=	Mean Alveolar Concentration
MAP	=	Mean Arterial Blood Pressure
mcg	=	Micrograms
mg	=	Milligrams
min	=	Minutes
ml	=	Millilitres
mm Hg	=	Millimetres of Mercury
NTG	=	Nitroglycerin
PCO_2	=	Partial Pressure of Carbon Dioxide
PO_2	=	Partial Pressure of Oxygen
RBF	=	Renal Blood Flow
SBP	=	Systolic Blood Pressure
SNP	=	Sodium Nitroprusside
SVR	=	Systemic Vascular Resistance
α	=	Alpha
β	=	Beta
%	=	Percentage

ABSTRACT

BACKGROUND: Intraoperative bleeding causing poor visibility of surgical field is a major concern during FESS and this may result in many complications. Controlled hypotension is a technique wherein arterial blood pressure is lowered in a deliberate but controlled manner to minimise blood loss and enhance operative field visibility.

AIM: The purpose of this study is to compare the hypotensive properties of Esmolol and NTG in FESS surgeries under General anaesthesia.

METHODS: 80 ASA grade I and II patients aged between 18-60 years undergoing FESS under GA were divided into 2 groups of 40 each to receive either Inj. Esmolol 500µg/kg over 30 seconds followed by infusion at 100-300 µg/kg/min or Inj. NTG at 5-10 µg/kg/min. All patients were premedicated with oral Alprazolam and Ranitidine on the previous night. In the operation theatre, all patients were premedicated with i.v.Glycopyrrolate, i.v. Midazolam and i.v. Fentanyl, and then induced with i.v.Propofol. Laryngoscopy and intubation was facilitated by i.v.Succinyl choline. Anaesthesia was maintained with Isofluranevapour in nitrous oxide/oxygen mixture and i.vVecuronium for muscle relaxation. Heart rate, blood pressure, average category scale for operative visibility were assessed at 5, 10, 15 minutes and every 15 minutes from the start of infusion till completion of surgery.

RESULTS: Both drugs produced desired hypotension but ideal operative conditions were achieved at MAP of 80.5 ± 2.5 mm Hg in ESM group, while same operating conditions were achieved at MAP of 70.8 ± 1.2 mm Hg in NTG group. ACS scores were significantly low in ESM group compared to NTG group ($p < 0.001$). Mean duration of surgery was less in ESM group than NTG group ($p < 0.001$).

CONCLUSION: Esmolol is a safe and superior agent to NTG for controlled hypotension in FESS under GA, as it minimizes surgical blood loss, enhances operative visibility and reduces duration of surgery at higher MAP without causing any adverse effects.

KEYWORDS: Functional Endoscopic Sinus Surgery; Controlled hypotension;Nitroglycerin; Esmolol; Average Category Scale;Fromme.

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INTRODUCTION

Bleeding is a major operative problem in surgeries especially of the paranasal sinuses, middle ear cavity and the spine. It is pertinent to minimise this bleeding electively than subject the patient to the risks associated with blood transfusion.[1]

Controlled hypotension is a technique wherein arterial blood pressure is lowered in a deliberate but controllable manner to minimize surgical blood loss and enhance the operative field visibility.[2] Synonyms for controlled hypotension are **elective hypotension, deliberate hypotension, induced hypotension** and **controlled circulation.** The difference between deliberate hypotension and hypovolaemic shock is that in the former; tissue oxygenation is maintained by a controlled MAP and vasodilatation but severe vasoconstriction and microcirculatory changes in shock lead to hypoxia and tissue damage.

The advantages of controlled hypotension to the anaesthesiologist are reduced intraoperative bleeding and hence a minimization of the need for blood transfusion and a reduced duration of anaesthesia. The surgeon enjoys a dry (bloodless) operative field with minimal use of diathermy and suturing and an overall reduction in the surgical duration.

Functional Endoscopic Sinus Surgery (FESS) [3,4] is a minimally invasive procedure for conditions like chronic sinusitis and polypous rhinosinusitis where classical local anaesthesia is gradually being replaced with general anaesthesia for these advantages –

- An immobile operative field.
- Airway and ventilatory control.
- Optimal analgesia

In FESS, haemostasis of the rhino-sinusoidal region poses special problems where capillary bleeding is a serious limitation because it decreases operative visibility of the surgical field. This impaired visibility prolongs the overall surgical duration and promotes haemotransfusion. Transfusion and prolongation of surgical and anaesthetic duration increase the risk of various infections and complications.[1,2]

There are several pharmacological and non-pharmacological techniques of inducing hypotension the mechanical ones being; tourniquets, table positioning and IPPV.[2]

α receptor agonists like Dexmedetomidine and antagonists like Phentolamine, β receptor antagonists like Esmolol, nitrovasodilators like Sodium nitroprusside and Nitroglycerin are the most commonly used to control the circulation.[5]

Nitroglycerin chiefly used to treat angina, has also been tried for hypotensive anaesthesia. It is a directly acting nitrovasodilator that dilates capacitance vessels; reducing venous return with concomitant reductions in stroke volume and cardiac output and thereby causing hypotension. The main advantage of NTG over SNP is the avoidance of invasive monitoring, sparing of platelet function and minimisation of the possibility of cyanide toxicity.[2,5]

Esmolol, a cardio selective β_1 adrenergic antagonist, has a main advantage of ultra short action,[2,5] rapid onset of action leading to a decrease in heart rate, cardiac output and blood pressure. Other than its use in tachyarrhythmias and perioperative hypertension, it has been used for the induction of hypotension.

Not many studies have been performed in India with these two pharmacological agents and hence there is a need for a clinical comparison of these two drugs in terms of reduction in blood pressure, overall duration of surgery and the clarity of the operative field.

AIM & OBJECTIVES

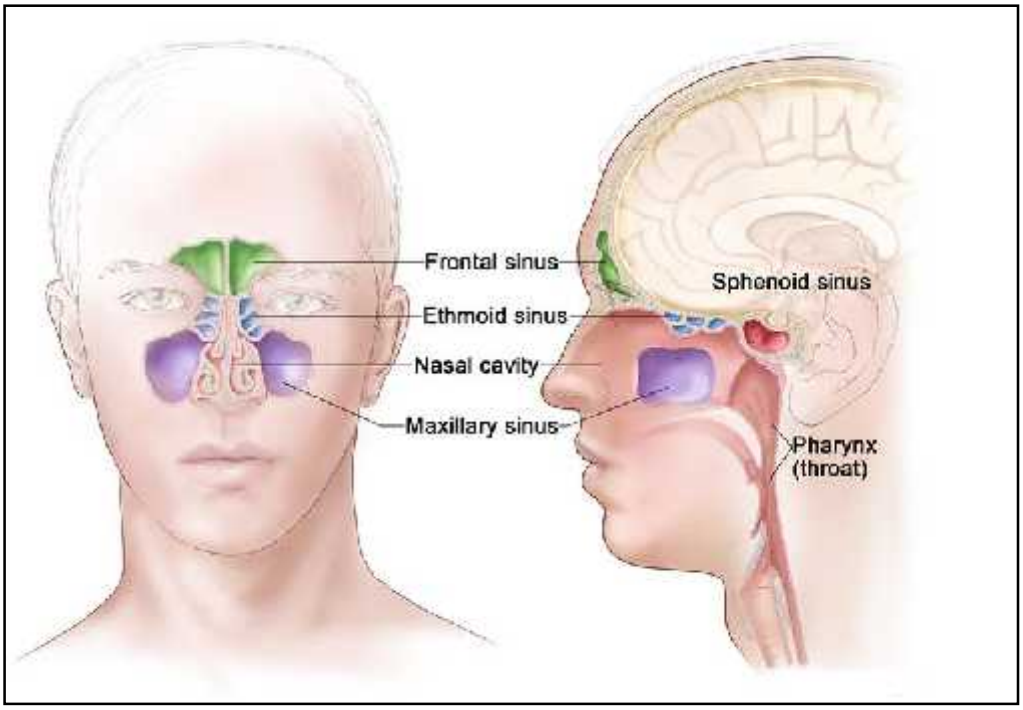
AIM: To compare the hypotensive efficacies of intravenous Nitroglycerin and intravenous Esmolol when performing elective FESS under general anaesthesia.

OBJECTIVES: To study the hypotensive properties of these two drugs in terms of

- Reduction in blood pressure.
- Surgeon's assessment of the quality of operative field.
- Surgical duration.
- Complications if any.

REVIEW OF LITRATURE

ANATOMY OF PARANASAL SINUSES[6,7,8]



ANTERIOR AND LATERAL VIEW OF THE PARANASAL SINUSES

Embryologically, the nose and paranasal sinuses are interlinked. Development of the head and neck along with face, nose and paranasal sinuses takes place simultaneously.

At about 25 – 28 weeks of gestation, three medially directed projections arise from the lateral wall of the nose. This serves as the beginning of the development of paranasal sinuses.

These medial projections of the lateral nasal wall form the following structures-

- The anterior projection forms the agger nasi.
- The inferior projection forms the inferior turbinate and maxillary sinus.
- The superior projection forms the superior turbinate, middle turbinate, ethmoidal air cells and their corresponding drainage channels.

The maxillary sinus is the first to develop amongst the sinuses. These structures are usually fluid-filled at birth. The growth of these sinuses is biphasic i.e. during years 0-3 and 7-12. In the later phase, pneumatization spreads inferiorly as the permanent teeth take their place.

The frontal sinus may develop as a direct continuation of embryonic infundibulum and frontal recess superiorly during the 16^{th} week. This sinus remains as a small blind sac within the frontal bone till the child is about 2 years of age when secondary pneumatization begins. When the child reaches 9 years, the development of the frontal sinus reaches completion.

The ethmoidal sinuses are well-delineated, fluid-filled structures in a newborn child. During foetal development, the anterior cells form first followed by the posterior cells. The cells grow gradually and are adult size by 12 years. They are not usually seen on radiographs in the first year. The septa gradually become thin and pneumatization spreads as the child ages.

The sphenoid sinuses are unique in that they do not arise from the out-pouchings of the nasal cavity. These sinuses arise from within the nasal capsule of the embryonic nose. They remain undeveloped till 3 years. By 7 years, pneumatization reaches the sella turcica and by 18 years, the sinuses reach their full size.

FUNCTIONS OF THE PARANASAL SINUSES -

- Resonating chamber for voice
- Decrease the weight of the skull
- Warming and moistening of air
- Shock absorbers
- Immune system

THE LATERAL NASAL WALL[6,7,8]

Inferior Turbinate

This structure is composed of a separate bone, the inferior concha which has an irregular surface, perforated and grooved by vascular channels to which the mucoperiosteum is firmly attached. The bone has a maxillary process which articulates with the inferior margin of the maxillary hiatus. It also articulates with the ethmoid, palatine and lacrimal bones, completing the medial wall of the nasolacrimal duct. The inferior concha has its own ossification centre which appears around the fifth intrauterine month. The turbinate possesses an impressive submucosal cavernous plexus with large sinusoids under autonomic control which provides the major contribution to nasal resistance. The turbinate is covered by respiratory epithelium, with a high number of goblet cells.

Inferior Meatus

The inferior meatus is that part of the lateral wall of the nose lateral to the inferior turbinate. It is the largest meatus, extending almost the entire length of the nasal cavity. The nasolacrimal duct opens into the inferior meatus usually just anterior to its highest point.

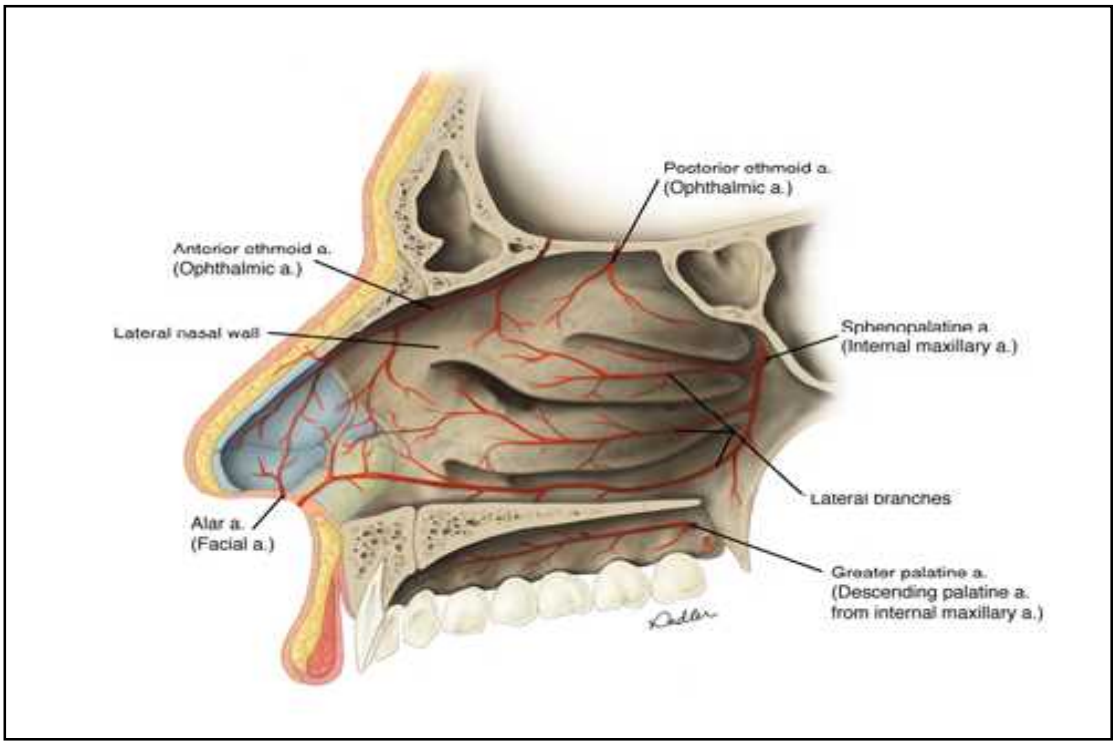
Blood Supply of the Lateral Nasal Wall[6,7]

The external and internal carotid arteries supply the lateral wall. The sphenopalatine artery (from the maxillary artery and thus external carotid artery) contributes the majority of the supply to the turbinates and meatus. It enters through the sphenopalatine foramen which lies just inferior to the horizontal attachment of the middle turbinate. Its branches to the respective turbinates and meatus enter posteriorly. In the inferior meatus, the sphenopalatine branch dips below the level of the palate to re-emerge anteriorly, leaving the central portion of the meatus relatively

avascular. An area anteriorly is supplied by a branch from the facial and part of the lateral wall adjacent to the palate receives blood from the greater palatine arteries.

The internal carotid artery contribution is via the ethmoidal arteries which supply the superior lateral wall. There is considerable overlap between the internal and external carotid arterial systems on each side and between the right and left sides which may complicate attempts at arterial ligation in the management of epistaxis. The vascular supply to the nose is well-developed and this is enhanced by cavernous plexus found in the lamina propria, in particular on the inferior and middle turbinates, which is controlled autonomically.

The veins of the plexus are between 0.1 and 0.5 mm wide and anastomose with each other. In addition, numerous arteriovenous anastomoses are found in the deep mucosa and around the glands. Venous drainage is to the sphenopalatine veins via facial and ophthalmic vessels, intracranially via the ethmoidal veins to the veins on the dura and to the superior sagittal sinus via the foramen caecum.



BLOOD SUPPLY OF THE LATERAL NASAL WALL

Nerve Supply of the Lateral Nasal Wall[6,7]

Apart from the olfactory supply on the superior concha, the lateral wall receives ordinary sensation from the anterior ethmoidal nerve anterosuperiorly and from branches of the pterygopalatine ganglion and anterior palatine nerves posteriorly. There is a small area innervated by the infraorbital nerve anteriorly and an area of overlap between the ethmoidal and maxillary nerves.

Middle Turbinate

It is a convoluted structure bending in different planes. It can be divided into 3 parts, depending on its attachment and its orientation in three dimensional space:

The anterior one third is in the sagittal plane and is attached to the cribriform plate at the junction of medial and lateral lamella. It also takes a small anterior attachment to the frontonasal process of the maxilla.

The middle one third is in the coronal plane and is attached to the lamina papyracea. It separates the anterior ethmoidal cells from the posterior ethmoidal cell.

The posterior third lies in the horizontal plane and is attached to the lamina papyracea and the perpendicular plate of palatine bone extending to upto the roof of the posterior choana.

Middle Meatus

The middle meatus is that portion of the lateral nasal wall lying lateral to the middle turbinate. It receives drainage from the frontal, maxillary and anterior ethmoidal sinuses.

In a disarticulated skull, the maxillary bone has a large opening in its medial wall, the maxillary hiatus. In the articulated skull this is filled in by adjacent bones:

- Inferior: the maxillary process of the inferior turbinate bone.
- Posterior: the perpendicular plate of the palatine bone.

- Anterosuperior: a small portion of the lacrimal bone.
- Superior: the uncinate process and bulla of the ethmoid.

A portion of the maxillary hiatus is filled by the mucous membrane of the middle meatus, the mucous membrane of the maxillary sinus and the intervening connective tissue - the membranous portion of the lateral wall. This membranous area can be defined as lying anterior or posterior to the uncinate process, constituting the anterior and posterior fontanelles, respectively. It is in the fontanelles that accessory ostia are found. Incidence for accessory ostia is probably 4-5 percent in the general adult population, increasing to 25 percent in patients with chronic rhinosinusitis. Accessory ostia are found most frequently in the posterior fontanelle which is generally larger than its anterior counterpart.

Superior Meatus

This meatus is defined by its relationship to the superior turbinate. The posterior ethmoidal cells open into this region. A supreme turbinate is discernible above the superior meatus. Drainage occurs to the corresponding supreme meatus from the posterior ethmoidal system.

Blood Supply and Nerve Supply of the Ethmoidal Sinuses[6,7]

The vascular supply is derived from the sphenopalatine and ethmoidal arteries and drains by corresponding veins. The ethmoid sinuses are innervated by the anterior and posterior ethmoidal nerves with additional supply from the orbital branches of the pterygopalatine ganglion. Lymphatics drain to the submandibular and retropharyngeal lymph nodes.

Blood Supply and Nerve Supply of the Sphenoidal Sinuses[6,7]

The sphenoid sinuses are supplied by the posterior ethmoidal vessels and nerves, with additional supply from the orbital branches of the pterygopalatine ganglion. Lymphatics drain to the retropharyngeal nodes.

Blood Supply and Nerve Supply of the Maxillary Sinuses[6,7]

Small branches of the facial, maxillary, infraorbital and greater palatine arteries and veins supply the maxilla. Venous drainage is to the anterior facial vein and pterygoid plexus. The maxillary division of the trigeminal nerve supplies sensation via the infraorbital, superior alveolar and greater palatine nerves. The posterior superior alveolar nerves arise from the maxillary nerve in the pterygopalatine fossa and enter the maxilla through the posterior wall to supply the adjacent mucosa and molar teeth. The middle superior alveolar nerve arises from the infraorbital nerve in its canal and supplies the lateral wall of the sinus and upper premolar teeth. The posteromedial wall of the sinus is supplied by the greater palatine nerve and the roof by perforating branches from the infraorbital nerve.

PHYSIOLOGY OF CONTROLLED HYPOTENSION

The principle objectives of FESS are to restore mucociliary clearance and promote drainage and aeration of the sinuses. The term 'functional' distinguishes FESS from conventional non-endoscopic surgical methods.[4] In this procedure, the sinus cells and sinus ostia are opened under direct visualization using an endoscope.[3]

Capillary bleeding is a major impediment to the endoscopic exploration in FESS. Even minimal bleeding interferes with operative visibility and prolongs the duration of surgery and anaesthesia. Prolonged interventions have been associated with several complications[3,4] some of which are dreaded and debilitating. In order to avoid these complications and to optimize the quality of anaesthetic and surgical intervention, controlled hypotensive anaesthesia becomes necessary.

PHYSIOLOGY OF CONTROLLED HYPOTENSION[9-15]

In order to perform safe and efficient hypotensive anaesthesia for the optimal benefit of the patient, it is necessary to have an understanding of the regulation of blood flow to the vital organs. Controlled hypotension rarely results in damage because blood flow to the vital organs especially the brain and the heart is normally well maintained within safety limits.

Flow is a function of both MAP and autoregulation in the cerebral, myocardial and renal beds. Using the concept of MAP (rather than SBP), the physiology of these 3 systems is studied separately to determine which is the critical 'weak link' i.e. the system that sets the minimal permissible pressure.

The mechanisms of autoregulation include:

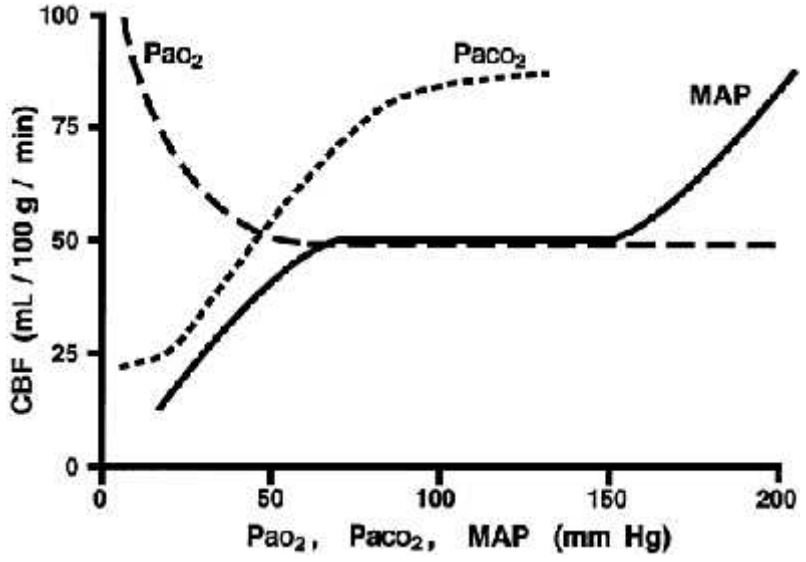
- **Stretch**: myogenic mechanism, where the smooth muscle in the vasculature responds to altered tension.

- **Passive mechanical**: applies to encapsulated organs, where expansion of the organ with increasing pressure compresses thin walled vessels and leads to an increase in vascular resistance.
- **Metabolic**: changes in pressure produces vasoactive substances.

Those organs capable of autoregulation are able to maintain their perfusion over a wide range of pressure changes, and it is only when the pressure decreases to relatively lower levels that adequate perfusion cannot be maintained. This critical pressure varies from vessel to vessel, organ to organ, and from individual to individual.

CONTROLLED HYPOTENSION AND THE CEREBRAL CIRCULATION[9,10]

Perfusion of the cerebral circulation is the critical factor that limits MAP reduction. This is probably because even minimal derangements in the post operative function of this organ are unacceptable. Through autoregulation, the normal CBF is maintained at 45-50ml/100g/min, within a MAP range of 50-150 mmHg.



RELATION BETWEEN MAP, PaO_2, $PaCO_2$, AND CBF[10]

The absolute value for the CBF below which cerebral ischaemia and hypoxia occurs is not exactly known but several studies have allowed the estimate to be made.

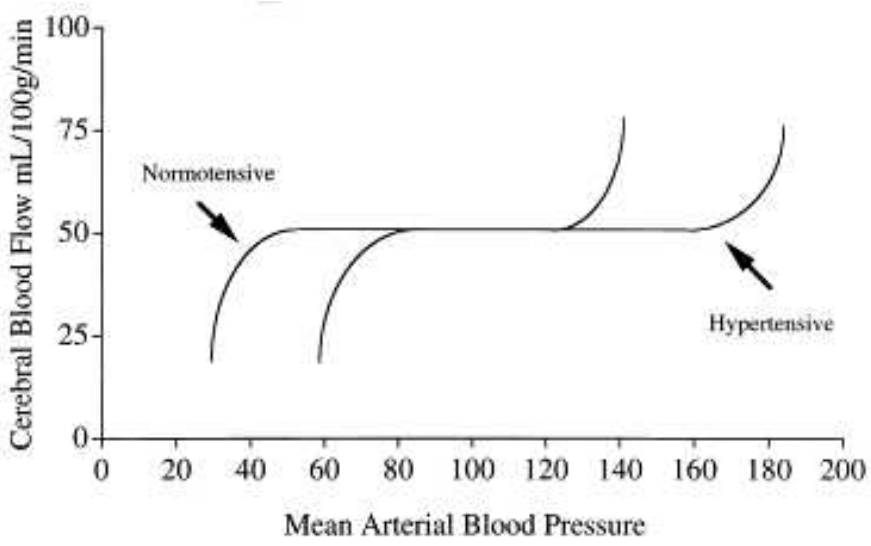
ANAESTHETIC FACTORS INFLUENCING THE CBF[10,11,15]

- **$PaCO_2$:** Within the range of autoregulation, the arterial PCO_2 is the most important factor in determining CBF. For every 1 mmHg increase in $PaCO_2$, there is an increase in CBF in the order of 1ml/100gm/min. These effects of carbon dioxide should be remembered when hypocapnia is a part of controlled hypotensive anaesthesia because the combination of hypotension and cerebral vasoconstrictive effects of a low $PaCO_2$ could be detrimental.
- **PaO_2:** Changes in the arterial oxygen tension also affect the CBF. In situations where high concentrations of oxygen are administered especially in hyperbaric conditions, the brain protects itself by means of vasoconstriction. Inhalation of 100% O_2 reduces the CBF by one fifths. If the arterial oxygen tension decreases below normal, the CBF increases through vasodilatation and vice versa. Hence, higher concentrations of oxygen could be detrimental.
- **TEMPERATURE**: A linear relationship exists between CBF and temperature. Hypothermia causes cerebral vasoconstriction whereas an increase in body temperature causes cerebral vasodilatation. CBF changes 5-7% per degree centigrade change in temperature.
- **VOLATILE AGENTS:** Volatile anaesthetic agents attenuate or abolish the cerebral autoregulation in a dose dependent manner in the following order- HALOTHANE >>> ENFLURANE >>> ISOFLURANE.
- **VASODILATORS**: Vasodilators such as SNP and NTG attenuate the autoregulation of CBF in a manner similar to that of volatile agents.

Since the skull limits the volume of blood that can be accommodated, events that increase blood flow to areas of normal perfusion may displace flow to the areas of marginal perfusion. Because of this uncertainty of regional blood flow distribution,

it should be safe to lower the MAP to 50-55 mmHg with no significant decrease in the CBF.

The hypertensive patient deserves special attention since it has been shown that the autoregulatory curve is shifted higher at both ends. Theoretical safe limits of hypotension may be calculated based on this shifted curve. However, these patients do pose an increased risk, even when the elevated MAP is accounted for. Therefore, hypertension becomes a relative contraindication to the technique of controlled hypotension.



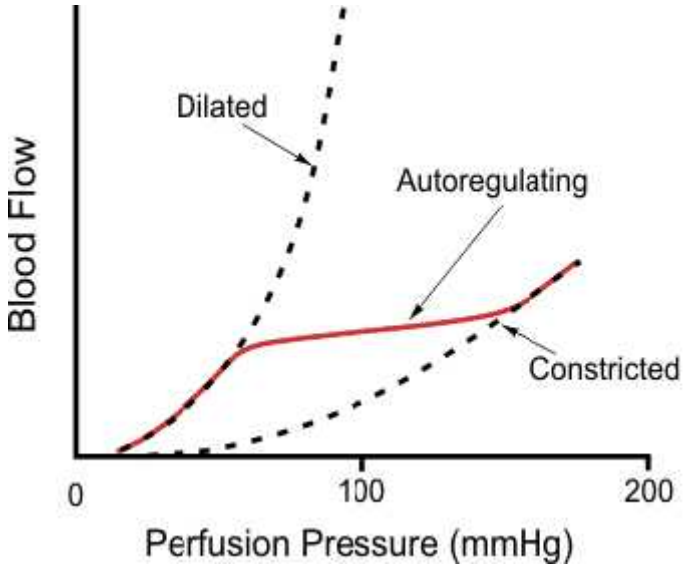
EFFECTS OF HYPERTENSION ON THE CBF

Lastly, elevation of the head during controlled hypotensive anaesthesia can aggrevate the decrease in CBF. The perfusion pressure decreases by 2 mmHg for every 2.5 cm elevation from the level of the heart.

CONTROLLED HYPOTENSION AND THE CORONARY CIRCULATION[10,12,13]

The heart has the highest oxygen consumption per tissue mass of all human organs (8 ml/min/100 gm) with a resting coronary blood flow of 0.8-1 ml/min/gm of cardiac tissue.

Coronary blood flow is dependent upon the aortic DBP and the coronary vascular resistance. Control of the coronary blood flow is autoregulated predominantly by means of alteration in coronary vascular resistance that are made to meet myocardial oxygen demands. Even at rest the myocardium extracts most of the oxygen delivered to it. Hence, any increase in myocardial oxygen demands requires a parallel increase in the coronary artery blood flow.



CORONARY AUTOREGULATION

Controlled hypotension may substantially decrease coronary blood flow. However, it simultaneously decreases myocardial oxygen demand due to the reduction in afterload and/or preload. Furthermore, coronary autoregulation ensures adequate myocardial blood flow. Studies have shown that during hypotensive anaesthesia, there is a poor correlation between the lowest degree of hypotension achieved and the development of ischaemic ECG changes. In a study done by **Rollason and Hough**[13] there was no ECG evidence of myocardial damage following controlled hypotension with ganglion blocking agents although about 40% of cases showed evidence of transient myocardial ischaemia. These changes were observed in

elderly patients or patients with pre-existing hypertension when the SBP fell below 60 mmHg.

Patients with coronary artery disease may have some areas of myocardium that are entirely dependent upon pressure to supply adequate blood flow. In addition, the use of vasodilators in these patients may induce a steal phenomenon. Hence, controlled hypotension is accompanied by a significant intraoperative risk of myocardial infarction and therefore, patients with heart conditions are contraindications for controlled hypotensive anaesthesia.

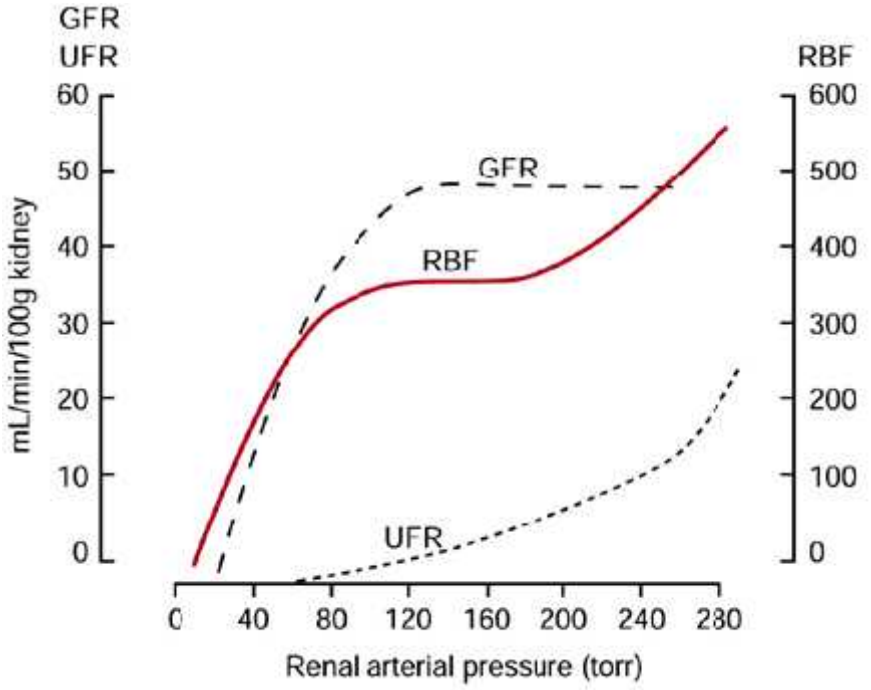
CONTROLLED HYPOTENSION AND THE RENAL CIRCULATION[10,14,15]

Renal blood flow is controlled in two ways - extrinsic autonomic and hormonal mechanisms and intrinsic autoregulation.

Miles, Ventom and De Wardener[14] showed that there was autoregulation of blood flow between the range 80-180 mmHg.

If the arterial blood pressure drops below these values, renal blood flow may decrease to a point where urine flow stops. When the MAP falls below 75 mmHg, the GFR falls too.

In addition, most opioids and inhalational agents stimulate the secretion of ADH. All these factors result in oliguria but it has been shown that following termination of controlled hypotension, GFR and urine formation return to normal provided the patient was euvolaemic to begin with.



EFFECTS OF RBF ON THE GFR and UFR

CONTROLLED HYPOTENSION AND HEPATIC CIRCULATION[9,10,11]

Most of the hepatic blood flow (70%) is via the portal vein. The remainder is supplied from the hepatic artery. The splanchnic circulation is richly innervated by the sympathetic nervous system. In contrast to the brain and kidney, the liver is not an autoregulated organ. Therefore a decrease in arterial pressure will lead to a decrease in liver blood flow. In addition, an increase in $PaCO_2$ or a decrease in PaO_2 will lead to a catecholamine response which causes splanchnic vasoconstriction and therefore a decrease in the hepatic blood flow. Also, hypocapnia produced incidentally by hyperventilation during IPPV leads to a decrease in the hepatic blood flow as a result of the mechanical effects. Apart from the effects of hypotension itself, the hepatic blood flow may be directly altered by the effects of the volatile anaesthetic agents on the splanchnic blood flow. Regardless of the above, deliberate hypotension seems to be well tolerated by the liver and there are no reports showing morbidity or mortality from hepatic hypoperfusion during controlled hypotension.

CONTROLLED HYPOTENSION AND THE RESPIRATORY SYSTEM[9,10,11]

During controlled hypotensive anaesthesia, the following pulmonary events occur –

- Pulmonary blood flow gravitates to the dependent areas of the lungs. Hence, the non dependent regions are ventilated but not adequately perfused thus increasing dead space. This scenario is aggravated by the head up position.
- The use of vasodilators to induce hypotension inhibits the hypoxic pulmonary vasoconstriction response thereby increasing intra-pulmonary shunting.

All these factors result in hypercarbia, an increase in arterial end-tidal CO_2 gradient and hypoxaemia. Hence, regular $PaCO_2$ and end tidal CO_2 measurements are necessary during controlled hypotension.

BLOOD PRESSURE GOALS[9,10,11,15]

The aim of hypotensive anaesthesia is to reduce blood loss and provide a 'dry' operating field. Hence, the degree of hypotension should be individualised. The hypotension should be considered satisfactory when bleeding appears to be minimal and organ perfusion adequate. Theoretically, as long as the MAP exceeds the sum of colloid osmotic pressure and venous pressure, the blood flow should be adequate to meet the tissue needs. Thus, a MAP of 32 mmHg should suffice but this may probably be way below the safe limit due to specific organ flow requirements and the possibility of disease and other causes.

With reference to the physiology of the various systems described previously, it is desirable that a deliberate induction of hypotension to a MAP of 30% below a patient's usual MAP, with a minimum of 60 mmHg in young ASA I and II patients and 80 mmHg in the elderly is clinically acceptable.

CONTRAINDICATIONS TO THE USE OF CONTROLLED HYPOTENSION[12,15]

- Cardiac disease
- Diabetes mellitus
- Anaemia and haemoglobinopathies
- Cerebrovascular disease
- Hepatic disease
- Renal disease
- Respiratory insufficiency
- Hypertension
- Known allergy to the hypotensive agents
- Lack of understanding the technique
- Lack of expertise
- Lack of monitoring facilities
- Lack of resuscitation facilities

TECHNIQUES OF CONTROLLED HYPOTENSION[2,5,9,11,15]

The key equations in the induction of elective hypotension are:[2]

Mean Arterial Pressure = Cardiac Output x Systemic Vascular Resistance

Cardiac Output = Stroke Volume x Heart Rate

MAP can be manipulated by reducing either SVR or cardiac output or both. Inducing hypotension purely by a reduction in cardiac output is not ideal because the maintenance of tissue blood flow is essential.

SVR can be reduced by peripheral vasodilatation while cardiac output can be reduced by lowering venous return, reducing the heart rate and/or myocardial contractility or a combination of these.

The techniques can broadly be classified as pharmacological and non-pharmacological.

The mechanical non-pharmacological methods of blood flow reduction are:[2,9]

1) **Tourniquet**: These can only be applied on limbs including fingers and toes. Their use involves monitoring of two critical parameters – the duration of application and the pressure applied. The pressures commonly applied are 250 mmHg for the upper limbs and 300 mmHg for the lower limbs with a time limitation of 60 min and 90 min respectively.
2) **Positioning**: Elevation of the site of operation allows easy venous drainage from the surgical area. Elevation of the head above the level of the heart reduces the arterial blood pressure and there is a fall by 0.7-0.8 mmHg for every 1 cm of vertical height above the level of the heart.
3) **IPPV**: Positive pressure ventilation with high tidal volumes, prolonged inspiratory times and raised positive end expiratory pressure would certainly reduce venous return and cause hypotension. However, this could compromise cerebral venous return and might raise the intracranial tension and also increase respiratory dead space because of large tidal volumes.

The pharmacological methods of deliberate hypotension are:[2,5,9,11]

1) **Local Infiltration**: Adrenaline in the concentrations of 1:200,000 to 1:400,000 are used commonly to cause local vasoconstriction. The total dose should not exceed 500 mcg and intravascular injections can prove to be fatal especially in conjunction with volatile agents.
2) **Central Neuraxial Blocks:** Pharmacological sympathectomy using local anaesthetic agents to produce either a subarachnoid block or an epidural block is an effective way of inducing a conduction block hypotension. The limitation is

the type of surgery. This method cannot be used for surgeries on the head and face.

3) **Sympathetic Ganglion Blocks**: Autonomic ganglion blockade by competitive inhibition of acetylcholine is another option for elective hypotension. Drugs like Trimetaphan and Pentolinium are injected but tachycardia and tachyphylaxis limit the use of this technique.

4) **Volatile Inhalational Agents**: With Halothane, the overall reduction in vascular resistance is approximately 15-20%. In addition, bradycardia caused by halothane further reduces the cardiac output. Its use however as a sole hypotensive agent is discouraged because large and lethal doses would be required. Unlike Halothane, Isoflurane has minimal effects on the myocardium and the vasodilator effects can be easily adjusted with alterations in the inspired concentration and hence Isoflurane has become more popular than halothane.

5) **Alpha Adrenoreceptor Blockers:** Phentolamine, Phenoxybenzamine, Chlor-promazine and Droperidol produce vasodilatation by competitive blockade of post synaptic noradrenergic receptors. However, some of these drugs cause intense sedation and the effects of Phenoxybenzamine may last for days. Phentolamine increases myocardial oxygen demand.

6) **Nitrovasodilators**: These include directly acting vasodilators like SNP and NTG. The advantage of SNP is its evanescent duration of action, allowing rapid reduction of the arterial blood pressure and equally rapid restoration to normal values. The element of cyanide toxicity, platelet dysfunction and the need for invasive arterial blood pressure monitoring however makes SNP the second choice after NTG.

7) **Beta Adrenoreceptor Blockers:** They produce what is known as a ‘rheostatic hypotension’ This is owing to the slowing of heart rate without any additional hypotension which considerably reduces operative bleeding without compromising on tissue needs.

PHARMACOLOGY OF NITROGLYCERIN[5, 9,16,17,18]

Intravenous NTG has been used since 1969 when its safety and effects were studied. NTG was first synthesized in 1846 by Sobrero. In 1857, T. Lauder Brunton of Edinburgh administered amyl nitrite by inhalation and noted that anginal pain was relieved within 30 to 60 seconds. William Murrell surmised that the action of Nitroglycerin mimicked that of amyl nitrite and established the use of sublingual NTG for the relief of an acute anginal attack. The importance of nitric oxide as a signalling molecule in the cardiovascular system was recognized by the awarding Nobel Prize in medicine to Robert Furchgott, Louis Ignarro, and Ferid Murad in 1998.

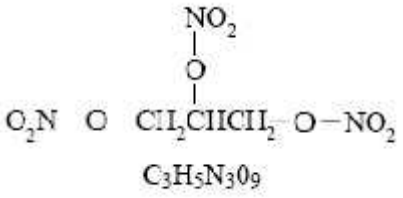
MECHANISM OF ACTION

NTG generates nitric oxide which activates guanyl cyclase which in turn increases cellular cGMP. In the smooth muscles, the net result is reduced phosphorylation of myosin light chain, reduced calcium concentration in the cytosol, and relaxation. In contrast to SNP however, which spontaneously produces nitric oxide, NTG requires the presence of thio-containing compounds.

CHEMISTRY

NTG is 1,2,3 – propanetriol trinitrate; an organic nitrate which is a polyol ester of nitric acid. Its empirical formula is $C_3H_5N_3O_9$ and it has a molecular weight of 227.09.

STRUCTURAL FORMULA



PHYSICOCHEMICAL PROPERTIES:

NTG is available as an oily yellow liquid in a 5 mg/ml solution in 5 ml and 10 ml ampoules.

PHARMACOKINETICS:

The duration of action of intravenous NTG is short with a distribution half life of 3 minutes and an elimination half life of 1.5 minutes. The volume of distribution is 3 litres/kg and a clearance rate of 230 ml/min/kg following an infusion.

NTG is reductively hydrolyzed by hepatic glutathione-organic nitrate reductase. More recent studies have implicated a mitochondrial aldehyde dehydrogenase enzyme in the biotransformation of NTG.

PHARMACODYNAMICS

Cardiovascular Effects

NTG affects both systemic arterial and venous systems but the predominant effect is on the venous capacitance vessels which causes peripheral pooling of blood and diminished venous return which causes a reduction in the preload. This reduction is accompanied by a diminished distension of the right atrium and a reduction of

diastolic ventricular wall tension. The decreased arteriolar tone on the other hand causes a reduction in the after load. Both these effects reduce left ventricular wall tension and heart size which ultimately reduce myocardial oxygen demand.

Higher doses will cause further venous pooling and further decrease arteriolar resistance thereby decreasing systolic and diastolic blood pressure and cardiac output and causing pallor, weakness, dizziness, and activation of compensatory sympathetic reflexes. The reflex tachycardia and peripheral arteriolar vasoconstriction tend to restore systemic vascular resistance. Coronary blood flow may increase transiently as a result of coronary vasodilatation but may decrease subsequently if cardiac output and blood pressure decrease sufficiently.

Other Effects

NTG acts on almost all smooth muscles. Bronchial smooth muscle, muscles of the biliary tract, including those of the gallbladder, biliary ducts, and sphincter of Oddi, Smooth muscle of the GI tract, including that of the oesophagus can be relaxed and its spontaneous motility is decreased by NTG. The effect may be transient and incomplete but abnormal spasm is reduced. Similarly, NTG can relax ureteral and uterine smooth muscle, but these responses are of uncertain clinical significance.

USES OF NTG

1) Angina Pectoris: Sublingual NTG is the most useful of the organic nitrates for the acute and chronic treatment of angina pectoris due to atherosclerotic coronary artery disease or coronary artery vasospasm. The ability of NTG to selectively dilate large conductive coronary arteries may be an important mechanism in the relief of angina pectoris due to vasospasm.
2) Congestive heart failure

3) Acute myocardial infarction

4) Sphincter of Oddi spasm

5) Controlled hypotension

CONTRAINDICATIONS:

1) Early myocardial infarction

2) Head injuries and increased intracranial tension

3) Constrictive pericarditis and pericardial effusion

4) Glaucoma

5) Severe anaemia

6) Patients on phosphodiesterase inhibitors particularly PDE-5

7) Known allergies to NTG

ADVERSE EFFECTS

- **Cardiovascular:** Chest pain, Reflex tachycardia, and rebound hypertension.
- **Central Nervous System:** Anxiety, agitation and confusion.
- **Gastrointestinal system:** Nausea and vomiting
- **Haematopoeitic:** Methaemoglobinaemias
- **Miscellaneous:** Xerostomia and skin rash

PHARMACOLOGY OF ESMOLOL[5,11,16,17,18]

Competitive antagonists of beta adrenergic receptors, or simply β blockers, have received enormous clinical attention because of their efficacy in the treatment of hypertension, ischemic heart disease, congestive heart failure, and arrhythmias.

β blockers are classified as nonselective for β_1 and β_2 receptors (Propranolol, Nadolol, Timolol, Pindolol) and cardioselective (Metoprolol, Atenolol, Acebutolol, Betaxolol, Esmolol, Bisoprolol) for β_1 receptors. Cardioselective drugs are better suited for administration to patients with a reactive airway disease.

MECHANISM OF ACTION

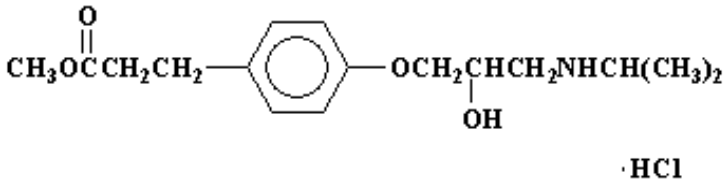
β_1 receptor blockade is associated with a slowing of the sinus rate, slowing of conduction of cardiac impulses and a decrease in inotropy. Ultimately, there is a reduction in cardiac output and thence hypotension.

CHEMISTRY

Esmolol is available as Esmolol hydrochloride which has the empirical formula $C_{16}H_{25}NO_4$.HCL with a molecular weight of 331.8.

STRUCTURAL FORMULA

$C_{16}H_{25}NO_4 \cdot HCl$



PHYSICOCHEMICAL PROPERTIES

It is a white crystalline powder which is relatively hydrophilic. Esmolol hydrochloride injection is a clear, colourless to light yellow, sterile, non-pyrogenic iso-osmotic solution of Esmolol hydrochloride in sodium chloride. It is available as a 10 mg/ml solution in a 10 ml vial.

PHARMACOKINETICS

Esmolol is rapidly metabolized by hydrolysis of the ester linkage primarily by the esterases in the cytosol of the red blood cells. It has a rapid distribution half life of 2 minutes and an elimination half life of 9 minutes.

The onset and cessation of β blockade with Esmolol are rapid and peak haemodynamic effects occur within 6 to 10 minutes of administration of a loading dose, and there is substantial attenuation of β blockade within 20 minutes of stopping an infusion. Heart rates typically reach the pre-drug level within 15 minutes.

Esmolol is metabolized to the corresponding free acid and methanol. The acid metabolite has $1/500^{th}$ of the potency of the parent drug and consistent with the high rate of blood based metabolism, less than 2% of Esmolol is excreted unchanged in the urine. Within 24 hours of the end of infusion, 75-90% of the dosage has been accounted for in the urine as the acid metabolite of Esmolol hydrochloride. The plasma protein binding is 55% while the acid metabolite is only 10% bound.

PHARMACODYNAMICS

Cardiovascular Effects: Esmolol produces a reduction in the heart rate at rest and during exercise and blood levels of esmolol hydrochloride have been shown to correlate with the extent of β blockade. In human electrophysiological studies, esmolol produced a decrease in heart rate, increase in the sinus cycle length, prolongation of the sinus node recovery time, prolongation of the AH interval during the normal sinus rhythm and an increase in antegrade Wenckebach cycle length. Esmolol when administered at 200 mcg/kg/min causes a reduction in the heart rate, systolic blood pressure, rate pressure product, left and right ventricular ejection fraction and the cardiac index.

USES

1) Supraventricular tachycardias
2) Intraoperative and post-operative tachycardia/hypertension
3) Suppression of cardiac dysrhythmias
4) Prevention of excessive sympathetic nervous system activity
5) Preparation of hyperthyroid patients
6) Controlled hypotension

CONTRAINDICATIONS

1) Sinus bradycardia
2) Heart block
3) Cardiogenic shock
4) Overt heart failure
5) Bronchospastic disorders

ADVERSE EFFECTS

- **Cardiovascular System:** Symptomatic hypotension (diaphoresis, dizziness), pallor, flushing, bradycardia, chest pain, syncope, pulmonary oedema and heart block.
- **Central Nervous System:** dizziness, somnolence, confusion, agitation, fatigue, paraesthesia, asthenia, depression, anxiety, anorexia and light headedness.
- **Gastrointestinal System:** Nausea, vomiting, dyspepsia, constipation, dry mouth, abdominal discomfort and cacogeusia.
- **Skin (Infusion Site):** Inflammation, induration, erythema, oedema, thrombophlebitis, burning and local skin necrosis.
- **Miscellaneous:** Urinary retention, speech disorders, abnormal vision, rigors and fever.

HISTORY OF CONTROLLED HYPOTENSIVE ANAESTHESIA

The definition of controlled hypotensive anaesthesia is taken from the very early studies done by **Eckenhoff and Rich** in 1966.[19,20] and it takes into account the level required to produce the controlled hypotensive effect but at the same time is limited by safety. This safety limit is individualised based on the hypotensive technique, each patient's limitations and the extent of intraoperative bleeding and its interference with the operative field.

Evolution of Controlled Hypotension[2,9,11]

1917: Deliberate hypotension was first introduced by **Harvey Cushing** in order to provide a bloodless field for neurosurgery.

1944: The technique of arteriotomy and reinfusion was described by **Kohlstadt** and **Page**.

1946: The concept of induced hypotension using arteriotomy to produce a bloodless field was introduced by **Gardner**.

1948: High spinal anaesthesia was use to induce hypotension and create a dry field by **Griffith** and **Gillies**.

1949: **Randall** described the hypotensive effects of thiophanium derivatives.

1950: Davidson used pentamethonium to produce hypotension.

1951: The high epidural block was introduced.

1952:Enderby used short acting sympatholytic and adrenolytic drugs like trimethaphan.

1962: Sodium nitroprusside was first used to induce hypotension during anaesthesia.

Hypotensive anaesthesia with a sole volatile agent like isoflurane is also used.[21]

Propofol has also been tried for the purpose of controlling hypotension during anaesthesia.[22]

In current practice, nitrovasodilators, β blockers, calcium channel blockers, opioids and α adrenergic agonists and antagonists are used more frequently.

RISKS OF CONTROLLED HYPOTENSION

In a retrospective review of nearly 30000 cases done by **Little DM** [23] in 1954, controlled hypotensive anaesthesia was associated with a morbidity of 1 in 31 and mortality of 1 in 291. By far, the commonest causes of mortality were compromise of the circulation to vital structures such as the kidney, brain and the heart. Other causes of mortality included reactionary haemorrhage, high spinal anaesthesia and over heparinization. The vast majority of cases in this study (>90%) were performed with a systolic blood pressure less than 80 mmHg which would probably account for the high morbidity and mortality rates. Subsequent studies by **Eckenhoff JE, Rich JC** (1965)[19,20] **Madsen JB, Cold GE, Hansen ES, Bardrum B** (1987) [24] and **Yamada S, Brauer F, Knierim D, Purtzer T** (1988) [25] have shown that controlled hypotension is safe provided the safety limits are adhered to.

One of the earliest convincing studies on controlled hypotension in nasal surgeries were performed and documented by **Eckenhoff** and **Rich JC** (1965)[20] who undertook a study of 115 patients out of which 74 were posted for rhinoplasty, 44 of whom were subjected to deliberate hypotension wherein the systolic blood pressure was lowered down to a range of 50-80 mmHg from a basal of 100-140 mmHg. They found that the average blood loss in the hypotensive group was only 25% of the average blood loss in the normotensive group. Even the duration of surgery in the hypotensive group was 25% less than in the normotensive group. There were no intra-operative / post-operative complications.

Cincikas D, Ivaskevicius J, Martinkenas JL, Balseris S (2001)[1] described in detail the role of an anaesthesiologist in reducing surgical bleeding in nasal endoscopic surgeries like FESS. They have opined that owing to the peculiar anatomical characteristics of the paranasal sinuses especially the ethmoidal, surgical bleeding in these areas greatly compromises the operative field visibility and this is directly related to dangerous vascular, orbital and intracranial complications. They are of the view that the controlled hypotension caused by Esmolol in FESS is better than SNP with respect to bleeding and working conditions, because Esmolol blocks the adrenergic effect of vasoactive amines released during hypotension. In their opinion, amongst the organic nitrates, NTG is a better than SNP because of its sparing effects on platelet function. They conclude that the role of an anaesthesiologist is extremely important in improving conditions of surgical intervention especially in nasal endoscopic surgeries.

Testa LD, Tobias JD (1995) [5] described various pharmacological agents for controlled hypotension. In their definition, controlled hypotension should be a reduction in systolic blood pressure to 80-90 mm Hg and a reduction in MAP by $1/3^{rd}$ or upto 50-65 mmHg. In summarising the advantages of NTG particularly it's rapid onset and offset and easy titratability, they recommended a dose range of 0.5-10 mcg/kg/min for the purpose of controlled hypotension. The advantages of β blockers especially Esmolol are its rapid onset and offset, decreased myocardial O_2 consumption, no pulmonary shunting or increase in ICP. They noted that with large doses of NTG and excessive decreases in the blood pressure, the renin-angiotensin system may get activated. NTG inhibits Hypoxic pulmonary vasoconstriction and increases intrapulmonary shunting. These changes reflected by a decreased PaO_2 and increased alveolar – arterial oxygen gradient are offset by an increase in the FiO_2.

The effect on platelet aggregation is less than that seen with SNP and even if occurs is clinically insignificant. They noted that while the cardiovascular and catecholamine responses during Esmolol induced hypotension were similar to those produced by combined SNP-Esmolol technique, there was a greater reduction in blood loss and drier field in the Esmolol category. The shorter half life of Esmolol allows for its easy titration and control of heart rate and blood pressure than can be achieved with single bolus doses. Additionally, its short half life allows for quick reversibility in the event of any adverse effects. An additional advantage of Esmolol is its selective β_1 activity which makes it a comparatively safer drug in patients with increased airway reactivity. They concluded that despite the fact that controlled hypotension has been practised for several decades, there isn't one ideal technique or pharmacological agent yet the majority of experience is with the use of nitrovasodilators like SNP and NTG.

Mutch WAC, Culligan JD, Cote DC, Thomson IR (1982) [26] studied 22 patients undergoing coronary artery bypass grafting in a randomized double blinded trial comparing the haemodynamic effects of intravenous NTG versus placebo. After a 20 minute infusion period, the MAP, MPAP, MCWP, CVP, stroke index and left ventricular stroke volume index were studied. They found that NTG administered at an intravenous rate of 0.5 mcg/kg/min significantly reduced all the above parameters but the cardiac index remained unchanged which indicated improved ventricular function despite a marked reduction in filling pressures. They also noted that the endocardial viability ration (DPTI/SPTI) also improved with NTG, suggesting a favourable myocardial oxygen balance. On increasing the dosage, the effects were similar but more profound in character. They concluded that these effects of NTG were compatible with the predominantly venodilator effect of drug and they also

attributed apparent increased potency of NTG to the use of an infusion system that does not adsorb the drug.

Menkhaus PG, Reves JG, Kissin I, Alvis MJ, Govier AV, Samuelson PN (1985) [27] studied the cardiovascular effects of Esmolol, which was a newly introduced drug at that time. 40 patients of IHD with normal ventricular function were equally divided into 4 groups of 10 each. One of the four was the control group while the other three received three different doses of i.v. Esmolol. All patients were pre medicated with oral Diazepam 0.15 mg/kg, Morphine sulphate 0.1 mg/kg intramuscularly and Scopolamine 0.3-0.4 mg intramuscularly, 60-90 minutes before induction. Diazepam 0.5 mg/kg and Pancuronium 0.1 mg/kg was injected to facilitate intubation. Anaesthesia was maintained with 50% N_2O in O_2. Thereafter, all patients in the treatment groups received 500 mcg/kg/min Esmolol for the first minute. Group I received an additional 100 mcg/kg/min for 6 min Group II received an additional 500 mcg/kg/min for another minute followed by 200 mcg/kg/min for the next 5 min. Group III received an additional 500 mcg/kg/min for 2 min followed by 300 mcg/kg/min for 4 min. Laryngoscopy was done 3 minutes after induction. Haemodynamic measurements were made at baseline, 3, 6, 7, 9, 10, 15 and 25 min after induction. Cardiac output and plasma nor-epinephrine levels were measured at baseline, 3, 6, 9 and 25 min after induction of anaesthesia. Blood samples for Esmolol were drawn at 6, 9 and 25 min after induction. They concluded that all three doses of Esmolol attenuated heart rate responses to intubation. Rate pressure products were significantly lower in Esmolol treated groups than in control groups. They also derived that the rapid disappearance of the drug from the blood paralleled the short duration of heart rate, hence making Esmolol a unique beta adrenergic blocker for the perioperative period.

Fromme GA, Mackenzie RA, Gould AB, Lund BA, Offord KP (1986) [28] studies 56 patients requiring orthognathic surgery. Patients were divided into three groups. Group I patients received 66% N_2O in Enflurane and O_2 and were kept normotensive. Group II patients received i.v. Morphine sulphate in 2-4 mg increments upto 24 mg plus 66% N_2O in Enflurane and O_2. Group III patients received the same concentration of the three gases as the other groups and an intravenous infusion of SNP sufficient enough to maintain a MAP between 55-60 mmHg. The surgical team was blinded and was asked to evaluate the dryness of the operative field every 30 minutes. Blood loss was determined using volumetric and gravimetric methods. Fromme et al popularised the surgeon's scale for quality of surgical field which ranges between 0-5 with a total of 6 points, 0 being the best possible operating condition and 5 making surgery impossible. They did not find any significant differences in blood loss or surgical dryness in any of the groups and the results were statistically insignificant in terms of duration of surgery too. They however noted that hypotensive anaesthesia has three potential benefits namely; reduced blood loss, improved quality of operative field and reduced operative time.

Mandal P (2003) [21] studied hypotensive properties of Isoflurane in 60 patients posted for FESS under general anaesthesia. Patients were equally divided into two groups and where one group received only 0.4% isoflurane and the other received the maximum concentration of isoflurane to maintain a MAP between 55-60 mmHg, they noted that the former group maintained their preoperative blood pressure throughout the procedure. Both the group patients had received lactated ringer's solution at 4ml/kg/hr. They found that the blood loss in the first group was much less (225ml) compared to the other group (750ml).There was a rise in heart rate in the first group after incision and a significant drop in the other group. He

concluded that higher concentrations of isoflurane produced hypotensive conditions good enough to facilitate a dry operative field and a fixed concentration (0.4%) did not alter the preoperative basal blood pressure.

Boezaart AP, Merwe van der J, Coetzee A (1995) [29] compared the surgical conditions for FESS under general anaesthesia during induced hypotension using either i.v. SNP or Esmolol and compared their findings with reference to the MAP and the average category scale of Fromme et al. Twenty patients posted for FESS under general anaesthesia were randomly divided into two groups, to receive either SNP (0.25 mcg/kg/min) or Esmolol (100-300 mcg/kg/min). They concluded that Esmolol provided better surgical conditions than SNP for FESS under general anaesthesia. All patients received a standard medication of oral Midazolam 15 mg an hour before induction of anaesthesia which was done with i.v. propofol at 2 mg/kg. Alcuronium at 0.2 mg/kg was used to facilitate intubation. All the patients were mechanically ventilated to maintain an $ETCO_2$ of 35 ± 2 mmHg. Anaesthesia was maintained with 50% N_2O in oxygen and Isoflurane. Patients of both groups received topical applications of Epinephrine on well rung out cotton pledges.

Ornstein E, Young WL, Ostapkovich N, Matteo RS, Diaz J (1990) [30] conducted a randomised controlled study in 22 patients posted for the surgical removal of intracranial arteriovenous malformation were all premedicated with oral diazepam 10 mg 90 min before arrival to the operating room and midazolam 2-5 mg once an i.v. access was established. Anaesthesia was maintained with Thiopentone, Vecuronium and 0.75% Isoflurane vapour in Nitrous oxide and Oxygen. Hypotension was induced with either Isoflurane 4% or SNP upto 8 mcg/kg/min or Esmolol 24 mg/min. In each group the end point of hypotension was a drop from baseline by 25%. Invasive monitoring was carried out throughout the surgery. They

found that all three pharmacological agents produced hypotension by different mechanism though. They noted that SNP caused an increase in cardiac output and heart rate while these were unchanged with Isoflurane and decreases with Esmolol. They concluded that amongst the three agents, Esmolol seemed most favourably affecting the myocardial oxygen balance with caution warranted in cases of compromised myocardial function.

Kadam PP, Saksena SG, Jagtap SR, Pantavaidya SM (1993) [31] studied 30 patients posted for spinal surgeries by dividing them into two groups. All patients received an intramuscular dose of Pethidine 1 mg/kg and Promethazine hydrochloride 0.5 mg/kg an hour before the surgery. Invasive blood pressure monitoring through the radial artery was secured. A standard technique of general anaesthesia was employed consisting of nitrous oxide, oxygen and pancuronium bromide as muscle relaxant with controlled ventilation. All the patients were catheterised to measure urine output. Halothane 0.5-2.5% was administered by Fluotec Mark III vaporiser to patients in one group. NTG solution was prepared by addition of 25 mg to 500 ml of 5% dextrose. The infusion was begun at the rate of 1 mcg/kg/min and then adjusted upto 2 mcg/kg/min for patients in the second group. The systolic blood pressure was lowered to 80-100 mmHg before the skin incision and maintained throughout the surgery in both the groups. 8-10 ml of Hartmann's solution was flown to maintain a urine output of 50 ml/hr or more. The surgeon was asked to grade the dryness of the surgical field on a scale 1-10; 1 being "dry and ideal" with little or no oozing and 10 being "wet and hopeless" which interfered with the surgical dissection. The blood loss was replaced by whole blood when the loss exceeded 10% of the estimated blood volume. It was assessed by weighing sponges and measuring the volume of blood in the suction bottle during surgery.

Postoperative drainage from the operation site within next 24 hours was also noted. The authors found that the hypotension achieved by NTG appeared to be more sustained than that by Halothane. They also noted an average blood loss of 202 ml in the NTG group and 602 ml in the Halothane group. Nine patients in this group needed blood transfusion. The surgeon's score (2.2+1.5) and operating time (143+57 min) were significantly less in the NTG group. The patients receiving NTG were alert at the end of the operation whereas six patients were drowsy for 4-6 hours following halothane. There was no evidence of tachyphylaxis or tolerance to the action of NTG. They concluded that i.v. nitroglycerin 1-2 mcg/kg/min is a safe and useful adjuvant to anaesthesia as suggested by less blood loss, better working field for the surgeon, reduced operative time and faster recovery.

Cincikas D, Ivaskevicius J (2003)[32] compared intraoperative haemorrhage and visibility of the operative field during normotensive and hypotensive anaesthesia in FESS by employing oral Captopril (6.25 mg) and i.v. NTG (0.5-5 mcg/kg/min) and compared findings with the control group with reference to MAP, intraoperative blood loss and surgical field visibility (Fromme scale) and they concluded that arterial hypotension induced by Captopril and NTG during general anaesthesia in FESS reduced bleeding and improved quality of surgical field. Fifty two patients posted for FESS were divided into two groups the hypotensive and the normotensive. All patients received premedication of 5 mg intramuscular midazolam 30 minutes before anaesthesia. The hypotensive group received 6.25 mg of oral Captopril one hour before anaesthesia. Induction was carried out with i.v. Fentanyl 1-2 mcg/kg and i.v. thiopentone 6-8 mg/kg. Patients were intubated employing either 0.5-0.7 mg/kg of i.v. Atracurium or 1.5 mg/kg of i.v. Succinyl choline. Anaesthesia was maintained with Halothane vapour (upto 1.5 MAC) in equal ratio of Oxygen and Nitrous oxide. For

patients of the hypotensive group, NTG was started at the rate of 0.5-5 mcg/kg/min and upon achieving a target MAP of 50-60 mmHg, surgical intervention was allowed to start. All patients were infiltrated locally with 1% Lignocaine in adrenaline. Haemorrhage was measured from the suction pumps and the surgical field was rated using the Fromme scale. NTG was discontinued 15-20 minutes before end of the surgery. The authors noted that the average blood pressure values as well as the heart rates differed statistically and the blood loss in the hypotensive group was on average 208 ml while that in the normotensive group was 349.2 ml. The visibility of operative field was on average one point better in the normotensive group. They concluded that captopril and NTG reduced the arterial blood pressure significantly and also reduced blood loss in FESS.

Kamal HM, Abd El-Rahman AS (2008) [33] conducted a study on 40 adults posted for FESS by dividing them into two groups. All patients received a standard anaesthetic technique in the form of i.v. Lignocaine 1 mg/kg, i.v. Fentanyl 1-2 mcg/kg, i.v. Propofol 2-3 mg/kg and i.v. Vecuronium 0.08 mg/kg to facilitate intubation. Anaesthesia was maintained with 1-1.5% isoflurane in 100% O_2. The Clevidipine group received an infusion of the same at 0.4-0.8 mcg/kg/min and the NTG group received i.v. NTG at 0.05 mcg/kg/min and gradually titrated upto 10 mcg/kg/min. In both groups, the infusions were adjusted to attain a MAP of 55-65 mmHg and the authors compared their findings with reference to heart rate, MAP, cardiac index, stroke index, SVR and surgical field visibility (Fromme scale) to conclude that Clevidipine was more effective in inducing controlled hypotension in FESS and it offered a better surgical field than NTG. They also suggested that although nitrovasodilators inhibit platelet function, it is unclear whether that was the contributing factor for the increased bleeding encountered by them in the NTG group.

Shams T, Bahnasawe M, Abu-Samra M, El-Masry R (2013) [34] performed a study upon 40 patients posted for FESS. They were randomly assigned to receive either dexmedetomidine 1mcg/kg over 10 min before induction followed by 0.4-0.8 mcg/kg/min maintenance or Esmolol 1mg/kg followed by 0.4-0.8 mcg/kg/min infusion to create a MAP between 55-65 mmHg. Anaesthesia was maintained with Sevoflurane 2-4% and the surgical field was rated using the average category scale. The average blood loss was estimated too. Emergence time and total recovery from anaesthesia were recorded using the Aldrete score. Sedation score was determined at 15, 30 and 60 min after tracheal extubation. They found that both the groups reached the target MAP with no intergroup differences in MAP or heart rate. In both the groups, there was no need of an additional hypotensive agent. Scores for bloodless surgical field were low for both groups and the median range was 1-3. They concluded that both drugs were efficient for controlled hypotension acting through two very different mechanisms with dexmedetomidine giving the added benefit of inherent analgesic, sedative and anaesthetic sparing effect.

Guney et al (2012)[35]employed 40 patients for their study involving the hypotensive properties of Esmolol and NTG. All patients were connected to the ECG, pulse oximetry, capnometry and an intra-arterial line for invasive monitoring. Through the intravenous line, 0.9% NaCl infusion was started at the rate of 5 ml/kg/hr. All patients were sedated with 0.03 mg/kg of i.v. Midazolam. They were then pre-oxygenated with 100% O_2 and induced with i.v. Propofol 2.5 mg/kg and 2 mcg/kg of i.v. Fentanyl. Rocuronium at 0.6 mg/kg was used to facilitate intubation. Anaesthesia was maintained with 6% Desflurane in an equal proportion of Nitrous oxide and Oxygen. Intravenous Remifentanil at 0.1 mcg/kg/min was infused as well. Normocapnoeic ventilation (32-35 mmHg) was practised for all the patients.

Desflurane was synchronised with a BIS of 40-60. All patients were given infiltration with lignocaine in adrenaline 1:100,000. E group received an infusion of Esmolol at 25-300 mcg/kg/min after an initial bolus of 500 mcg/kg over 30 seconds. The N group received an infusion of NTG at 0.5-2 mcg/kg/min. The blood pressure targets for both groups were a systolic blood pressure of 80 mmHg or a MAP of 60-65 mmHg. The period was logged until the target values were achieved for all patients. The total Esmolol and NTG used throughout the procedure was also noted. In case of bradycardia < 40, a 0.5 mg bolus of atropine was administered. The administered dose was reduced by half when the MAP went below 60 and the infusion was stopped altogether if no response was obtained within 5 minutes. Any side effects observed were recorded. The operative site was evaluated by the surgeon using the 5 point scale (0-5). The results were as follows. A comparison between SAP, DAP and MAP values and values prior to the hypotensive period yielded no difference between the groups. However, the decrease in heart rate in group E was found to be higher. Evaluation of surgical site haemorrhage during the hypotensive period did not yield any significant difference between the groups. Nausea/vomiting were observed in 6 patients in group E and 3 in group N. The authors concluded that Esmolol could be safely used as an alternative to NTG owing to its heart rate control related surgical site quality. In addition, Esmolol produced easy control of hypotension with no rebound tachycardia or hypertension.

Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A (2013) [36] compared the hypotensive properties of Esmolol and Nitroglycerine with reference to the surgical conditions. Fifty two adult consenting patients of both genders of ASA I and II requiring FESS under general anaesthesia were divided into two groups: the ESM group or the NTG group. Patients with bleeding disorders, hepatic,

renal or cardiovascular dysfunction and pregnancy were excluded from the study. All patients were starved and administered oral Alprazolam 0.25-0.5 mg on the night before surgery. All patients were connected to a non-invasive cuff, 5 lead ECG, pulse oximeter, temperature probes and the capnometer. Every patient received a similar general anaesthesia with Midazolam, Glycopyrrolate and Fentanyl 3-5 minutes before induction with Propofol. Laryngoscopy and intubation were facilitated with i.v. Vecuronium and anaesthesia was maintained on Isoflurane, Nitrous oxide, Oxygen and Fentanyl. All patients received a local infiltration with 4 ml of 2% Lignocaine and 1 ml of 1:1000 epinephrine before commencement of surgery. Now, group NTG received an i.v. infusion of 2-5 mcg/kg/min. Group ESM first received a bolus of 0.5 mg/kg followed by an infusion at 100-300 mcg/kg/min. In both the groups, the MAP was reduced in steps until the surgeon reported a category scale of 2-3 or until a predetermined lowest MAP of 60 mmHg was achieved. On attaining a target MAP of 60 mmHg or a visual score of 2-3 the infusion rates were maintained with fine adjustments. In both the groups, the hypotensive drugs were continued till the surgery was complete. The surgeon assessed the quality of operative field using the Fromme et al scale. An average category scale of 2-3 was considered ideal for surgery. The blood loss was estimated by collecting the surgical blood into the suction jars and weighing the soaked gauzes. Heart rate, SBP, DBP and MAP were recorded at regular intervals. All patients received lactated ringer's solution at 3-5 ml/kg/hr. The authors noted that the time to attain a target ACS of 2-3 was significantly shorter in the ESM group. The intraoperative SBP, DBP and MAP did not differ significantly in both the groups. The intraoperative heart rates remained lower in the ESM group. Ideal operating conditions were attained faster in the ESM group. The average blood loss in the ESM

group and no blood transfusion was needed in any group. The authors concluded that both Esmolol and NTG are safe drugs for controlled hypotension. However, Esmolol was better as it provided optimum surgical condition with only mild reduction in the blood pressure.

METHODOLOGY

This clinical study entitled "**Comparative Study of Nitroglycerin and Esmolol for Controlled Hypotension in FESS**" was carried out at Shri B.M Patil Medical College, Vijayapur during the period from December 2015 to August 2017.

This study was only undertaken on consenting patients after obtaining the ethical clearance from institutional ethical committee.

Eighty normotensive patients aged 18-60 years; scheduled for an elective FESS belonging to ASA grade I and II were included in this study.

SAMPLE SIZE: 80 patients

INCLUSION CRITERIA

- Elective FESS under general anaesthesia.
- Patients aged 18-60 yrs.
- Patients of ASA grade I and II
- Malampatti grade I and II
- Patients consenting for study.

EXCLUSION CRITERIA

- Patients of ASA grade III and above.
- Anaemic, diabetic and hypertensive patients.
- Cardiovascular and cerebrovascular diseases.
- Renal, hepatic and peripheral vascular diseases.
- Known or suspected allergy or intolerance to study drugs.
- Anticipated difficult airway.

Patients were randomly divided into two groups with 40 patients in each.

NTG Group – Nitroglycerin group (n=40): Received an i.v. infusion of NTG at 5-10 mcg/kg/min after intubation.

ESM Group – Esmolol group (n=40): Received an initial bolus of i.v. Esmolol at 500 mcg/kg over 30 seconds followed by an infusion at 100-300 mcg/kg/min after intubation.

All patients were assessed on the previous day before surgery.

The routine pre-anaesthetic evaluation consisted of the following:

- General condition of the patient.
- Nutritional status and weight.
- Airway assessment of the patient by Mallampatti grading.
- A detailed examination of the respiratory and cardiovascular system.
- A detailed examination of the alimentary and renal system.
- An explicit informed and written consent for anaesthesia and the clinical study.

The following investigations were done in all patients:

- Complete hemogram
- Standard 12 lead ECG
- Chest X ray
- Blood sugars
- Renal function tests
- Hepatic function tests

Patients with subnormal or abnormal laboratory reporting were excluded from the study.

All patients received Tab. Ranitidine 150 mg before and Tab. Alprazolam 0.5 mg after their evening meals after which they were advised to be nil by mouth for a minimum of 8 hours from midnight.

On the day of surgery, two i.v. accesses were secured on both hands – one meant for the hydrating fluids and the other for the hypotensive drug. An infusion of RL at 4 ml/kg/hr was given through one line. All patients were catheterized for monitoring urine output. Monitors were attached for continuous recording of heart rates and rhythm, non-invasive blood pressure (SBP, DBP and MAP), end tidal CO_2 and oxygen saturation.

All patients were premedicated with i.v. Glycopyrrolate at 0.01 mg/kg, i.v. Midazolam at 0.02 mg/kg and i.v. Fentanyl at 2 mcg/kg. They were then preoxygenated with 100% oxygen for 5 minutes.

Anaesthesia was induced with i.v Propofol 2 mg/kg. Direct laryngoscopy and endotracheal intubation were facilitated with a 1 mg/kg bolus of i.v. Succinyl Choline. Care was taken to ensure a smooth, dextrous and gentle laryngoscopy so as to avoid any haemodynamic variations from the basal values.

After intubation, normocapnoeic ventilation (30-35 mmHg) was carried out.

Anaesthesia was maintained with 0.4% Isoflurane in balanced N_2O/O_2 mixture and Vecuronium boluses at appropriate intervals. The dial concentration of isoflurane was kept constant (0.4%) throughout the anaesthetic duration.

NTG group (n=30) received i.v. Nitroglycerin (5 - 10 mcg/kg/min) and ESM group (n=30) received i.v. Esmolol 100-300 mcg/kg/min (after a bolus of 500 mcg/kg over 30 seconds) through syringe pumps. NTG solution was prepared by adding 50 mg (10 ml) of injectable NTG to 40 ml of 0.9% saline to make a 50 ml NTG solution (1 mg/ml). Esmolol solution was prepared by loading 500 mg (50 ml) of injectable

Esmolol hydrochloride solution in a 50 ml syringe (10 mg/ml). These hypotensive agents were administered using the EMCO SIP 850 syringe pump.

MAP was gradually reduced in decrements of 5 mmHg. The infusions were adjusted and steadied when the MAP reached 60-65 mmHg or when the surgeon gave 2 points for the operative visibility on the average category scale (ACS) of **Fromme et al**., [28] whichever was earlier.

Surgery was allowed to commence at the 5^{th} minute of infusion. Local infiltration of Lignocaine with adrenaline was given by the surgeon.

Patients who developed severe hypotension (MAP<60 mmHg) were first observed for 5 minutes after discontinuation of the hypotensive agent and if the low MAP persisted or did not improve, they were promptly treated with a 6 mg bolus of Inj. Ephedrine. These patients were excluded from the study. Similarly any patients in the Esmolol group, who developed bradycardia (HR <50/min) received Inj. Atropine and were excluded from this study.

Heart rate, ECG, SBP, DBP, MAP, SpO_2, capnography and urine output were monitored throughout the surgery

Infusion of the hypotensive agent was stopped 10 minutes before the anticipated end of surgery. Isoflurane was stopped 5 minutes before the end of the surgery. The balanced N_2O/O_2 mixture was gradually converted to 100% O_2 to avoid diffusion hypoxia.

At the end of the surgery, the residual neuromuscular paralysis of all patients was reversed with i.v. Neostigmine 0.05 mg/kg and i.v. Glycopyrrolate 0.01 mg/kg. All patients were extubated on the table and shifted to PACU for further monitoring.

The surgeon's opinion was sought throughout the surgery and at the end of the procedure.

MONITORING

The following parameters were recorded in all patients:

- Heart rate
- SBP, DBP and MAP
- Average category scale of visual surgical field rating (surgeon's assessment)

Basal readings of heart rate, SBP, DBP and MAP were noted followed by readings every 5 minutes for the first 15 minutes (following treatment with the hypotensive agent) followed by every 15 min until the infusions were stopped.

The average category scale (ACS) was assessed by the surgeon first at the 10th min of infusion and then every 15 minutes till closure. This ACS was based on the 6 points (0-5) assessment tool proposed and popularized by Fromme et al[28]

This average category scale is as follows:

5 – Massive uncontrollable bleeding. Surgery impossible. Constant suctioning required.

4 – Heavy but controllable bleeding that interferes with dissection. Prompt suctioning required.

3 – Moderate bleeding that moderately compromises surgical dissection. Frequent suctioning required.

2 – Moderate bleeding but without interference with accurate dissection. Surgical field not threatened. Occasional suctioning required.

1 – Bleeding, so mild it is not even a surgical nuisance. No suctioning.

0 – No bleeding, virtually bloodless field.

STATISTICAL ANALYSIS:

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/ Freeman-Halton Fisher exact test was employed to determine the significance of differences between groups for categorical data. The difference of the means of analysis variables between two independent groups was tested by unpaired t test. The difference of the means of analysis variables between two time points in same group was tested by paired t test. The difference of the means of analysis variables between more than two independent groups was tested by ANOVA and F test of testing of equality of Variance. If the p-value was < 0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0. and Microsoft office.

RESULTS

Table 1: Comparison of Mean Age between study groups

Parameter	NTG group			ESM Group			p value
	Range	Mean	SD	Range	Mean	SD	
AGE IN YEARS	18-58	33.9	11.9	18-60	32.2	14.9	0.579

Chart A : Comparison of Mean Age between study groups

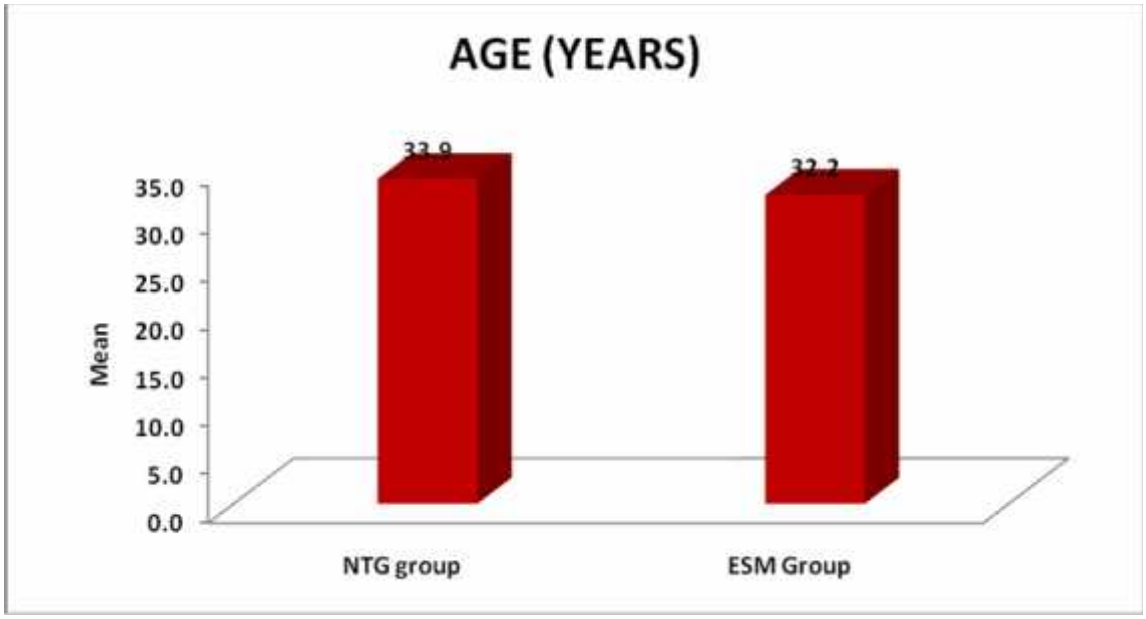


Table 1 and Chart A show mean age distribution among both groups. Both groups were comparable and p value was not statistically significant.

Table 2: Distribution of cases according to Sex between study groups

Sex	NTG group		ESM Group		p value
	N	%	N	%	
Male	20	50.0	22	55.0	0.654
Female	20	50.0	18	45.0	
Total	40	100.0	40	100.0	

Chart B: Distribution of cases according to Sex between study groups

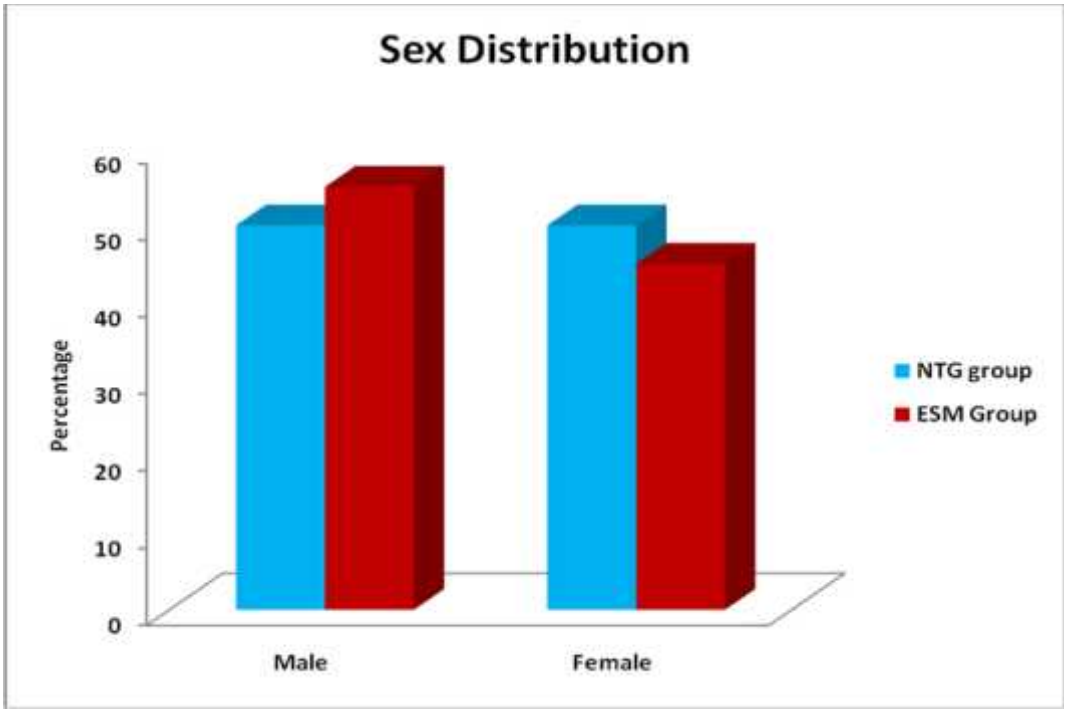


Table 2 and Chart B show sex distribution among both groups. Both groups were comparable and p value was not statistically significant

Table 3: Comparison of Mean Weight between study groups

Parameter	NTG group			ESM Group			p value
	Range	Mean	SD	Range	Mean	SD	
WEIGHT IN KG	43-75	60.7	8.8	45-75	59.8	9.0	0.652

Chart C: Comparison of Mean Weight between study groups

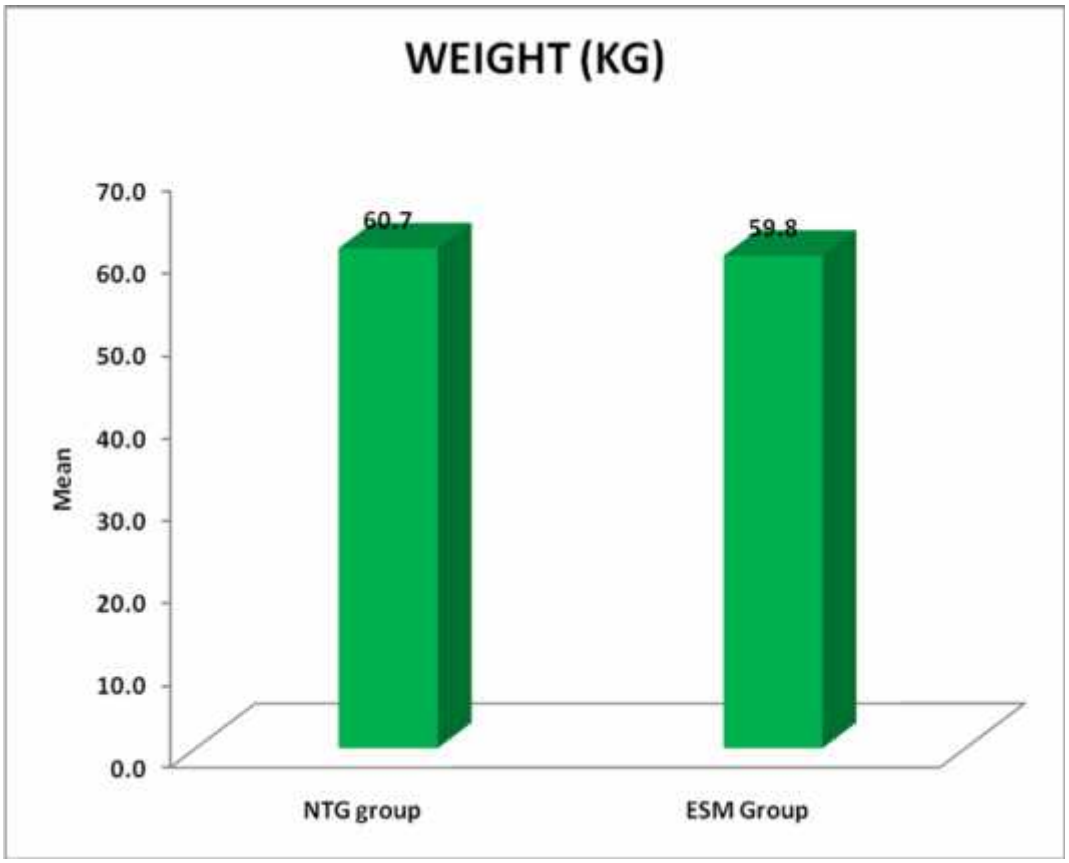


Table 3 and Chart C show weight distribution among both groups. Both groups were comparable and p value was not statistically significant

Table 4: Change in Mean heart rate (HR) between study groups

HR	NTG group		ESM Group		p value
	Mean	SD	Mean	SD	
BASAL	85.2	9.9	82.9	10.5	0.312
5 minutes	109.3	7.5	81.9	7.5	**<0.001***
10 minutes	96.3	7.9	75.3	5.1	**<0.001***
15 minutes	92.0	7.9	71.8	4.8	**<0.001***
30 minutes	87.4	5.7	68.4	5.3	**<0.001***
45 minutes	86.5	5.3	67.3	5.7	**<0.001***
60 minutes	87.4	8.2	66.6	4.9	**<0.001***
75 minutes	84.3	7.7	66.1	4.8	**<0.001***
90 minutes	84.3	7.5	68.3	35.3	**<0.001***
105 minutes	85.4	6.7	77.3	4.2	**0.002***
120 minutes	90.5	9.8	85.0	7.1	0.463

Note: *means significant at 5% level of significance ($p<0.05$)

Chart D: Change in Mean heart rate between study groups

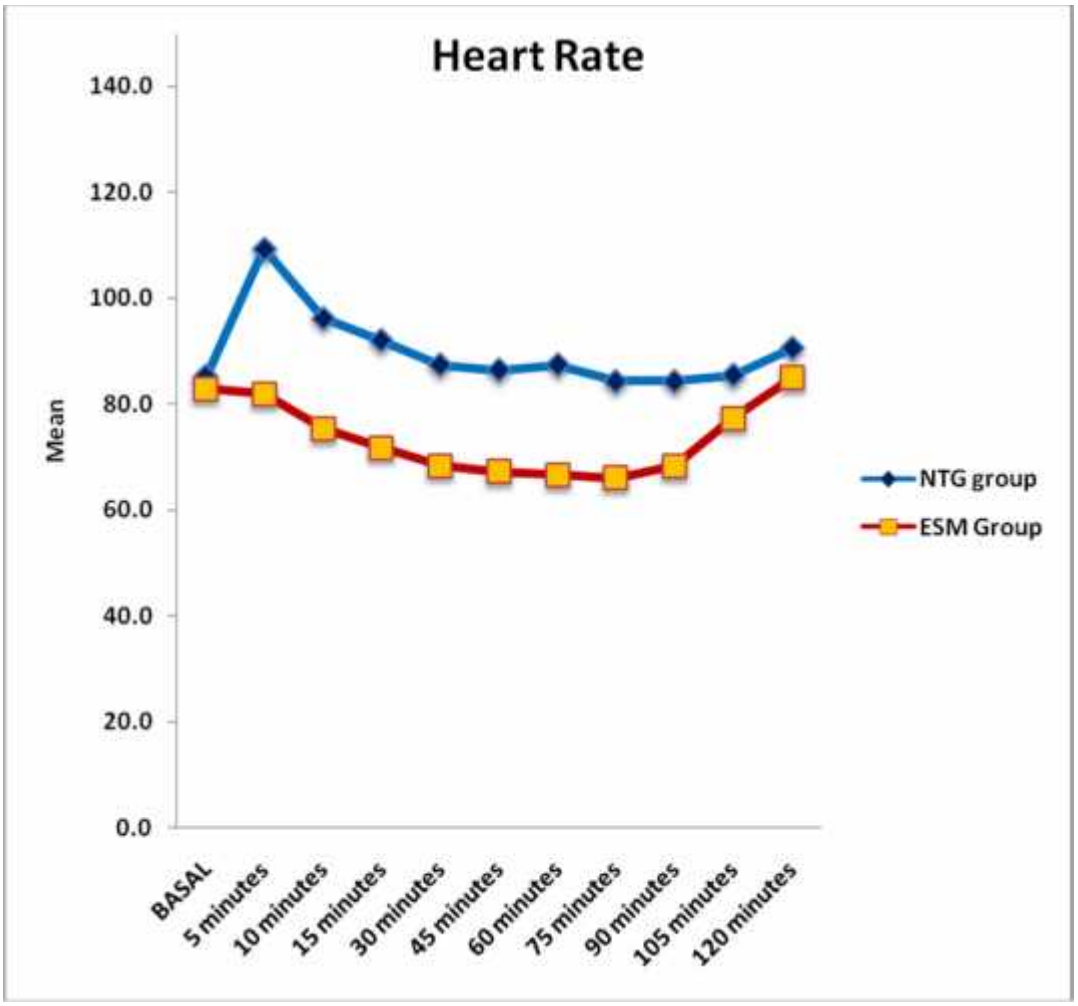


Table 4 and Chart D show mean Heart rate among both groups.

Significant p value is shown in bold.

Mean basal heart rate in NTG group was 85.2 ± 9.9 and in ESM group was 82.9 ± 10.5.

Mean heart rate in ESM group decreased from 5 minutes of surgery up to 120 minutes with significant value of **< 0.05.**

Table 5: Change in Mean Systolic blood pressure (SBP) between study groups

SBP	NTG group		ESM Group		p value
	Mean	SD	Mean	SD	
BASAL	127.1	5.3	121.2	7.6	**<0.001***
5 minutes	127.1	4.6	125.2	6.9	0.158
10 minutes	104.8	3.4	115.7	5.4	**<0.001***
15 minutes	95.3	5.4	100.2	5.2	**<0.001***
30 minutes	87.3	3.8	95.1	2.1	**<0.001***
45 minutes	84.3	2.8	93.9	2.1	**<0.001***
60 minutes	83.0	2.7	93.8	2.3	**<0.001***
75 minutes	85.2	3.0	94.0	2.1	**<0.001***
90 minutes	88.1	2.9	93.4	2.9	**<0.001***
105 minutes	91.5	3.3	97.2	2.5	**<0.001***
120 minutes	95.3	4.3	101.5	7.8	0.106

Note: *means significant at 5% level of significance ($p<0.05$)

Chart E: Change in Mean SBP between study groups

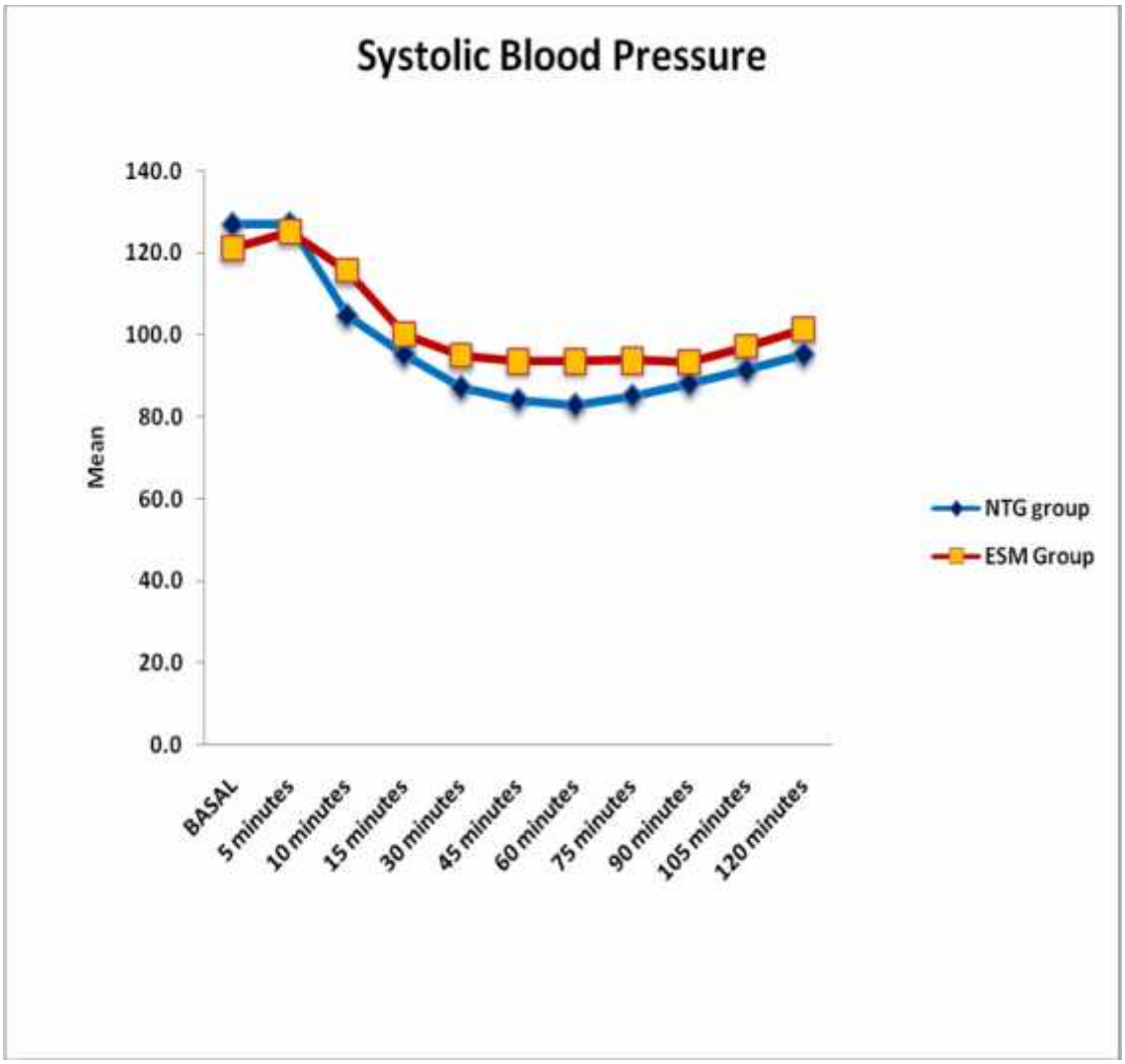


Table 5 and Chart E shows mean Systolic blood pressure among both groups.

Significant p value is shown in bold.

Significant decrease in systolic blood pressure was seen ESM group from 10 minutes of start of infusion up to 105 minutes with statistically significant p value of **< 0.001**

Table 6: Change in Mean Diastolic blood pressure (DBP) between study groups

DBP	NTG group		ESM Group		p value
	Mean	SD	Mean	SD	
BASAL	77.8	6.2	79.3	5.4	0.247
5 minutes	86.7	7.2	82.7	4.4	**0.003***
10 minutes	78.9	8.5	73.0	3.5	**<0.001***
15 minutes	63.6	2.7	68.1	3.6	**<0.001***
30 minutes	57.7	3.5	64.7	1.6	**<0.001***
45 minutes	54.8	1.9	64.2	1.3	**<0.001***
60 minutes	55.2	2.1	65.6	1.6	**<0.001***
75 minutes	55.1	2.3	65.9	1.9	**<0.001***
90 minutes	56.1	2.0	68.2	3.1	**<0.001***
105 minutes	57.6	2.3	68.4	0.9	**<0.001***
120 minutes	58.7	1.7	70.0	0.0	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart F: Change in Mean DBP between study groups

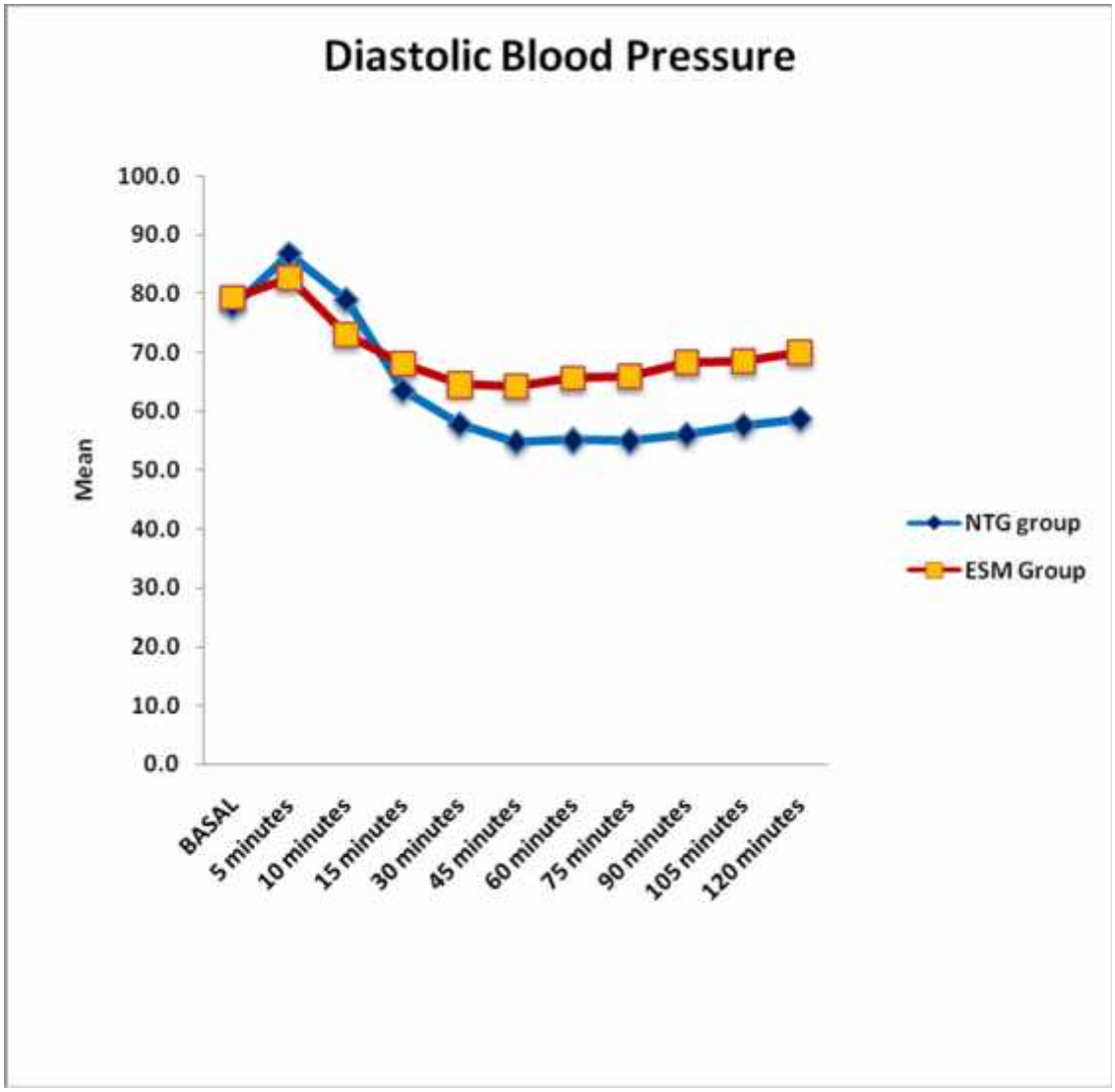


Table 6 and Chart F shows mean Diastolic blood pressure among both groups.

Significant p value is shown in bold.

Significant decrease in diastolic blood pressure was seen ESM group from 5 minutes of start of infusion up to 120 minutes with statistically significant p value of **< 0.05**

Table 7: Change in Mean arterial pressure (MAP) between study groups

MAP	NTG group		ESM Group		p value
	Mean	SD	Mean	SD	
BASAL	93.8	5.5	93.2	4.3	0.558
5 minutes	103.2	6.2	96.8	3.9	**<0.001***
10 minutes	95.2	5.7	87.2	3.1	**<0.001***
15 minutes	74.1	3.1	78.7	3.6	**<0.001***
30 minutes	67.6	3.2	74.8	1.2	**<0.001***
45 minutes	64.4	2.0	70.6	15.8	**0.016***
60 minutes	64.4	1.7	74.9	1.3	**<0.001***
75 minutes	65.1	1.9	75.4	1.3	**<0.001***
90 minutes	66.5	1.6	76.7	1.2	**<0.001***
105 minutes	68.7	1.6	78.1	1.0	**<0.001***
120 minutes	70.8	1.2	80.5	2.5	**<0.001***

Note: *means significant at 5% level of significance ($p<0.05$)

Chart G: Change in Mean arterial pressure between study groups

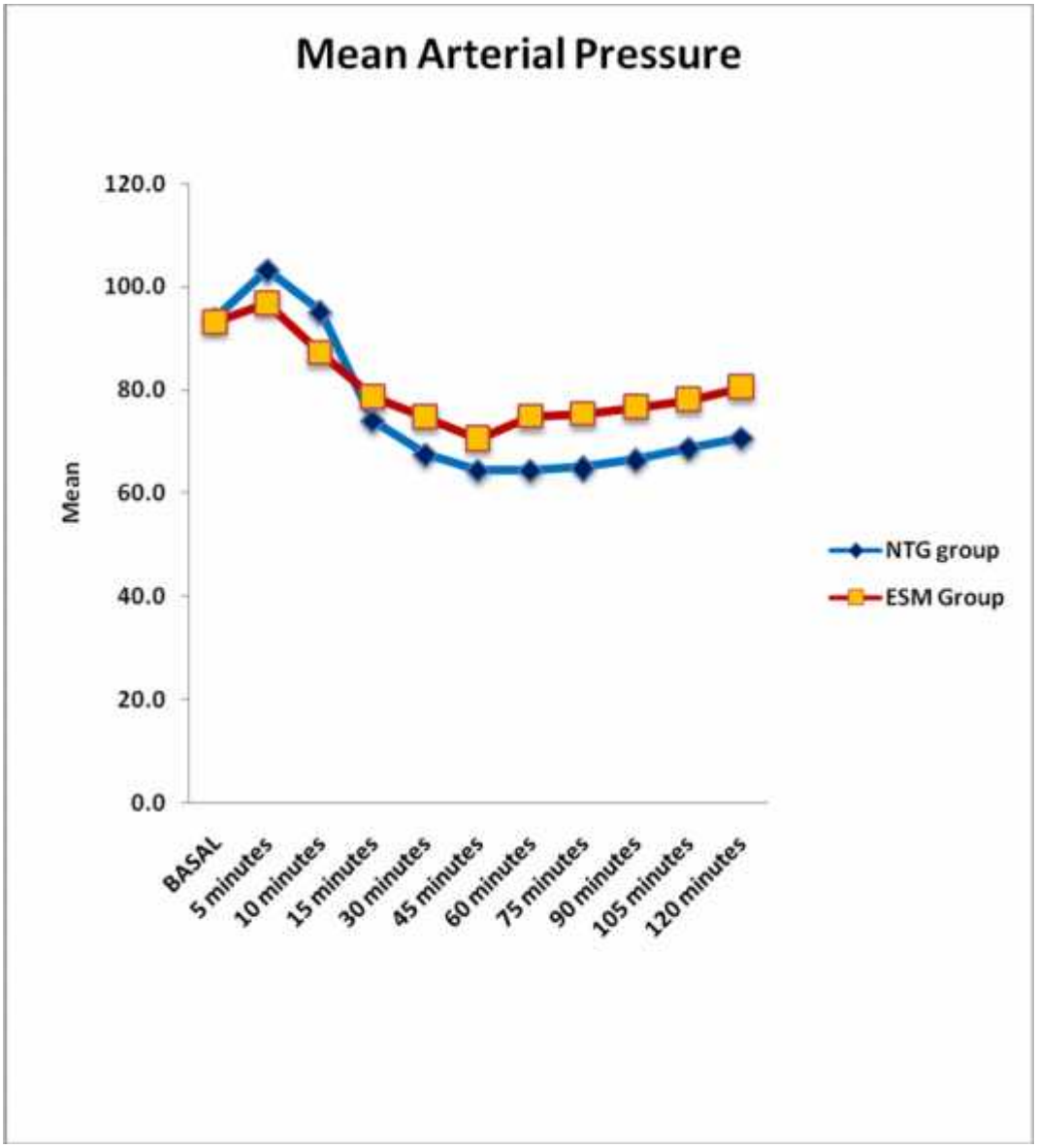


Table 7 and Chart G shows mean arterial blood pressure among both groups.

Significant p value is shown in bold.

Significant decrease in systolic blood pressure was seen ESM group from 5 minutes of start of infusion up to 120 minutes with statistically significant p value of **< 0.05.**

Table 8: Change in Mean Average category scale (ACS) between study groups

ACS	NTG group		ESM Group		p value
	Mean	**SD**	**Mean**	**SD**	
10 minutes	3.9	0.6	2.9	0.6	**<0.001***
15 minutes	3.2	0.5	2.3	0.5	**<0.001***
30 minutes	2.3	0.4	2.0	0.0	**0.001***
45 minutes	2.1	0.5	1.8	0.4	**<0.001***
60 minutes	2.0	0.4	1.8	0.4	**0.003***
75 minutes	2.0	0.2	1.6	0.7	**0.007***
90 minutes	2.0	0.2	1.9	0.3	0.813
105 minutes	1.9	0.3	2.0	0.0	0.459
120 minutes	2.0	0.0	2.0	-	-

Note: *means significant at 5% level of significance ($p<0.05$)

Chart H: Change in Mean ACS between study groups

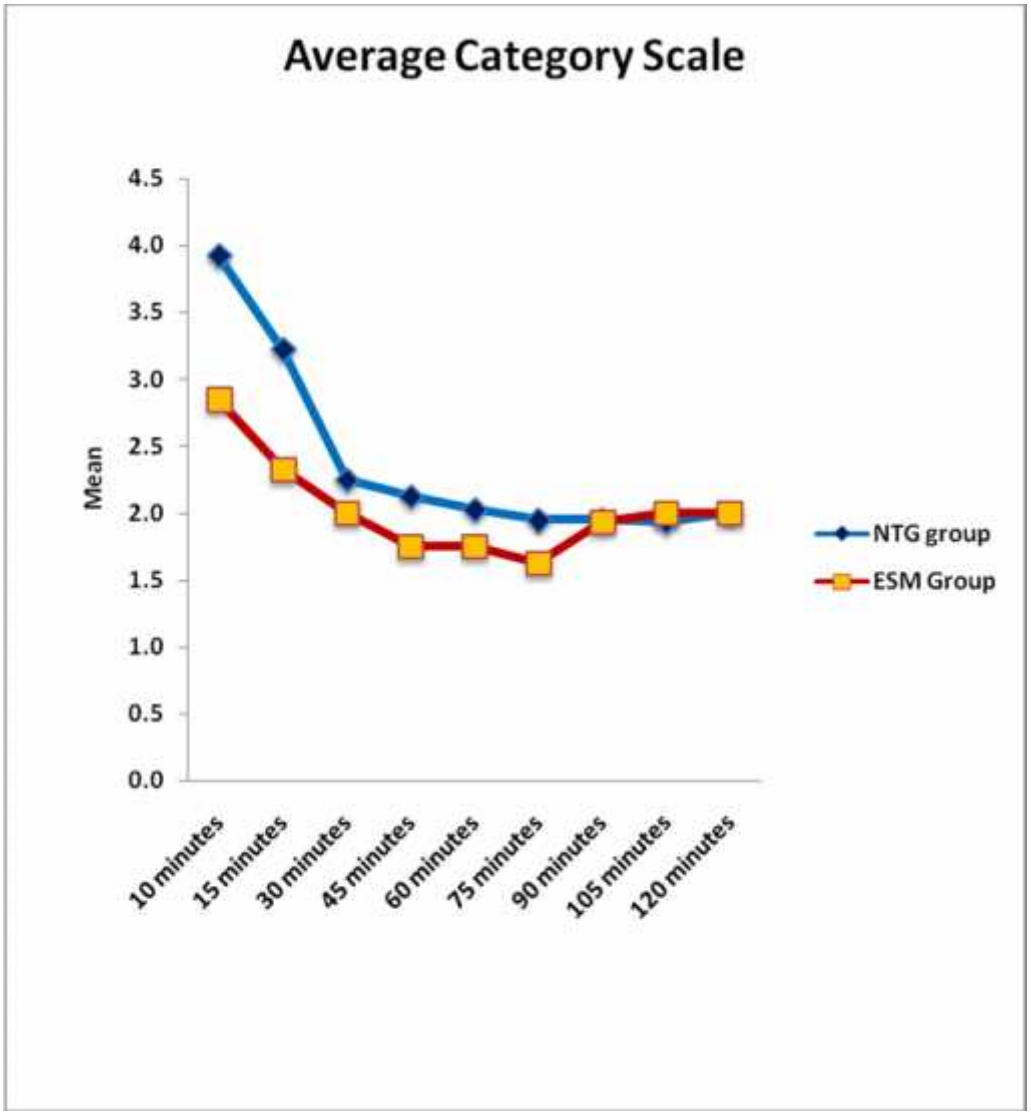
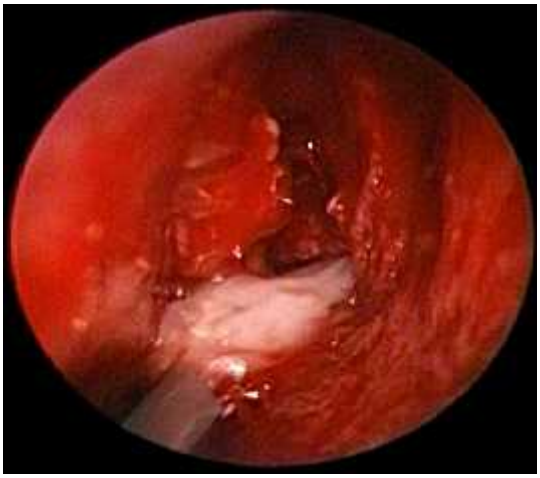


Table 8 and Chart H show mean Average category scale between both groups.

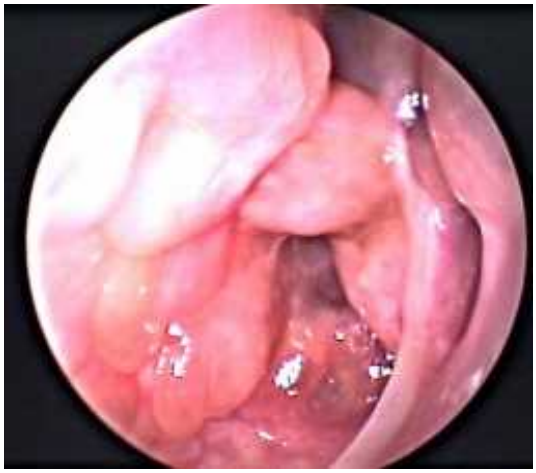
Significant p value is shown in bold.

ESM group had lower ACS score compared to NTG group from 10 minutes of start of infusion up to 75 minutes with statistically significant p value of **< 0.001.**

QUALITY OF SURGICAL DRYNESS IN MAJORITY OF CASES



NTG GROUP



ESM GROUP

From the above figures, it can be concluded that at 10 minutes, while most patients in the NTG group were given a surgical score of 4, an almost equal number of patients of the ESM group had 3 which is superior in terms of surgical dryness. At 30 min, all patients of the ESM group had a score of 2 while most patients in the NTG group had a score of 3. None of the patients in the NTG group ever had a score of 0, which was observed in a few patients of the ESM group. In the figure, the surgical field of the ESM group seems much superior to NTG group.

Table 9: Mean Duration of Surgery between study groups

Parameter	NTG group		ESM Group		p value
	Mean	SD	Mean	SD	
SURGICAL DURATION (min)	111.1	9.3	96.3	8.8	<0.001*

Note: *means significant at 5% level of significance (p<0.05)

Chart I: Mean Duration of Surgery between study groups

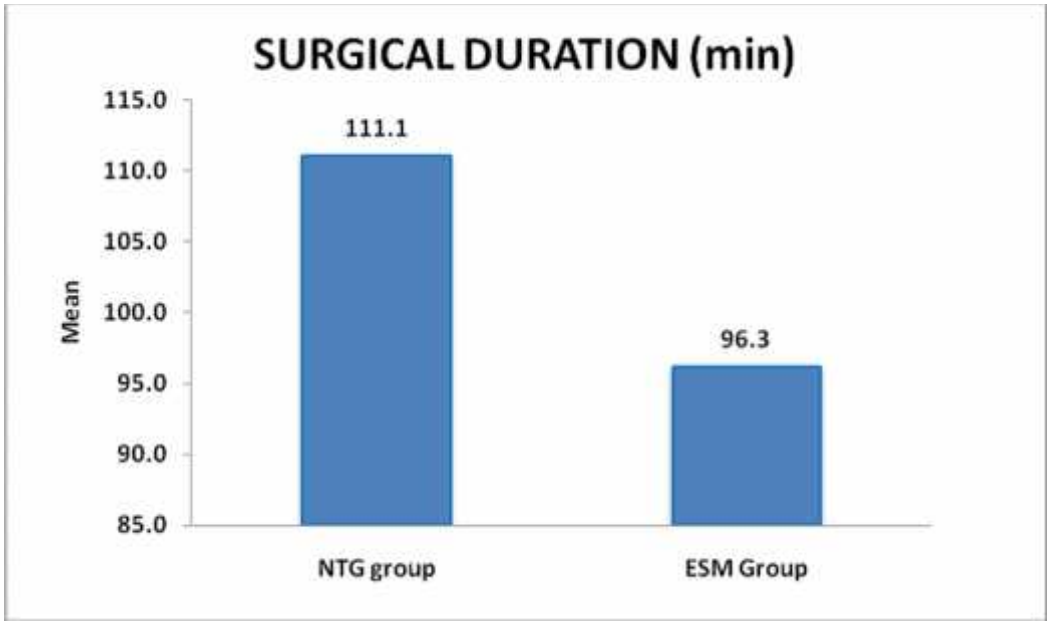


Table 9 and Chart I show mean duration of surgery among both groups.

Significant p value is shown in bold.

Mean duration of surgery was 111.1 ± 9.3 minutes in NTG group and 96.3 ± 8.8 minutes in ESM group.

p value was statistically significant (**< 0.001**)

Table 10: Complications

Complications	
NTG group	Nil
ESM Group	Nil

Patients in both study groups had no complications in the perioperative period.

DISCUSSION

FESS is a routinely employed for common conditions like rhino-sinusitis and polypus sinusitis. Bleeding is an impediment to quality intervention because it impairs operative field visibility and prolongs the duration of surgery and anaesthesia.[1,2]

Deliberate controlled hypotension is a tried and tested anaesthetic technique wherein the arterial blood pressure is lowered in a predictable manner to reduce the operative blood loss and improve the surgeon's field.[2]

Several hypotensive techniques have been tried and invented. The earlier ones included mechanical methods like tourniquets and positioning. High spinal and epidural anaesthesia have also been used. Later, various pharmacological agents including ganglion blockers, sympatholytic and adrenolytic drugs have been employed successfully.[2]

Nitrovasodilators like NTG dilate the capacitance vessels and reduce the venous return with concomitant reductions in stroke volume and cardiac output thereby causing hypotension. NTG has been tried by various authors for inducing hypotension[31,32,33,35,36,37]

Esmolol produces hypotension by reducing the heart rate, cardiac output and blood pressure. Other than its use as an anti-arrhythmic agent, it has also been found useful by several authors for the induction of controlled hypotension.[27,29,30,34,35,36,37]

Our clinical study compared the hypotensive effects of the nitrovasodilator NTG and the ultra short acting β-adrenergic blocker esmolol in elective FESS under general anaesthesia.

The present study was undertaken to compare the hypotensive properties of both drugs in terms of the total duration of surgery and surgical dryness.

The study population involved 80 consenting normotensive adults who were randomly divided into two groups with 40 patients each. The NTG Group received an i.v. infusion of NTG 5-10 mcg/kg/min after intubation and ESM Group received an initial bolus of intravenous Esmolol at 500 mcg/kg over 30 seconds followed by an infusion at 100-300 mcg/kg/min after intubation.

TABLE 11: DOSES OF NTG AND ESMOLOL EMPLOYED IN VARIOUS STUDIES

SL.NO.	AUTHOR AND YEAR	NTG DOSE USED
1	Cincikas D et al[32] 2003	0.5-5 mcg/kg/min
2	Kamal et al[33] 2008	0.05-10 mcg/kg/min
3	Guney at al[35] 2012	0.5-2 mcg/kg/min
4	Dongre et al[37] 2012	1 mcg/kg/min
5	Srivastava U et al[36] 2013	2-5 mcg/kg/min
6	**PRESENT STUDY**	5-10 mcg/kg/min
SL.NO.	**AUTHOR AND YEAR**	**ESMOLOL DOSE USED**
1	Ornstein et al[30] 1991	24 milligrams/min
2	Boezaart AP et al[29] 1995	500 mcg/kg loading bolus followed by infusion of 100 - 300 mcg/kg/min
3	Guney at al[35] 2012	500 mcg/kg loading bolus followed by infusion of 25 - 300 mcg/kg/min
4	Srivastava U et al[36] 2013	500 mcg/kg loading bolus followed by infusion of 100 - 300 mcg/kg/min
5	Shams T. et al[34] 2013	1000 mcg/kg loading bolus followed by infusion of 400-800 mcg/kg/min
6	**PRESENT STUDY**	500 mcg/kg loading dose followed by infusion of 100 - 300 mcg/kg/min

Cincikas D, Ivaskevicius J[32] showed that induced hypotension produced by Nitroglycerin combined with Captopril during general anaesthesia in endoscopic rhinosurgery reduces bleeding and improves operative field visibility.

Kamal HM, Abd El-Rahman AS [33] in their study involving Clevidipine and NTG showed that NTG was less effective than Clevidipine in controlling hypotension and improving the surgical field visibility in FESS.

Boezaart AP, Merwe van der J, Coetzee A [29] compared SNP with Esmolol and concluded that esmolol provided better operating conditions that SNP.

Guney at al[35] demonstrated that Esmolol provided better haemodynamic stability than NTG in controlled hypotension and should be considered as an alternative to it in nasal surgeries.

Ornstein E, Young WL, Ostapkovich N, Matteo RS, Diaz J [30] suggested that a combination of Sodium nitroprusside, Esmolol and NTG was better than when used singly for deliberate hypotension for patients with intracranial malformations.

Dongre H, Sharma V, Premendran B, Dongre A, Tikde S [37] opined that both NTG and Esmolol can be used to produce a dry operative field in spine surgeries with comparable efficacy with NTG being a more economical option.

Shams T, Bahnasawe M, Abu-Samra M, El-Masry R [34] employed Dexmedetomidine and Esmolol for controlled hypotension in FESS and opined that although both drugs provided ideal surgical conditions, Dexmedetomidine had the added advantage of inherent analgesic, sedative and anaesthetic sparing properties.

Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A [36] in their comparison of NTG and Esmolol were of the opinion that Esmolol offered better operative conditions with only minimal reductions in the mean arterial blood pressure when performing FESS under general anaesthesia.

METHOD OF ADMINISTRATION

In the present study, both NTG and Esmolol were infused through a syringe pump (EMCO SIP 850). In case of Esmolol, only the loading dose was pushed manually. The method of administration used here is similar to the administration by the various authors cited above.

CHANGES IN THE HEART RATE AND BLOOD PRESSURE

In the NTG group, the basal heart rate was in the range of 85.2 ±9.9 and in the ESM group, it was 82.9 ±10.5. This difference was comparable but was statistically insignificant.

At the 10^{th} minute of infusion however, the heart rates in group ESM were much lower (75.3 ±5.1) compared to the NTG group (96.3 ± 7.5). This difference was highly significant ($p<0.001$). This fall in heart rates in the ESM group is attributed to the beat-adrenergic blocking effects of Esmolol. Throughout the surgery, the mean heart rates in the ESM group were much lower than in the NTG group. The mean heart rates in the NTG group are consistent with the fact that NTG causes either no change or a slight increase in heart rates during a continuous infusion as a reflexive phenomenon which is the baroreceptor mediated response secondary to the hypotension. One patient in group NTG had a consistent tachycardia throughout the surgery. This is probably the reflex tachycardia that is seen with NTG. Studies by **Guney at al**[35] also showed a similar trend in their study. They found a drop in heart rates by 18% for the esmolol group. **Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A** [36] in their study found that the mean heart rates in esmolol group were 83.87±7.58 compared to 90.88±8.54 in the NTG group. Our results with regards to the trend and drop in heart rates in the Esmolol group are similar to the study results by the aforesaid authors. None of the patients in the Esmolol group suffered from

clinically significant bradycardia (<50/min). These results are comparable with the findings of **Ornstein E, Young WL, Ostapkovich N, Matteo RS, Diaz J** [30]

The mean basal values of SBP of the NTG group were 127.1 ± 5.3 while that of Esmolol were 121.2 ± 7.6. These values were statistically significant. It is noteworthy that on an average, the NTG group achieved a fall in SBP much earlier than in the Esmolol group (at 10^{th} min, NTG = 104.8 ± 3.4 and ESM = 115.7 ± 5.4) This difference was highly significant ($p<0.001$) This is purely attributed to the mechanism of hypotension caused by each drug. NTG has a venodilatory action while esmolol reduces the cardiac output by negative chronotropism. The latter mechanism takes some time. Even though the SBP fall is higher in the NTG group, the surgical dryness was superior in the Esmolol group. The mean basal DBP values of NTG and ESM group were 77.8 ±6.2 and 79.3 ± 5.4 respectively. Throughout the hypotensive period, the difference in DBP between the two groups was highly significant.

The basal MAP values of NTG and ESM group were 93.8 ± 5.5 and 93.2 ± 4.3 respectively. This difference was comparable but clinically insignificant. On examining the mean MAPs of both groups, we found that the ESM group achieved the target SFR of 2 or below at higher MAP values and hence, the MAPs were not further lowered in this group. To achieve similar operative dryness, the MAP had to be reduced much lower in the NTG group. On an average, the mean MAPs of ESM group in the hypotensive period was 80.5 ± 2.5 while for NTG, it was 70.8 ± 1.2.

Our results pertaining to the trends in heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure are in agreement with the studies conducted by **Boezaart AP, Merwe van der J, Coetzee A** [29] **Guney et al,**[35] **Dongre H, Sharma V, Premendran B, Dongre A, Tikde S** [37] and **Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A**. [36]

A close relationship between reduced MAP values surgical field quality has been shown by **Sieskiewicz A, Drozdowski A, Rogowski M** [38] Improved surgical field quality with a MAP of 50-60 mmHg with NTG in nasal surgeries has also been the observation of **Cincikas D, Ivaskevicius J**[32] In their study comparing the effects of esmolol and SNP with a target MAP of 55-65 mmHg during orthognathic surgery, **Blau WF, Kafer ER, Anderson JA** [39] reported the average MAP as 58.7±0.7 with Esmolol and said that the reduction of blood loss with esmolol was more effective. On an average, we found that similar operative visibility was obtained in the Esmolol group with much higher MAPs than in the NTG group. These findings are in agreement with those of **Guney at al**[35] and **Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A.** [36]

SURGICAL FIELD VISIBILITY AND DURATION OF SURGERY

Several authors have opined that the quality of operative field is improved with controlled hypotension but all have suggested that it is difficult to accurately measure and compare the minute blood losses. Hence the **Fromme et al**[28] scoring system was accepted to enable the surgeon to make his own assessment of the operative field. This average category scale consists of 6 points (0-5) with 0 being the driest and 5 making surgery impossible. In this visual scale, the surgeon opines on the quality of the surgical field and gives scores. This scoring system has been used by almost all authors who have attempted to study hypotensive anaesthesia.

The mean average category scale score for NTG group at 10^{th} min was 3.9 ± 0.6 while in the Esmolol group was 2.9 ± 0.6. At 30 min, patients of the Esmolol group had a mean score of 2 compared to NTG group that had mean score of 2.3 ± 0.4. It is also worthwhile to note that at 30 min, the MAPs in the ESM group was 74.8 ± 1.2 versus a 67.6 ± 3.2 in the NTG group. The average surgical duration in the NTG

group was 111.1 ± 9.3 min while it was 96.3 ± 8.8 min in the ESM group. This difference is significant. The shorter duration in the ESM group is probably owing to the superior operative field.

Capillary bleeding is the major impediment in FESS. Esmolol blocks the adrenergic effect of vasoactive amines released during hypotension. During esmolol induced hypotension, unopposed alpha-adrenergic effects causes vasoconstriction of arterioles and pre-capillary sphincters leading to the nasal mucosal blood vessels to contract and cause less oozing and thus providing for a superior operative field via its heart rate control related bleeding and surgical site quality in FESS.

In contrast, the endogenous catecholamines have minimal effect on vascular smooth muscles when NTG is used. This might result in vasodilatation[40] with the consequence of more oozing and surgical blood loss. In addition, reflex tachycardia will further contribute to this. These factors contribute to more oozing and a longer duration of surgical intervention.

Our findings on surgical duration are comparable to the findings of **Srivastava U, Dupargude AB, Kumar D, Joshi K, Gupta A** [36]

None of the patients of either group presented with the need for intraoperative haemotransfusion or suffered any post operative complications.

CONCLUSION

From our study, we conclude that-

1) Both Esmolol and NTG produced hypotension required for FESS.
2) Optimum operative conditions with better surgical field visibility were achieved at higher MAPs with Esmolol whereas similar operative conditions were achieved only with more reduction in MAP with NTG.
3) Better surgical field dryness with reduced intraoperative bleeding was seen in the Esmolol group compared to NTG group with a statistical significant difference between both groups.
4) The average duration of surgery was lower in the Esmolol group.
5) No complications were noted with either drug.

Hence, we conclude that, Esmolol is a safe and superior agent to NTG for controlled hypotension in FESS as it minimizes surgical blood loss, enhances the operative field visibility and reduces overall duration of surgery at higher MAPs compared to NTG.

LIMITATIONS:

- Our study was done only in ASA I and II patients aged between 18-60 years.
- More studies are needed to focus on the effects of Esmolol in debilitated patients and paediatric population.

SUMMARY

This clinical study entitled "COMPARATIVE STUDY OF NITROGLYCERIN AND ESMOLOL FOR CONTROLLED HYPOTENSION IN FESS" was carried out at Shri B.M Patil Medical College, Hospital & Research centre, Vijayapur from December 2015 through August 2017. 80 consenting patients (aged 18-60 years) scheduled for elective FESS under general anaesthesia were included in this study. Patients with anaemia, hypertension, diabetes and other systemic disorders were excluded from this study. The study population was randomly divided into two groups.

Group NTG – Nitroglycerin group (n=40): After intubation received an intravenous infusion of NTG at 5-10 mcg/kg/min.

Group ESM – Esmolol group (n=40): After intubation received an initial bolus of intravenous Esmolol at 500 mcg/kg over 30 seconds followed by an infusion at 100-300 mcg/kg/min.

All patients were premedicated with i.v. Glycopyrrolate, i.v. Midazolam and i.v. Fentanyl. Patients were preoxygenated with 100% oxygen and then induced with i.v. Propofol. Laryngoscopy and intubation were done after giving i.v. Succinyl Choline. The infusions were finely adjusted and steadied when the MAP reached 60-65 mmHg or when the surgeon gave 2 points for the operative visibility on the average category scale (ACS) popularised by Fromme et al[28], whichever was earlier.

The basal values of heart rate, SBP, DBP and MAP were recorded followed by those at 5, 10, 15 minutes and then every 15 minutes following the hypotensive infusion. The average category scale was assessed at 10^{th} and 15^{th} minute and every 15 minutes following the infusion.

There was a marked decrease in the HR in the ESM group compared to NTG group. SBP, DBP and MAP decreased in NTG group compared to ESM group. The surgical blood loss and duration of surgery was lower in the ESM group.

Both NTG and Esmolol are useful for controlled hypotensive anaesthesia but Esmolol given in the dose of 100-300 mcg/kg/min (after a bolus of 500 mcg/kg) effectively reduced the surgical blood loss and duration in a superior manner because it gave better results at much higher MAPs. It also enhanced the operative visibility better. There was no clinically significant bradycardia or any other side effects or complications noted with Esmolol.

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ANNEXURE – I

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

NO/58/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17/11/2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title "Comparative study of nitroglycerine and esmolol for controlled hypotension in fess"

— x — x —

Name of P.G. Student : Dr. Rahul. S.
Dept of Anaesthesiology.

Name of Guide/Co-investigator : Dr. R. R. Kusugal.
Assoc prof. Anaesthesiology

DR.TEJASWINI VALLABHA
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical College,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

ANNEXURE - II

INFORMED CONSENT FORM

TITLE OF THE PROJECT: **"COMPARATIVE STUDY OF NITROGLYCERIN AND ESMOLOL FOR CONTROLLED HYPOTENSION IN FESS"**

PRINCIPAL INVESTIGATOR : **Dr. RAHUL S**,

Department of Anaesthesiology,

Email: rahulgowda251988@yahoo.com

PG GUIDE : **Dr. R.R. KUSUGAL**,

Associate Professor,

Department of Anaesthesiology,

B.L.D.E University's

Shri B.M. Patil Medical College,

Hospital & Research Centre,

Vijayapur, Karnataka.

I have been informed that this study is **"COMPARATIVE STUDY OF NITROGLYCERIN AND ESMOLOL FOR CONTROLLED HYPOTENSION IN FESS"**

I have been explained about this study in the language which I understand. I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have been told that my participation in the above study is voluntary and I am aware that I can opt out of the study at any time without having to give any reasons for doing so. I am also informed that my refusal to participate in this study will not affect my treatment by any means.

I agree to participate in the above study and cooperate fully. I agree to follow the Doctor's instructions about my treatment to the best of my ability.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audio tapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time and Dr. Rahul S is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for my careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr. Rahul S will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/ my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided. I understand that by my agreement to participate in this study, I am not waiving any of my legal rights. I have been explained about the purpose of this research, the procedures required and the possible risks and benefits, in my own language. I have been explained all the above in detail and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

Patient's Signature: Witness Signature

Name: Name:

Date: Date:

Dr. R.R.KUSUGAL **Dr. RAHUL S**

(Guide) (Investigator)

ANNEXURE - III

PROFORMA

- **PATIENT DETAILS**

NAME OF THE PATIENT: AGE: GENDER:

IP NO: DATE OF ADMISSION: DATE OF SURGERY:

DIAGNOSIS:

ASA GRADE: WEIGHT:

HB: TLC: DLC: BLOOD GROUP:

BT: CT:

RFT:

ECG: CXR:

- **BASAL PARAMETERS**

HEART RATE: SBP: DBP: MAP:

- **HYPOTENSIVE AGENT DETAILS-**

DRUG TO BE USED- LOADING: MAINTENANCE:

CALCULATED DOSE (for weight) LOADING: MAINTENANCE:

- **DETAILS OF ANAESTHESIA (Time)-**

PRE-MEDICATION: PREOXYGENATION: INDUCTION:

INTUBATION:

- **OPERATIVE DETAILS (Time)-**

HYPOTENSIVE AGENT ADMINISTRATION: BEGINNING OF SURGERY:

TERMINATION OF HYPOTENSIVE AGENT: COMPLETION OF SURGERY:

- **TOTAL DURATION OF SURGERY (mins):**
- **INTRA/POST-OP COMPLICATIONS (if any):**

INTRAOPERATIVE RECORDINGS

TIME (minutes)	HR	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	ACS	TIME (minutes)	HR	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	ACS
5						95					
10						100					
15						105					
20						110					
25						115					
30						120					
35						AVG					
45											
50											
55											
60											
65											
70											
75											
80											
85											
90											

NITROGLYCERIN (NTG) GROUP

SERIAL NUMBER	AGE IN YEARS	GENDER	WEIGHT IN KG	HEART RATE (Beats per minute)											SYSTOLIC BLOOD PRESSURE (mm Hg)											DIASTOLIC BLOOD PRESSURE (mm Hg)											MEAN ARTERIAL BLOOD PRESSURE (mm Hg)											AVERAGE CATEGORY SCALE (Fromme)										SURGICAL DURATION (min)	COMPLICATIONS (Y/N)
				BASAL	NTG INFUSION @ 5-10 mcg/kg/min										BASAL	NTG INFUSION @ 5-10 mcg/kg/min										BASAL	NTG INFUSION @ 5-10 mcg/kg/min										BASAL	NTG INFUSION @ 5-10 mcg/kg/min										NTG INFUSION @ 5-10 mcg/kg/min											
					5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes		5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes		5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes		5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes		
1	37	M	73	76	99	92	90	77	84	81	73	79	85	90	122	118	100	90	96	88	87	84	82	89	92	70	70	80	70	65	55	54	56	58	60	62	87	89	90	76.7	75.3	66	65	65.3	66	69.7	72	3	3	2	2	2	2	2	2	2	120	N
2	30	F	50	92	117	98	94	90	88	84	87	90	95	-	128	128	107	93	87	83	80	86	90	94	-	72	84	88	63	57	52	57	53	55	58	-	92	101	101	73	67	62.3	64.7	64	66.7	70	-	5	4	3	2	2	2	2	2	-	115	N
3	20	M	60	80	104	98	98	90	82	78	75	83	-	-	128	124	104	100	90	88	85	89	90	-	-	72	72	78	67	65	55	56	59	60	-	-	90	92	93	78	73.3	66	65.7	69	70	-	-	4	3	2	2	2	2	2	-	-	95	N
4	24	M	65	90	99	90	88	88	84	87	82	83	85	-	126	123	104	100	90	85	80	85	86	90	-	86	94	70	65	60	55	58	57	58	62	-	100	108	94	76.7	70	65	65	66	67	71	-	4	3	2	2	2	2	2	2	-	110	N
5	28	M	65	86	106	108	106	84	83	87	84	87	90	-	128	120	105	100	90	86	80	88	85	90	-	80	80	82	65	55	54	56	57	59	60	-	95	96	99	76.7	66.7	64.7	64	67.3	67.7	70	-	4	3	2	2	2	2	2	2	-	110	N
6	24	F	56	80	108	96	90	93	87	80	83	81	76	-	132	118	104	93	87	86	85	80	83	87	-	70	94	62	58	55	52	50	53	56	58	-	86	108	84	69.7	65.7	63.3	61.7	62	65	67.7	-	4	3	2	2	2	2	2	2	-	105	N
7	42	M	74	72	114	102	100	77	81	79	73	70	-	-	130	138	110	105	90	85	87	80	90	-	-	78	78	80	67	56	55	53	52	58	-	-	96	96	99	79.7	67.3	65	64.3	61.3	68.7	-	-	5	4	3	3	2	2	2	-	-	100	N
8	38	F	63	96	102	88	85	85	82	78	79	77	73	-	132	126	102	91	85	80	82	86	90	95	-	90	90	82	63	56	55	58	52	53	57	-	105	105	96	72.3	65.7	63.3	66	63.3	65.3	69.7	-	3	3	2	1	1	1	1	1	-	110	N
9	53	M	67	86	116	98	90	87	85	83	80	83	-	-	128	128	109	94	88	83	82	84	90	-	-	80	90	88	65	58	59	55	54	58	-	-	95	101	101	74.7	68	67	64	64	66.7	-	-	3	2	2	2	2	2	2	-	-	105	N
10	31	F	56	86	108	106	99	90	88	86	87	83	88	94	119	128	101	97	85	82	87	85	88	90	95	79	92	78	60	55	52	58	56	55	53	58	92	110	94	72.3	65	62	67.7	65.7	66	65.3	70.3	4	3	2	2	2	2	2	2	2	120	N
11	47	M	59	71	108	88	82	86	90	105	93	87	80	-	124	130	103	91	87	84	80	82	85	89	-	70	94	102	64	56	55	53	57	55	59	-	83	94	111	73	66.3	64.7	62	65.3	65	69	-	4	3	2	2	2	2	2	2	-	110	N
12	35	F	58	104	118	103	98	84	87	96	88	86	-	-	118	128	109	101	97	88	84	83	85	-	-	80	90	76	65	61	56	54	57	53	-	-	98	108	93	77	73	66.7	64	65.7	63.7	-	-	4	3	2	3	2	2	2	-	-	120	N
13	18	F	45	80	109	96	88	90	97	95	88	87	85	-	121	126	106	93	84	87	84	89	89	92	-	74	94	74	62	58	53	57	54	57	58	-	92	108	91	72.3	66.7	64.3	66	65.7	67.7	69.3	-	4	3	2	2	2	2	2	2	-	115	N
14	50	F	61	86	116	86	80	81	84	86	81	90	89	-	128	130	107	100	92	90	85	80	83	90	-	70	90	92	65	60	55	56	52	54	59	-	89	107	105	76.7	70.7	66.7	65.7	61.3	63.7	69.3	-	4	4	3	3	2	2	2	2	-	115	N
15	40	F	54	94	116	96	94	94	90	86	80	83	83	99	128	126	107	103	92	87	80	88	85	90	92	80	78	78	67	66	53	55	52	57	58	61	94	96	94	79	74.7	64	63.3	64	66.3	68.7	71.3	4	3	2	2	2	2	2	2	2	120	N
16	18	M	64	94	118	98	94	90	84	86	83	80	-	-	128	128	104	83	86	81	83	87	88	-	-	86	94	88	60	56	54	57	55	58	-	-	100	108	101	67.7	66	63	65	65.7	68	-	-	4	3	2	2	2	2	2	-	-	105	N
17	50	M	75	70	98	99	92	87	88	84	80	79	77	76	128	128	104	93	84	82	80	84	88	90	91	76	84	72	63	55	54	54	56	54	57	58	91	105	92	73	64.7	63.3	62.7	65.3	64	67.3	68.7	4	3	2	2	2	2	2	2	2	120	N
18	40	F	56	90	108	94	90	87	88	94	97	100	98	-	140	128	106	94	87	81	82	87	85	90	-	74	94	72	60	52	54	56	58	53	57	-	90	111	90	71.3	63.7	63	64.7	67.7	63.7	68	-	4	3	2	2	2	2	2	2	-	110	N
19	18	F	56	82	106	94	86	88	90	104	100	95	90	88	130	128	100	90	82	80	83	88	90	95	100	86	84	71	60	57	56	54	55	57	58	57	98	105	90	70	65.3	64	63.7	66	68	70.3	71.3	4	4	3	3	3	2	2	2	2	120	N
20	40	F	45	80	109	96	88	90	97	95	88	87	85	-	121	126	106	93	84	87	84	89	89	92	-	74	94	74	62	58	53	57	54	57	58	-	92	108	91	72.3	66.7	64.3	66	65.7	67.7	69.3	-	4	3	2	2	2	2	2	2	-	115	N
21	20	M	67	94	116	103	97	94	86	87	82	89	85	98	128	136	118	108	95	85	80	87	88	90	93	82	92	80	67	58	53	55	58	55	57	60	103	111	98	80.7	70.3	63.7	63.3	67.7	66	68	70	4	4	3	2	2	2	2	2	2	120	N
22	23	F	56	82	106	94	86	88	90	104	100	95	90	88	130	128	100	90	82	80	83	88	90	95	100	86	84	71	60	57	56	54	55	57	58	57	98	105	90	70	65.3	64	63.7	66	68	70.3	71.3	4	4	3	3	3	2	2	2	2	120	N
23	23	M	74	72	114	102	100	77	81	79	73	70	-	-	130	138	110	105	90	85	87	80	90	-	-	78	78	80	67	56	55	53	52	58	-	-	96	96	99	79.7	67.3	65	64.3	61.3	68.7	-	-	5	4	3	3	2	2	2	-	-	100	N
24	21	M	60	80	104	98	98	90	82	78	75	83	-	-	128	124	104	100	90	88	85	89	90	-	-	72	72	78	67	65	55	56	59	60	-	-	90	92	93	78	73.3	66	65.7	69	70	-	-	4	3	2	2	2	2	2	-	-	95	N
25	52	F	43	78	112	94	88	77	70	69	72	78	-	-	130	128	105	100	85	84	80	84	90	-	-	72	95	89	62	55	52	53	57	55	-	-	90	108	98	74.7	65	56	62	66	66.7	-	-	4	4	3	3	3	2	2	-	-	95	N
26	58	F	48	106	118	108	106	89	83	87	82	84	88	104	128	128	107	94	87	83	81	90	95	100	102	84	84	80	62	57	58	52	54	56	54	57	99	105	93	72.7	67	66.3	61.7	66	67.7	69.3	72	4	3	2	2	2	2	2	2	2	120	N
27	30	F	56	86	108	106	99	90	88	86	87	83	88	94	119	128	101	97	85	82	87	85	88	90	95	79	92	78	60	55	52	58	56	55	53	58	92	110	94	72.3	65	62	67.7	65.7	66	65.3	70.3	4	3	2	2	2	2	2	2	2	120	N
28	24	F	63	96	102	88	85	85	82	78	79	77	73	-	132	126	102	91	85	80	82	86	90	95	-	90	90	82	63	56	55	58	52	53	57	-	105	105	96	72.3	65.7	63.3	66	63.3	65.3	69.7	-	3	3	2	1	1	1	1	1	-	110	N
29	25	M	70	94	116	98	95	90	85	95	90	93	95	-	130	120	103	95	87	87	81	85	88	90	-	80	80	70	62	55	57	55	57	56	55	-	96	95	86	73	65.7	67	63.7	66.3	66.7	66.7	-	3	3	2	2	2	2	2	2	-	115	N
30	28	F	54	92	114	86	88	86	86	82	88	73	-	-	140	128	105	90	84	87	80	82	88	-	-	78	84	72	60	54	53	57	52	57	-	-	94	105	92	70	64	64.3	64.7	62	67.3	-	-	4	3	2	2	2	2	2	-	-	100	N
31	28	M	67	90	99	90	88	94	87	83	82	87	-	-	126	123	104	92	85	86	88	90	92	-	-	86	94	80	63	55	54	56	53	52	-	-	100	108	94	72.7	65	64.7	66.7	65.3	65.3	-	-	5	4	3	2	2	2	2	-	-	90	N
32	24	M	69	68	96	90	82	80	84	87	80	84	86	76	110	118	106	92	83	80	82	84	87	91	96	70	89	80	67	58	55	52	51	57	59	60	87	106	90	75.3	66.3	63.3	62	62	66	69.7	72	5	4	3	2	2	2	2	2	2	120	N
33	26	M	65	90	99	90	88	88	84	87	82	83	85	-	126	123	104	100	90	85	80	85	86	90	-	86	94	70	65	60	55	58	57	58	62	-	100	108	94	76.7	70	65	65	66	67	71	-	4	3	2	2	2	2	2	2	-	110	N
34	28	F	53	86	116	86	85	90	94	94	85	80	-	-	126	130	101	89	83	84	83	85	90	-	-	70	96	88	64	57	58	56	53	55	-	-	89	111	102	72.3	65.7	66.7	65	63.7	66.7	-	-	3	3	2	2	2	2	2	-	-	90	N
35	55	F	48	106	118	108	106	89	83	87	82	84	88	104	128	128	107	94	87	83	81	90	95	100	102	84	84	80	62	57	58	52	54	56	54	57	99	105	93	72.7	67	66.3	61.7	66	67.7	69.3	72	4	3	2	2	2	2	2	2	2	120	N
36	45	M	72	92	114	86	84	80	83	90	87	81	85	90	128	128	105	103	92	85	87	80	88	86	90	78	84	65	66	67	58	55	58	55	59	60	94	105	92	78.3	75	67	65.7	65.3	66	68	70	4	3	2	2	2	2	2	2	2	120	N
37	25	F	60	80	129	122	115	108	100	95	106	110	99	-	124	131	101	91	82	81	83	85	90	95	-	74	81	80	64	57	53	58	55	57	55	-	92	103	97	73	65.3	62.3	66.3	65	68	65	-	3	3	2	2	2	2	2	2	-	115	N
38	49	M	75	70	98	99	92	87	88	84	80	79	77	76	128	128	104	93	84	82	80	84	88	90	91	76	84	72	63	55	54	54	56	54	57	58	91	105	92	73	64.7	63.3	62.7	65.3	64	67.3	68.7	4	3	2	2	2	2	2	2	2	120	N
39	42	M	68	80	106	88	83	89	94	84	87	83	80	-	128	132	102	91	85	87	88	82	86	90	-	70	78	73	63	58	57	55	57	56	59	-	89	96	96	72.3	67	67	66	65.3	66	69.3	-	3	3	2	2	2	2	2	2	-	115	N
40	45	M	59	71	108	88	82	86	90	105	93	87	80	-	124	130	103	91	87	84	80	82	85	89	-	70	94	102	64	56	55	53	57	55	59	-	83	94	111	73	66.3	64.7	62	65.3	65	69	-	4	3	2	2	2	2	2	2	-	110	N

ESMOLOL (ESM) GROUP

SERIAL NUMBER	AGE IN YEARS	GENDER	WEIGHT IN KG	HEART RATE (Beats per minute)											SYSTOLIC BLOOD PRESSURE (mm Hg)											DIASTOLIC BLOOD PRESSURE (mm Hg)											MEAN ARTERIAL BLOOD PRESSURE (mm Hg)											AVERAGE CATEGORY SCALE (Fromme)									SURGICAL DURATION (min)	COMPLICATIONS (Y/N)
					ESMOLOL INFUSION @ 100-300 mcg/kg/min											ESMOLOL INFUSION @ 100-300 mcg/kg/min											ESMOLOL INFUSION @ 100-300 mcg/kg/min											ESMOLOL INFUSION @ 100-300 mcg/kg/min										ESM INFUSION @ 100-300 mcg/kg/min										
				BASAL	5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes	BASAL	5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes	BASAL	5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes	BASAL	5 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes	10 minutes	15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes		
1	45	F	56	90	86	85	78	68	63	67	69	-	-	-	120	125	116	109	94	92	97	91	-	-	-	85	88	72	65	63	64	66	68	-	-	-	97	100	86.7	79.7	73.3	73.3	76.3	75.7	-	-	-	4	3	2	2	2	2	-	-	-	90	N
2	24	M	67	79	76	70	74	73	70	67	63	-	-	-	113	121	115	107	94	95	93	94	-	-	-	78	80	73	66	64	65	66	67	-	-	-	90	94	87	79.7	74	75	75	76	-	-	-	2	2	2	1	1	1	-	-	-	90	N
3	35	F	53	72	80	76	70	65	66	66	65	70	-	-	131	129	116	98	94	96	92	96	94	-	-	65	75	68	65	64	63	66	67	-	-	-	87	93	84	76	74	74	74.7	76.7	-	-	-	3	2	2	2	2	2	-	-	-	95	N
4	29	F	56	69	76	70	65	63	67	70	63	78	83	-	136	134	120	97	95	93	98	95	96	97	-	78	80	72	65	63	64	65	66	67	68	-	97	98	88	75.7	73.7	73.6	76	75.7	76.7	77.6	-	3	2	2	2	2	2	2	2	-	100	N
5	58	F	47	77	79	75	70	67	66	62	67	70	-	-	129	133	120	100	98	95	92	90	92	-	-	81	85	73	66	65	63	67	68	-	-	-	97	101	88.7	77.3	76	73.7	75.3	75.3	-	-	-	3	2	2	2	2	2	-	-	-	90	N
6	60	M	55	86	85	78	70	65	62	67	66	68	74	-	109	113	109	94	96	92	95	92	95	94	-	78	82	71	67	64	65	63	67	68	69	-	88	92	83.7	76	74.7	74	73.7	75.3	77	77.3	-	3	2	2	2	2	2	2	2	-	110	N
7	56	M	58	88	80	77	70	67	66	65	60	-	-	-	110	118	110	100	98	96	93	95	-	-	-	75	82	77	72	66	63	66	65	-	-	-	87	94	88	81.3	76.7	74	75	75	-	-	-	2	2	2	1	1	1	1	-	-	100	N
8	35	F	47	77	79	75	70	67	66	62	67	70	-	-	129	133	120	100	98	95	92	90	90	-	-	65	75	68	65	64	63	66	67	-	-	-	87	93	84	76	74	74	74.7	76.7	-	-	-	3	2	2	2	2	2	-	-	-	95	N
9	40	F	54	97	89	78	77	73	78	74	70	-	-	-	118	120	112	96	91	97	93	96	-	-	-	80	83	75	64	66	65	68	69	-	-	-	93	95	87.3	74.7	74.3	75.7	76.3	78	-	-	-	2	2	2	1	1	1	-	-	-	90	N
10	19	F	56	103	100	80	76	70	77	75	80	-	-	-	119	122	118	103	96	94	91	95	-	-	-	78	83	78	75	65	64	67	63	-	-	-	91	97	91.3	84.3	75.3	74	75	73.7	-	-	-	3	2	2	2	2	2	-	-	-	90	N
11	25	M	75	77	76	69	65	63	67	62	68	62	74	-	124	125	118	106	93	90	91	94	93	96	-	67	69	65	64	63	62	64	63	65	67	-	86	88	82.7	78	73	71.3	73	73.3	74.3	76.7	-	3	3	2	2	2	2	2	2	-	110	N
12	24	M	71	75	76	70	66	68	65	60	62	69	77	-	112	118	110	103	96	90	94	92	93	99	-	84	81	75	70	65	63	66	68	69	70	-	93	93	86.7	81	75.3	72	75.3	76	77	79.7	-	3	3	2	2	2	2	2	2	-	110	N
13	55	M	74	87	85	78	68	65	63	60	63	-	-	-	114	124	117	103	96	88	93	92	-	-	-	85	89	74	68	67	65	64	66	-	-	-	95	101	88.3	79.7	76.7	2.7	73.7	74.7	-	-	-	3	3	2	2	2	2	-	-	-	90	N
14	18	M	60	74	76	70	67	63	65	68	70	-	-	-	113	118	105	95	93	97	91	96	-	-	-	78	80	73	65	66	67	65	68	-	-	-	90	93	83.7	75	75	77	73.7	77.3	-	-	-	4	3	2	2	2	2	-	-	-	90	N
15	50	M	73	78	80	76	65	64	63	63	67	-	-	-	112	110	108	101	95	92	98	94	-	-	-	77	83	72	69	64	66	67	69	-	-	-	89	92	84	79.7	74.3	74.7	77.3	77.3	-	-	-	4	3	2	2	2	2	2	-	-	90	N
16	60	M	57	92	85	80	77	76	68	65	64	76	-	-	125	130	117	95	97	92	95	94	90	-	-	80	87	72	64	61	66	67	64	-	-	-	95	101	87	74.3	73	74.7	76.3	74	-	-	-	2	2	2	1	1	0	-	-	-	95	N
17	18	F	45	76	76	70	75	67	64	68	63	-	-	-	123	130	121	96	92	97	91	96	-	-	-	84	86	73	66	65	63	67	64	-	-	-	97	101	89	76	74	74.3	75	74.7	-	-	-	2	2	2	2	2	2	-	-	-	90	N
18	22	F	46	88	80	75	77	67	60	64	62	-	-	-	125	130	118	96	94	95	92	97	-	-	-	88	88	71	67	65	64	62	66	-	-	-	100	102	86.7	76.7	74.7	74.3	72	76.3	-	-	-	3	2	2	2	2	2	-	-	-	90	N
19	18	M	62	66	62	60	63	62	67	66	63	-	-	-	121	126	108	91	97	92	94	92	-	-	-	81	84	74	66	63	65	67	64	-	-	-	94	98	85.3	74.3	74.3	76	74	73.3	-	-	-	3	2	2	2	2	2	-	-	-	90	N
20	18	M	67	72	78	74	70	65	62	60	62	-	-	-	129	133	120	107	98	94	96	93	-	-	-	78	82	73	71	63	65	67	69	-	-	-	95	99	88.7	83	74.7	74.7	76.7	77	-	-	-	3	3	2	2	2	2	2	-	-	100	N
21	38	M	67	80	85	75	70	66	68	64	65	-	-	-	121	125	118	102	97	92	96	97	-	-	-	82	86	82	76	67	63	68	64	-	-	-	95	99	94	84.7	77	72.7	77.3	75	-	-	-	2	2	2	1	1	0	-	-	-	95	N
22	20	M	63	92	85	76	70	66	65	63	60	70	76	80	128	135	120	102	97	93	95	96	92	97	96	77	80	76	74	68	65	66	63	67	69	70	92	98	90.7	83.3	77.7	74.3	75.7	74	75.3	78.3	78.7	3	2	2	2	2	2	2	2	2	120	N
23	27	F	62	79	80	85	78	75	70	64	63	68	73	-	119	120	105	94	91	97	96	94	97	99	-	79	81	73	66	65	63	64	65	76	68	-	92	94	83.7	75.3	73.7	74.7	74.7	76.3	78.3	79	-	3	2	2	2	2	2	2	2	-	110	N
24	22	M	70	88	80	75	70	66	64	63	63	-	-	-	115	122	117	105	92	94	97	93	-	-	-	78	84	73	70	63	65	64	66	-	-	-	90	97	87.7	81.7	72.7	74.7	75	75	-	-	-	3	3	2	2	2	2	2	-	-	100	N
25	27	M	69	102	100	80	80	87	85	82	79	-	-	-	114	120	115	107	97	94	92	93	-	-	-	80	76	65	73	64	66	65	64	-	-	-	91	91	81	84.3	75	75.3	74	73.7	-	-	-	4	3	2	2	2	2	2	-	-	100	N
26	19	F	56	90	86	85	78	68	63	67	69	-	-	-	120	125	116	109	94	92	97	91	-	-	-	85	89	74	68	67	65	64	66	-	-	-	95	101	88.3	79.7	76.7	2.7	73.7	74.7	-	-	-	4	3	2	2	2	2	-	-	-	90	N
27	55	F	54	97	89	78	77	73	78	74	70	-	-	-	118	120	112	96	91	97	93	96	-	-	-	80	83	75	64	66	65	68	69	-	-	-	93	95	87.3	74.7	74.3	75.7	76.3	78	-	-	-	2	2	2	1	1	1	-	-	-	90	N
28	22	F	56	103	100	80	76	70	77	75	80	-	-	-	119	122	118	103	96	94	91	95	-	-	-	78	83	78	75	65	64	67	63	-	-	-	91	97	91.3	84.3	75.3	74	75	73.7	-	-	-	3	2	2	2	2	2	-	-	-	90	N
29	28	F	67	70	78	76	70	75	79	66	64	-	-	-	122	126	113	106	96	95	94	92	-	-	-	70	74	66	71	66	61	63	65	-	-	-	87	91	81.7	82.7	76	72.3	73.3	74	-	-	-	3	3	2	2	2	2	2	-	-	90	N
30	24	M	68	92	87	76	75	78	70	77	65	78	82	90	134	133	121	108	94	93	95	97	100	102	107	89	87	74	70	65	63	67	64	67	68	70	104	102	89.7	82.7	74.7	73	76.3	75	78	79.3	82.3	2	3	2	1	1	0	0	0	0	120	N
31	19	F	46	88	80	75	77	67	60	64	62	-	-	-	125	130	118	96	94	95	92	97	-	-	-	88	88	71	67	65	64	62	66	-	-	-	100	102	86.7	76.7	74.7	74.3	72	76.3	-	-	-	3	2	2	2	2	2	-	-	-	90	N
32	52	F	47	77	79	75	70	67	66	62	67	70	-	-	129	133	120	100	98	95	92	90	90	-	-	81	85	73	66	65	63	67	68	-	-	-	97	101	88.7	77.3	76	73.7	75.3	75.3	-	-	-	3	2	2	2	2	2	-	-	-	90	N
33	46	M	65	90	90	77	76	75	70	66	70	-	-	-	124	126	120	104	95	94	97	95	-	-	-	80	82	80	75	65	64	66	63	-	-	-	95	97	93.3	84.7	75	74	76.3	73.7	-	-	-	3	2	2	2	2	2	-	-	-	90	N
34	20	F	56	69	76	70	65	63	67	70	63	78	83	-	136	134	120	97	95	93	98	95	96	97	-	78	80	72	65	63	64	65	66	67	68	-	97	98	88	75.7	73.7	73.6	76	75.7	76.7	77.6	-	3	2	2	2	2	2	2	2	-	100	N
35	19	F	45	76	76	70	75	67	64	68	63	-	-	-	123	130	121	96	92	97	91	96	-	-	-	84	86	73	66	65	63	67	64	-	-	-	97	101	89	76	74	74.3	75	74.7	-	-	-	2	2	2	2	2	2	-	-	-	90	N
36	20	M	73	88	80	75	70	67	60	63	67	-	-	-	108	113	104	92	94	95	92	93	-	-	-	78	82	73	65	67	66	65	67	-	-	-	88	92	83.3	74	76	75.7	74	75.7	-	-	-	3	2	2	1	1	1	-	-	-	90	N
37	18	M	66	69	80	76	70	65	66	68	63	-	-	-	130	138	129	109	97	93	90	95	-	-	-	85	85	74	72	63	64	65	68	-	-	-	100	100	92.3	84.3	74.3	73.7	73.3	77	-	-	-	3	3	2	2	2	2	2	-	-	90	N
38	27	M	57	92	85	80	77	76	68	65	64	76	-	-	125	130	117	95	97	92	95	94	92	-	-	80	87	72	64	61	66	67	64	-	-	-	95	101	87	74.3	73	74.7	76.3	74	-	-	-	2	2	2	1	1	0	-	-	-	95	N
39	57	M	55	86	85	78	70	65	62	67	66	68	74	-	109	113	109	94	96	92	95	92	95	94	-	78	82	71	67	64	65	63	67	68	69	-	88	92	83.7	76	74.7	74	73.7	75.3	77	77.3	-	3	2	2	2	2	2	2	2	-	110	N
40	18	M	72	64	70	65	63	60	64	66	67	62	-	-	117	122	118	96	94	95	93	95	90	-	-	78	85	75	68	66	64	65	66	-	-	-	91	97	89.3	77.3	75.3	74.3	74.3	75.7	-	-	-	2	2	2	1	1	0	-	-	-	95	N