Study Of The Effectiveness Of Oral Clonidine And Oral Pregabalin In Attenuating The Hemodynamic Pressor Response During Laryngoscopy And Tracheal Intubation

by

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ABBREVIATION

ASA	American Society of Anaesthesiologists
Bpm	Beats per minute
CO	Cardiac Output
CO_2	Carbon Dioxide
P	Pregabalin
C	Clonidine
CSF	Cerebrospinal fluid
ECG	Electrocardiography
$ETCO_2$	End Tidal Carbon Dioxide
mmHg	milli meter of Mercury
HR	Heart Rate
i.v.	Intravenous
kg	kilogram
MAP	Mean Arterial Pressure
mcg	microgram
Min	minute
ml	millilitre
mg/dl	milligram per decilitre
N_2O	Nitrous Oxide
NIBP	Non-Invasive Blood Pressure
O_2	Oxygen
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
RPP	Rate Pressure Product

SPO_2	Arterial Oxygen Saturation
MAP	Mean arterial pressure
CVS	Cardiovascular system
RS	Respiratory system
CNS	Central nervous system
P/A	Per abdomen
ECG	Electrocardiogram
I.P. No.	Inpatient number
Inj	Injection

ABSTRACT

Background and objectives:

Laryngoscopy is a noxious and most invasive stimulus before endotracheal intubation.Manipulation of the respiratory tract such as during laryngoscopy and endotracheal intubation are associated with cardiovascular responses consisting of increased circulating catecholamines, raised heart rate and blood pressure, increased myocardial oxygen demand, and possible dysrhythmias. This study was carried out to compare the effect of oral Clonidine and oral Pregabalin premedication with respect to hemodynamic variables like HR, SBP, DBP, MAP and RPP in attenuating the hemodynamic stress response following laryngoscopy and endotracheal intubation.

Methods:

A prospective, randomized study was conducted on 90 adult consented patients aged 18 to 60 yrs with ASA I or II of either sex scheduled to undergo elective general surgical procedures under general anaesthesia, were randomized to receive Clonidine (300mcg) Group C, Pregabalin (75mg) Group P given 120 minutes before surgery as oral premedication. Anaesthetic technique was standardized and both groups were compared for the haemodynamic changes before study drug, after study drug administration at 30min, 60min, 90min, before induction, after laryngoscopy and intubation at 1min, 5min, 10min and 15min.

Results:

In this study, it was observed that Clonidine was found to be better than Pregabalin in lowering of systolic blood pressure, diastolic blood pressure, mean arterial pressure,rate pressure rate and heart rate changes associated with laryngoscopy and intubation. None of the premedicated patient has suffered from any postoperative side effects

Conclusion:.

Oral premedication with Clonidine 300µg was superior to Pregabalin 75mg resulting in hemodynamic stability during laryngoscopy and endotracheal intubation.

Keywords:

hemodynamic pressor response, laryngoscopy, intubation, clonidine, pregabalin

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INTRODUCTION

Laryngoscopy is a noxious and most invasive stimulus before endotracheal intubation[1]. Manipulation of the respiratory tract such as during laryngoscopy and endotracheal intubation are associated with cardiovascular responses consisting of increased circulating catecholamines, raised heart rate and blood pressure, increased myocardial oxygen demand, and possible dysrhythmias[2]. Rate pressure product is a measure of the stress put on the cardiac muscle based on the number of times it needs to beat per minute (Heart rate) and the arterial blood pressure that it is pumping against(Systolic blood pressure). It allows us to calculate the internal workload or hemodynamic stress.

The magnitude of the response is greater with increasing force and time of laryngoscopy. In patients with cardio-vascular and cerebral diseases these transient responses can result in morbidity and mortality from tachycardia and hypertension. Many preanaesthetic medications have been tried to attenuate the hemodynamic response.

Various methods used to attenuate pressor response are providing sufficient depth of anesthesia, keeping duration of laryngoscopy less than 15 seconds, use of vasodilators e.g. Nitrogycerine[3], Sodium nitroprusside, calcium channel blockers e.g. Diltiazem[4], local anesthetics like Lignocaine[5] (topical spray or intravenously[6]), opioids like Fentanyl[7], Remifentanil[8], beta blockers like Esmolol[9], Metoprolol[10].

Every method used to obtund the pressor response has its advantages and disadvantages.Deep planes of anaesthesia can be achieved by using additional doses of i.v induction agent, inhalational agents or narcotics. However, deep planes could prove hazardous in patients with myocardial ischemia and hypertension due to in advertent hypotension and myocardial depression.

Vasodilators and calcium channel blockers used can cause associated rise in heart rate that can be uncontrollable.

Esmolol (beta - blocker) possesses several properties to suggest that it might be valuable in obtunding responses to laryngoscopy and intubation. First,it is highly cardioselective, thus doing away with undesirable side effects of beta blockage eg:bronchospasm.Second,it is rapidly metabolized, thus having a short duration of action and rapid onset of action.

Clonidine is an imidazoline derivative directly acting α2 adrenoreceptor agonist. It has an antihypertensive effect and blunts catecholamine release and thus attenuate pressor response following laryngoscopy and tracheal intubation[11].

Pregabalin is structurally described as (s)-3 amino methyl-5-methylhexanoic acid, a compound of gabapentinoids. It functions by reducing the neurotransmitter glutamate synthesis to act on the central nervous system.It has analgesic, anticonvulsant and anxiolytic activity and is efficient in inhibiting the neuropathic element of acute nociceptive surgical pain.

In this study the efficacy of oral Clonidine and oral Pregabalin in attenuating hemodynamic pressor reponse to direct laryngoscopy and tracheal intubation has been compared with each other.

AIMS AND OBJECTIVES

AIMS:

To study and compare the effect of oral Clonidine and oral Pregabalin in attenuating the hemodynamic pressor response during laryngoscopy and tracheal intubation.

OBJECTIVES:

To study and compare the effect of oral Clonidine and oral Pregabalin with respect to following parameters:

a) Heart rate(HR)

b) Systolic blood pressure(SBP)

c) Diastolic blood pressure(DBP)

d) Mean arterial pressure(MAP)

e) Rate pressure product(RPP)

REVIEW OF LITERATURE

Burstein, LoPinto and Newman[12] studied the effect of laryngoscopy and intubation on electrocardiogram in 109 patients.There were transient ECG changes in 68% of cases.There was sinus bradycardia in 4 patients, sinus tachycardia in 43 patients, atrial fibrillation in 1 patient and ventricular tachycardia in 2 patients at the time of intubation. This was irrespective of the type of anesthesia used. Inadequate anaesthesia, prolonged laryngoscopy, multiple attempts at intubation enhanced the development of arrhythmias.

King et al[13] studied the reflex circulatory responses to direct laryngoscopy and intubation.They found that laryngoscopy and intubation invariably caused increase in heart rate and blood pressure and these responses were abolished by deep ether anaesthesia.

Stoelting[5,6] demonstrated the influence of duration of laryngoscopy on the severity of the pressor response. It was demonstrated that a short duration laryngoscopy (ideally less than 15 seconds) combined with laryngotracheal lignocaine just before intubation is an effective method to attenuate the mean arterial pressure increases during intubation.

GhignoneM, **QuintinL et al**[7] studied "Effects of Clonidine on narcotic requirements and hemodynamic response during induction of Fentanyl anesthesia and endotracheal intubation". Twenty-four patients undergoing aortocoronary bypass surgery (ACBS) with a history of arterial hypertension, coronary artery disease (NYHA class 3-4) and well-preserved left ventricular function were assigned randomly to either Group 1 (n=12), who received standard pre-medication , or Group 2 (n= 12), who received Clonidine 5mcg / kg orally in addition to standard premedication 90 min before estimated induction time. It was concluded that at a

similar anaesthetic depth, as assessed by the EEG shift into the lower frequency range (0.5-3Hz), a markedly reduced Fentanyl dose effectively prevented the hyperdynamic cardiovascular response to laryngoscopy and intubation in the group of patients premedicated with Clonidine. This is likely explained by the known synergistic inhibitory action of opiates and α2 adrenoceptor agonists on central sympathetic outflow.

Charles E.Laurito et al[14] studied the effectiveness of oral Clonidine as sedative / anxiolytic drug to blunt the hemodynamic responses to laryngocopy in a double-blinded randomized assignment for one of four treatment groups(Clonidine0.1mg, Clonidine0.2mg, triazolam0.25mg or placebo). Results showed that triazolam and both Clonidine doses improved sedation at 90 min compared to a placebo. Clonidine 0.2mg reduced anxiety at 90 min but not more than a placebo.Clonidine 0.2mg reduced systolic, mean and diastolic blood pressures at 90min but not heart rate. Clonidine 0.2mg also blunted the rise in systolic blood pressure but not in diastolic blood pressure or heart rate that accompanied laryngoscopy.There were no variations in therapy for postanaesthetic hemodynamics or duration of recovery. It was concluded that oral Clonidine 0.2mg was efficient in preopearatively decreasing the level of behavioral and hemodynamic reactions and in suppressing the systolic hypertension produced by prolonged laryngoscopy.

Kumkum Gupta et al[15] conducted a randomized prospective study on Pregabalin premedication- A new treatment option for hemodynamic stability during general anaesthesia." 80 patients of ASA I and II aged between 24 to 54 years undergoing surgeries under general anaesthesia were randomized to receive oral Pregabalin 150mg and other group with placebo capsule. Both the group were assessed for preoperative sedation and changes in heart rate and mean arterial blood

pressure before and after induction and after intubation. Preoperative sedation was higher with Pregabalin with no significant change in heart rate. Hence author concluded that oral Pregabalin premedication effectively leads to sedation and analgesia with successful attenuation of adverse and deleterious hemodynamic pressor response.

Gupta K, Sharma D, Gupta PK [16] in their study "Oral premedication with Pregabalin or Clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: A comparative evaluation" a total of 80 ASA I and II patients , aged between 20-60 years of both sexes for elective laparoscopic cholecystectomy were planned. All the patients were divided into two groups randomly. Group A received 0.3mg oral Clonidine and group B received 150mg oral Pregabalin, 60 minutes prior to the operation. Results showed that for laryngoscopy and tracheal intubation ,oral Clonidine 0.3mg and oral Pregabalin 150mg were effective in blunting haemodynamic stress reaction. In reducing systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate, Clonidine was found to be better than Pregabalin. They concluded that both the drugs can be used as an efficient premedicant to attenuate the sympathetic reaction to laryngoscopy and tracheal intubation without significant side effects and the added benefit of intraoperative and postoperative analgesia.

Rastogi Bhawna et al[17] conducted a randomized controlled study on "oral Pregabalin premedication for attenuation of hemodynamic pressor response of airway instrumentation during general anaesthesia." A total of 90 normotensive ASA grade 1 and 2 adult patients aged 24-56yrs of both sexes were planned for elective surgery under general anaesthesia and were randomly allocated into 3 groups of 30 patients. Group 1 received placebo, group 2 received Pregabalin 75mg and group 3 received

Pregabalin 150mg. Preoperative sedation level was assessed by the Ramsay sedation scale. Intraoperative heart rate, blood pressure were monitored before and after induction and immediately after intubation. In the 150mg Pregabalin group, Sedation was considerably greater. The heart rate increased in all groups immediately after laryngoscopy and intubation but was lowest in group 3. Intraoperatively, bolus doses of fentanyl were added to the control group where as no analgesic supplement was required for the Pregabalin group. There were no indications of any effects caused by drugs such as nausea, vomiting, any respiratory inadequacy or hemodynamic instability in the postanesthesia care unit. Accordingly, the author concluded that the attenuation of mean arterial blood pressure in the premedicated group was statistically significant as compared to control group, and that in group 3, 150mg oral Pregabalin was better received.

AyyaSyamaSundar et al[18] conducted a randomized double blind prospective study on "The effect of preemptive Pregabalin on attenuation of stress response to endotracheal intubation and opioid sparing effect in patients undergoing off-pump coronary artery bypass grafting". The study was comparison between 2 groups of 30 patients scheduled for elective off pump coronary artery bypass (OPCAB) surgery under general anaesthesia. In the control group, the patient were given placebo and in Pregabalin group with 150mg Pregabalin orally lhr before surgery. The patients were compared for hemodynamic changes after induction and after intubation. Study showed that a single oral dose of 150mg Pregabalin given attenuated the pressor response to tracheal intubation. Hence author concluded that Pregabalin suppresses reflex tachycardia and hypertension related to laryngoscopy and intubation of trachea in patient coming for elective OPCAB grafting and does not produce dizziness and visual disturbance.

Archana Raichurkar et al[19] conducted a randomized prospective study on "A Comparative Study of Oral Pregabalin and Clonidine for Attenuation of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation" Sixty patients of ASA Grade I or II and aged between 18-60 years, of either sex, who were posted for elective surgeries under general anaesthesia were selected. The patients were randomly divided into 2 groups of 30 each where Group C received 200mcg Clonidine and group P 150mg Pregabalin 90 mins before surgery. After three mins of preoxygenation with 100% oxygen, pre-medication given was 5mg/kg of IV Ivcopyrolate and 2.5mg/ kg IV Fentanyl was given for analgesia. Patients were induced with IV Thiopentone 5mg/kg followed by IV Suxamethonium 2mg/kg for intubation. Anaesthesia was maintained with Nitrous Oxide, Oxygen and Isoflu-rane. Muscle relaxation was achieved with IV Vecuronium 0.1mg/kg (loading dose) and 0.02mg/kg for maintenance dose. During laryngoscopy and endotracheal intubation the heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were recorded at 0,1,3,5 and 10 mins. Statistical difference between the two groups were analyzed using student's 't' test. Results showed attenuation of increase in BP was better in group P and sedation was more commonly obtained in Group P which were statistically significant. They concluded that both Pregabalin and Clonidine successfully attenuated the hemodynamic response to laryngoscopy and tracheal intubation. Pregabalin better attenuates pressor response.

Khan AA, Gani S, Munshi FA, Saleem B, Hameed S, Rather MA[20] in their study " A comparative trial studying the effectiveness of oral Clonidine and Pregabalin premedication in attenuation of haemodynamic response following laryngoscopy and endotracheal intubation" a total of 120 healthy adult individuals between ages 20to50 yrs with the American Society of Anesthesiologist (ASA)

physical status I were planned to undergo elective general surgical operations under general anaesthesia. Pateints were randomized for Clonidine (300µg) Group 1, Pregabalin (75mg) Group 2, or placebo Group 3, provided as oral premedication 120 minutes prior to surgery. The findings showed that oral Clonidine (300µg) provided 120 min before induction was efficient in attenuating the haemodynamic stress response to laryngoscopy and endotracheal intubation . Oral Pregabalin (75mg) administered 120 min prior to induction was not efficient in attenuating hemodynamic stress response to intubation, although it offered a moderate level of anxiolysis and minimal sedation relative to placebo. They concluded that, during laryngoscopy and endotracheal intubation, oral premedication with Clonidine 300µg was superior to Pregabalin 75mg leading to adequate sedation and pre-op anxiolysis along with hemodynamic stabilization without prolonging recovery time and side effects.

Chaudhary Asmita, Sanghvi Kinjal, Parikh Heena [21] in their study "Oral premedication with Pregabalin and Clonidine for hemodynamic stability during laryngoscopy: A comparative study" a total of 100 healthy patients aged 30-70 years with American Society of Anesthesiology Physical Status I and II of both gender, who met the inclusion criteria of general anaesthesia, randomly received Pregabalin (150 mg) Group I or Clonidine (100 µg) Group II, 60-70 mins before surgery as an oral premedication. The results showed that the incidence of hypotension and bradycardia were observed in 4% case in the Clonidine group. Pre-operative sedation level was higher in the Pregabalin group as compared to Clonidine group. $p>0.05$ which shows there is no difference in both the drugs in terms of control of HR and MAP perioperatively. They concluded that the hemodynamic pressure response of airway instrumentation was attenuated with Pregabalin and Clonidine oral premedication

without prolongation of recovery time and side effects.

Bahgat NM et al[22] in their study of "The effects of using Pregabalin versus Clonidine premedication in laparoscopic cholecystectomy" 60 adult patients aged 18-60 yrs with ASA physical status I of both sexes were posted for elective laparoscopic cholecystectomy and were randomized to receive Pregabalin 300 mg (group P), Clonidine 200 μg (group C), or placebo (group O), given 90 min before surgery as oral premedication. The results showed that perioperative sedation levels were higher with Pregabalin than with Clonidine, without prolongation of recovery time. Statistically significant attenuation of mean arterial pressure and heart rate to laryngoscopy was observed in the premedicated groups. This study shows that, during laparoscopic cholecystectomy , oral premedication with Pregabalin 300 mg or Clonidine 200mcg results in sedation and hemodynamic stabilization and a decrease in postoperative pain and analgesic use.

Parveen S, Negi DS, Kumar R, Bagwan MC[23] in their study of " Oral Clonidine vs Oral Pregabalin Premedication to Attenuate Pressor Response to Direct Laryngoscopy in Patients Undergoing Laparoscopic Cholecystectomy" A total of 80 ASA grade I and II patients, aged between 20-60 years of both sexes were scheduled for elective laparoscopic cholecystectomy. All the patients were randomly divided into two groups. Group A received 0.3mg of oral Clonidine and group B received 150mg of oral Pregabalin , 60 minutes prior to the surgery. The results showed that for laryngoscopy and tracheal intubation , both oral Clonidine 0.3mg as well as oral Pregabalin 150mg were efficient in blunting haemodynamic stress response . In reducing systolic blood pressure, diastolic blood pressure , mean arterial pressure and heart changes connected with laryngoscopy ,Clonidine was found to be effective than Pregabalin. They concluded that both the drugs can be used as an

efficient premedicant to attenuate the sympathetic response to laryngoscopy and tracheal intubation without significant side effects and the added benefit of intraoperative and postoperative analgesia.

Waikar C, Singh J, Gupta D, Agrawal A[24] in their study "Comparative Study of Oral Gabapentin, Pregabalin, and Clonidine as Premedication for anxiolysis, sedation, and attenuation of pressor response to endotracheal intubation" 90 adult patients between 18 and 60 years were enrolled in the study. Patients with American Society of Anesthesiologists Grade-I and Grade-II are included which are posted for elective surgery under general anesthesia. Patients were divided into three groups: A, B, and C and received oral drugs 90 min before induction of general anesthesia, Pregabalin 150, gabapentin 900mg, and Clonidine 200 mcg, respectively. The results showed that mean arterial pressure was well attenuated by Pregabalin than others, and mean heart rate following laryngoscopy and intubation was attenuated by Clonidine group significantly. They concluded that oral Pregabalin and gabapentin attenuate blood pressure response fairly well and heart rate significantly attenuated by Clonidine. All three drugs are very effective for relieving anxiety and improving sedation.

ANATOMY OF LARYNX[25]

In adult humans, the larynx is found in the anterior neck at the level of the C3–C6 vertebrae. It connects the inferior part of the pharynx (hypopharynx) with the trachea. The laryngeal skeleton consists of nine cartilages: three single (epiglottis, thyroid and cricoid) and three paired (arytenoid, corniculate, and cuneiform).The hyoid bone is not part of the larynx, though it is connected to it. The larynx extends vertically from the tip of the epiglottis to the inferior border of the cricoids cartilage. Its interior can be divided into supraglottis, glottis and subglottis.

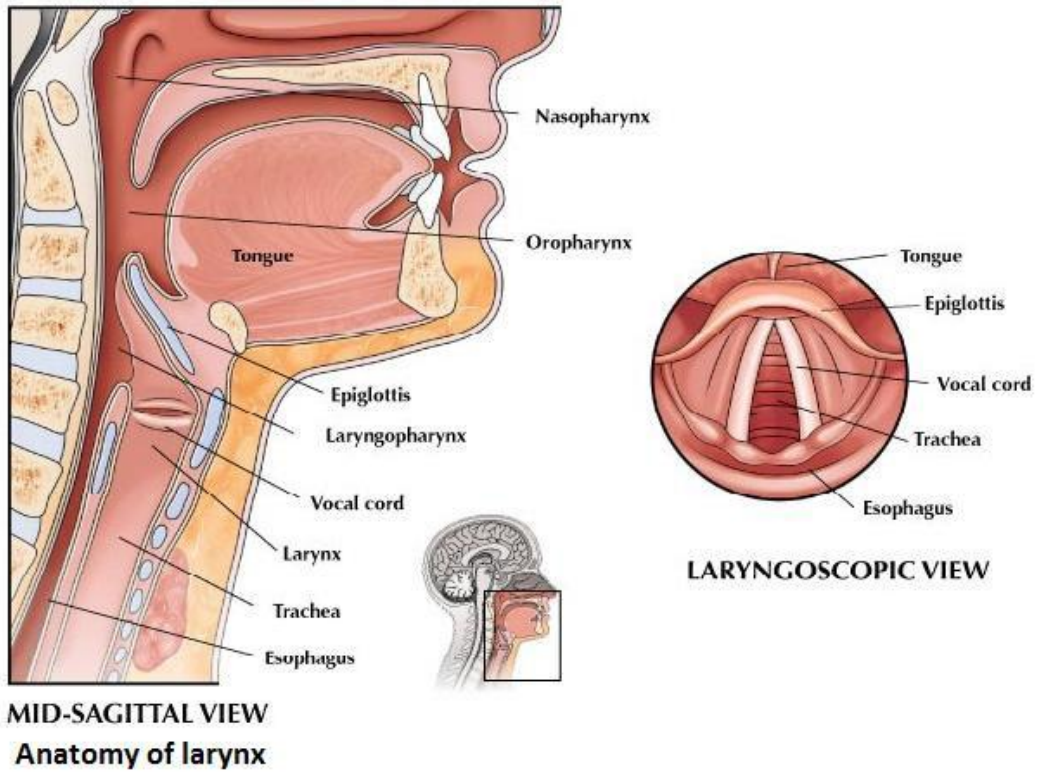

Fig no.1. Anatomy of Larynx

In newborn infants, the larynx is initially at the level of the C2–C3 vertebrae, and is further forward and higher relative to its position in the adult body.The larynx descends as the child grows.

Structure:

1. Cartilages

TABLE NO.1 CARTILAGES OF LARYNX

Single cartilages	Paired cartilages
Epiglottis	Arytenoid cartilages
Thyroid cartilage	Corniculate cartilages
Cricoid cartilage	Cuneiform cartilages

2. Joints: Cricothyroid joint Cricoarytenoid joints
3. Ligaments and membranes: Thyrohyoid membrane,Cricothyroid membrane, Cricotracheal membrane

Hyoid bone:

The hyoid bone is considered a lingual bone because the tongue musculature attaches to it.It also serves as an attachment for the larynx.

Thyroid cartilage:

This is the largest of the laryngeal cartilages.It is formed of two quadrangular laminae which fuse anteriorly forming a median projection called the laryngeal prominence (Adam's apple) which is more prominent in males than females.

Cricoid Cartilage:

This is smaller but thicker than the thyroid cartilage.It is the only cartilage that forms a complete ring in the larynx.

Epiglottis:

This is a thin leaf like lamella of elastic cartilage.It projects upwards behind the tongue and hyoid bone.

Arytenoid cartilages:

These are a pair of cartilage which lies on the upper border of the lamina of the cricoids cartilage.

Joints of the larynx:

Cricothyroid joints: between the inferior horn of the thyroid cartilage and the cricoids cartilage.

Cricoarytenoid joints: between the cricoid cartilage and the arytenoid cartilage.

Membranes and ligaments of the larynx:

Thyro-hyoid membrane:

This is a fibroelastic membrane connecting the upper border of the thyroid cartilage with the upper border of the posterior surface of the hyoid bone.

Crico-thyroid ligament:

This is an elastic band, which lies below and on the inner aspect of the thyroid cartilage. It is connected to the thyroid, cricoid and arytenoid cartilages.

Crico-tracheal ligament:

This is an elastic annular ligament, which connects the lower border of the cricoids cartilage with the first tracheal ring.

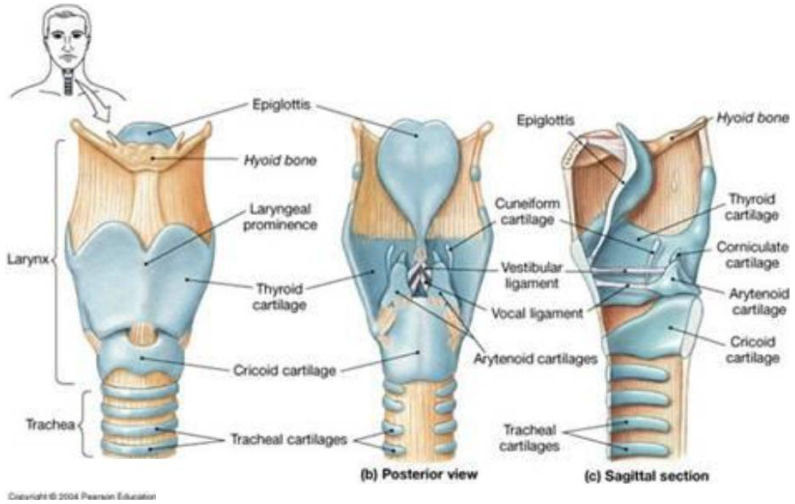

Fig.2. LARYNGEAL STRUCTURE

Interior of the larynx

The cavity of the larynx extends from the inlet to the lower border of the cricoids cartilage.

Inlet (aditus) of the larynx:

This is the opening through which the pharynx communicates with the larynx. It is directed backwards and upwards.It is bounded by:

- Anteriorly: epiglottis.
- Laterally: aryepiglottic folds
- Posteriorly: mucousmembrane between the arytenoids cartilages

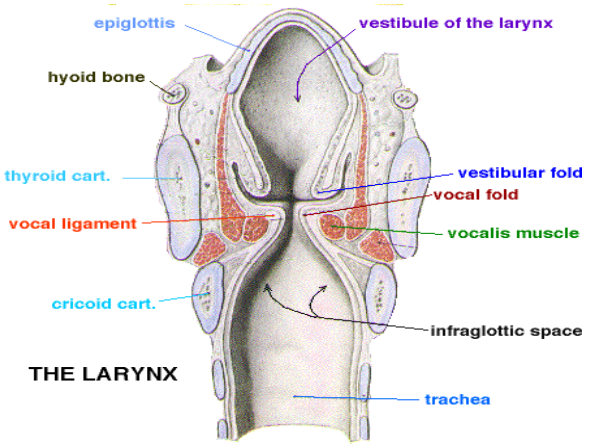

Fig no.3. INTERIOR OF LARYNX

Sidewall of the larynx:

Each side wall presents a pair of folds of mucous membrane.The upper one is called the vestibular fold and the lower one is called the vocal fold.

Vestibule of the larynx:

This is the part of the cavity between the inlet and the level of the vestibular folds.The vestibule is wider above and narrower below.

Vocal folds:

One on each side is a sharp and thin fold of mucous membrane,which stretches from the middle of the angle of the thyroid cartilage to the vocal process of the arytenoid cartilage.The fissure between the two vocal folds is called the rima glottides (theglottis), which is the narrowest part of the cavity.

Ventricle (sinus) of the larynx:

One on each side is a fusiform recess (cul-de-sac) between the vestibular and vocal folds.

Clinical subdivisions of the larynx:

Supraglottis: from the tip of the epiglottis to the junction between the respiratory and squamous epithelium on the floor of the ventricle.

Glottis: surrounded by the anterior commisure, the true vocal cords and the posterior commisure.

Subglottis: from the junction between the squamous and the respiratory epithelium on the undersurface of the true vocal cords to the inferior edge of the cricoid cartilage.

Muscles of the larynx:

The muscles of the larynx may be divided into extrinsic and intrinsic, which move the various cartilages of the larynx and regulate the mechanical properties of the vocal folds.

1- Extrinsic muscles**:**(Attach the larynx to the neighbouring structures and maintain the position of the larynx in the neck)

A- Suprahyoid muscles: attach the hyoid to the tongue and skull base

- Mylohyoid
- Geniohyoid
- Stylohyoid

- Stylopharyngeus
- Palatopharyngeus
- Salpingopharyngeus

B- Infrahyoid muscles: attach the hyoid bone to the larynx

- Thyrohyoid
- Sternothyroid
- Sternohyoid
- Omohyoid.

2- Intrinsic muscles**:** (Move laryngeal cartilages in relation to each other)

A. Adductors of the cords: Supplied by recurrent laryngeal nerve

- Lateral crico-arytenoid muscle
- Transverse arytenoid muscle
- Oblique arytenoid muscle

B. Abductors of the cords: Supplied by recurrent laryngeal nerve Posterior crico-arytenoid muscle (posticus)

C. Tensor of the cord: Supplied by the external laryngeal nerve Cricothyroid muscle.

Arterial supply of the larynx

- Superior laryngeal artery:It is a branch of the superior thyroid artery,derived from the external carotid artery. It pierces the thyro-hyoid membrane with the internal laryngeal nerve.
- Inferior laryngeal artery: It is a branch of the inferior thyroid artery,which originates from the thyrocervical trunk of the subclavian artery: It ascends deep to the lower border of the inferior constrictor muscle with the recurrent laryngeal nerve.

Venous drainage of the larynx:

- Superior laryngeal vein: Accompanies the superior laryngeal artery and eventually empties into the internal jugular vein.
- Inferior laryngeal vein**:** Accompanies the inferior laryngeal artery. It is a tributary of the thyrocervical trunk of the subclavian vein.

Nerve supply of the larynx:

- Superior laryngeal nerve: It is a branch of the vagus nerve.It has two terminal branches: External laryngeal nerve: Supplies the cricothyroid muscle.

  Internal laryngeal nerve: Supplies the upper part of the mucosa of the larynx to the level of the vocal folds.
- Recurrent laryngeal nerve: It is also a branch of the vagus nerve at the skull base. On the right side, it arises from thevagus, passes downwards to the root of the neck and recurs up around the first part of the subclavian artery. On the left side,it arises from the vagus, passes downwards to the thorax and then recurs up around the arch of the aorta just behind the ligamentum arteriosum.

  It has two branches: Motor branch: To all the intrinsic muscles of the larynx except cricothyroid muscle. Sensory branch: Supplies the mucosa of the larynx below the level of the vocal folds
- Glossopharyngeal nerve: It supplies the superior aspect of the epiglottis, posterior one third of the tongue and lower pharynx.

  The sensory impulses from the larynx ascend via internal and recurrent Laryngeal nerve to the nucleus of the tractus solitaries in the medulla.

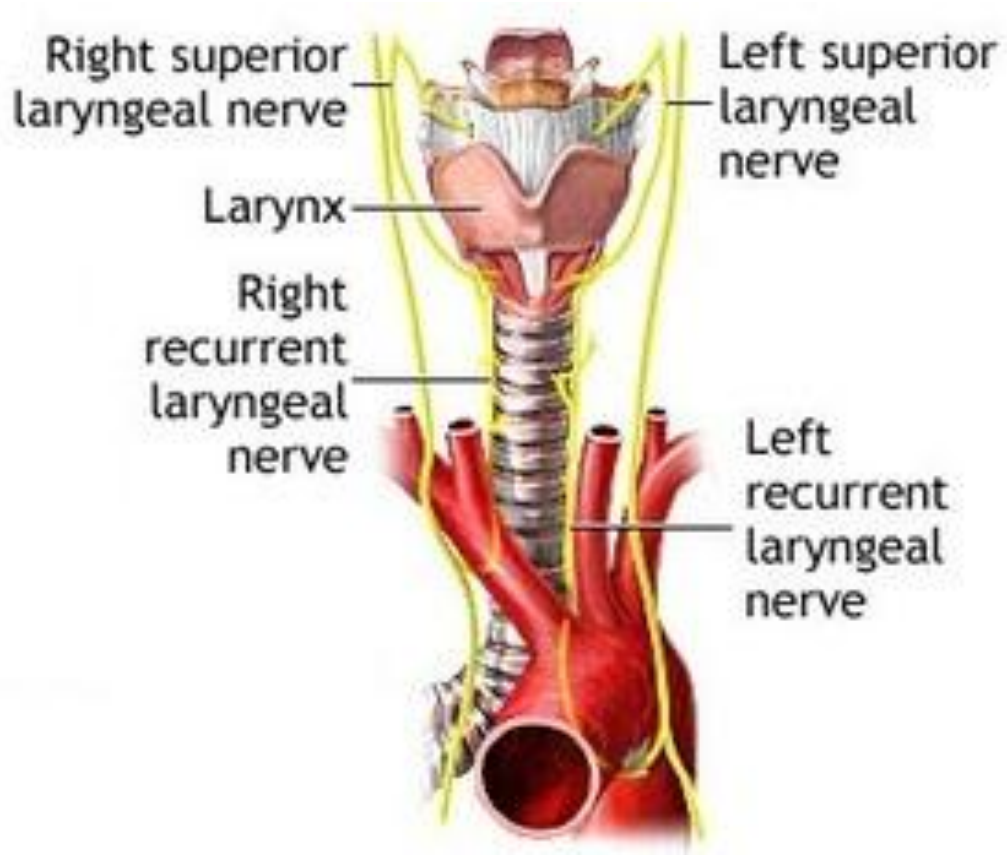

Fig no.4.Nerve supply of Larynx

Lymphatic drainage of the larynx:

The upper part of the larynx: Drains into the upper deep cervical nodes.

The lower part of the larynx: Drains into the lower deep cervical lymph nodes. Some vessels are interrupted in the infra-hyoid, pre-laryngeal and pre- tracheal lymphnodes. The vocal folds has minimal or no lymph drainage.

Function of the larynx:

1. **Protective:**

This is a vital function to prevent entrance of any substance into the air passages. Examples are:

a) Closure of the larynx during swallowing of food.

b) Closure of the larynx if any foreignbody reaches the pharynx. c)If a foreign body enters, it is expelled by the cough reflex.

2. **Respiratory**:

a) The larynx serves as an air channel.

b) The control of the width of the glottis regulates gas exchanges and carbon dioxide level in the blood.

3. Phonatory (sound production):

The air column from the chest causes vibration of the adducted vocal cords, there by producing a sound, which is articulated into speech.

4. **Circulatory:**

The alternating positive and negative intra-thoracic pressures help the blood circulation.

5. **Deglutitory:**

a) The constrictor muscles draw the larynx upward to grasp the bolus and force it downwards.

b) The shape of the epiglottis is to split the bolus or direct it into one or other pyriform fossa.

c) Closure of the larynx during swallowing.

6. **Tussive and expectorative:**

a) To try to expel inhaled foreign bodies.

b) To expel mucus or pus,the so-called“endogenous foreign bodies”.

PHYSIOLOGY OF HEMODYNAMIC RESPONSE

Autonomic nervous system is the biological house keeper of the internal milieu of the body. The adrenal medulla secretes around 0.2mcg/kg/minute adrenaline and 0.05mcg/kg/minute noradrenaline everyday.

The sympathetic nervous system plays an important role in flight and fight response. In stress, the hypothalamus stimulates the sympathetic nervous system, which in turn releases catecholamines leading to an increase in heart rate, blood pressure, cardiac output, bronchodilatation, shunting of blood away from skin, muscles to brain, heart and kidney.

Laryngoscopy and tracheal intubation are stressors stimulating inducing hypothalamic activity and causing sympathetic output leading to release of norepinephrine by post ganglionic sympathetic fibers and secretion from adrenal medulla[12].

The very first observation made by Reid and Brace[26] in 1940, was parasympathetic predominance manifestation as bradycardia. Later in 1950 Burstein et al[12] came to a conclusion that hypertension and tachycardia are manifestation of the sympathetic response. King et al[13] in 1951 suggested that they are due to a combined effect of both sympathetic and parasympathetic reflexes.

Various workers have measured the plasma catecholamine levels by using radioenzymatic assays and high pressure liquid chromatography.

W.J. Russell and R.G Mortis[27] studied changes in plasma catecholamine levels during laryngoscopy and intubation. The increases in arterial pressure were associated with increases in noradrenaline concentrations. Adrenaline and dopamine concentrations did not change significantly following intubation. The results suggest a predominantly sympathetic response during intubation.

The adrenergic response was maximum by one minute and had diminished by 5 min.

In adults the norepinephrine is released from terminals of adrenergic nerve and adrenaline from adrenal medulla, alongwith activation of renin angiotensin system through beta adrenergic fibres causes tachycardia and hypertension. In children bradycardia is seen commonly during laryngoscopy and intubation.

Laryngoscopy, Intubation and Cardiac Disease:

Laryngoscopy and intubation are stimuli of different intensity leading to different responses. Laryngoscopy alone, without intubation provides a supraglottic pressure stimulus causing increases in both systolic and diastolic pressures above the pre-induction control levels. Increases in heart rate are slight and are not significant due to laryngoscopy alone.

Intubation and placement of an endotracheal tube or a catheter in the trachea, stimulates infraglottic receptors and evokes an additional cardiovascular response with a further increase in catecholamines. The hemodynamic response is much greater, increasing by 36% from pre-induction control levels. The heart rate also significantly increases by about 20% with tracheal intubation, where as there is little rate response to laryngoscopy alone.[28,29]

Neuroendocrine response to endotracheal intubation leads to tachycardia and hypertension which causes a range of complications in hear disease patients.Myocardial ischemia in pateints with coronary artery insufficiency is the most common adverse cardiovascular issue related with intubation. Heart rate and blood pressure are the major determinants of rnyocardial oxygen demand. As endotracheal intubation causes marked increase in arterial pressure and heart rate, increase demand for myocardial oxygen must be encountered through increased supply of oxygenated

blood through coronary circulation. In individuals with coronary artery disease, the ability to meet an increase in myocardial oxygen demand is limited. Any abrupt rise in myocardial demand leads to ischemia of the tissue causing myocardial dysfunction and infarction.

In addition, arterial hypertension-induced ischemia may be compounded by increased left ventricular end-diastolic pressure resulting in further subendocardial tissue compromise of perfusion. These events are responsible in patients with atherosclerosis for episodes of ST segment depression in ECG and increased diastolic pressure of the pulmonary artery. These episodes ocassionally predispose to perioperative myocardial infarction.

During endotracheal intubation, patients with vascular anomalies that cause weakening of lining of major arteries are at risk. The integrity of cerebral and aortic aneurysms depends largely on transmural pressure; a sudden increase in blood pressure can lead to rupture of vessel and abrupt deterioration of patient's status. This results in significant blood loss for anaesthesiologists to replace and additional technical problems for surgeon attempting to inspect the lesion and insert a vascular prosthesis.

TABLE NO.2: PATHOPHYSIOLOGIC EFFECTS AND COMPLICATIONS OF LARYNGOSCOPY AND INTUBATION[30]

CARDIOVASCULAR SYSTEM	Dysrhythmia Hypertension Myocardial ischemia and infarction
RESPIRATORY SYSTEM	Hypoxia Hypercarbia Laryngeal spasm Bronchospasm
CENTRAL NERVOUS SYSTEM	Increase in intracranial pressure
EYE	Increase in intraocular pressure
MISCELLANEOUS	Toxic and adverse effects due to drugs related to Laryngoscopy and intubation

PHARMACOLOGY OF CLONIDINE[31]

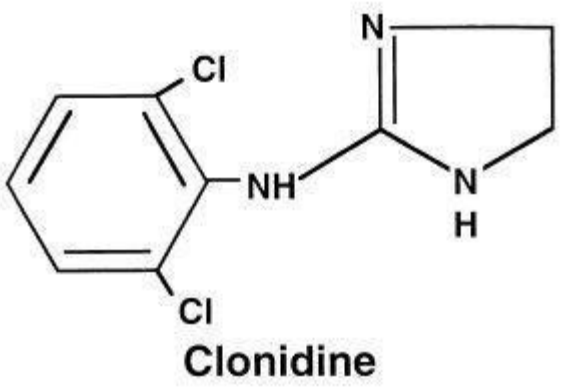

Fig no.5.CHEMICAL STRUCTURE OF CLONIDINE

N – (2,6 – dichlorophenyl) -4, 5 –dihydro – 1H – imidazol – z – amine

Clonidine is directly acting α2 agonist prescribed historically as an antihypertensive agent. In addition to its antihypertensive effect, in recent studies, Clonidine has been demonstrated to be an effective sedative and analgesic which reduces the amount of anaesthetic agents required when used as part of anaesthetic technique. Therefore, a reconsideration of possible new indications for Clonidine in clinical anaesthesiology is justified.

MECHANISM OF ACTION

Clonidine stimulates pre-synaptic α2 receptors and inhibits norepinephrine release from both central and peripheral adrenergic terminals. It also has some α1 agonist activity & in high oral doses may cause paradoxical hypertension by stimulating vascular α1 receptors.Its selectivity ratio of receptors is α2:1=220:1.

Under normal circumstances α2 effects predominate. The prominent antihypertensive effect is thought to be secondary to stimulation of α2 receptors in the vasomotor centers of the medulla oblongata.Peripherally there is decreased plasma renin activity as well as decreased epinephrine and norepinephrine levels. α2 receptors are abundant in pontine locus ceruleus which is an significant source of

sympathetic nervous system innervations of the forebrain and a vital modulator of vigilance. Clonidine's sedative effects most likely reflect this nucleus's inhibition.

Hemodynamics

Clonidine impacts blood pressure in a complex manner following neuraxial or systemic administration due to opposing actions at various locations. Activation of postsynaptic α2 adrenergic receptors decreases sympathetic drive in the nucleus tractus solitarius and locus coeruleus of the brainstem. It also activates non-adrenergic imidazoline preferring binding sites in the lateral reticular nucleus, there by giving rise to hypotension and an antiarrthymic action. In the periphery, its action on presynaptic α2-adrenoceptors at sympathetic terminals reduce the release of norepinephrine causing vasorelaxation and reduced chronotropic drive. These brainstem and peripheral effects of α2-adrenoceptor stimulation are counter balanced by direct peripheral vasoconstriction through its action on α1-adrenoceptors from circulating concentrations of Clonidine. As a consequence, the dose-response for Clonidine after neuraxial or systemic administration is U-shaped, with peripheral vasoconstriction from circulating drug concentrations at elevated doses opposing central sympatholysis. Clonidine decreases heart rate partly due to presynaptically mediated norepinephrine release inhibition at the neuroreceptor junction and partly by vagomimetic impact.

After neuraxial or systemic administration, the hemodynamic impacts of Clonidine start within 30 min and achieve a peak of 1-2 hrs and last about 6-8hrs after a single injection.Delayed onset of hypotension was not noted either alone or in combination with the use of Clonidine for analgesia.

Respiratory depression:

Even after overdose α2-adrenergic agonists do not induce deep respiratory depression nor do they potentiate respiratory depression from opioids.

Renal:

Salt and water retention can occur and is due to reduced sympathetic tone. Conversely a diuretic effect during general anaesthesia has been described after administration of oral Clonidine, 2.5 to 5.0 mcg/kg, as preanaesthetic medication.

GIT:

Constipation is also relatively common side effect of Clonidine and incidence is about 10% is due to antisecretory effect on the intestine.

Dermatological:

Rash, erythema, allergic contact dermatitis, angioneurotic edema, urticaria, alopecia and pruritus may occur. Skin reactions have been reported in up to 50% of patients using Clonidine transdermal patches.

Others:

Clonidine prevents opioid induced skeletal muscle rigidity and produces skeletal muscle flaccidity. α2 agonists have no effect on the responses evoked by neuromuscular blocking drugs. Clonidine hydrochloride has been associated with acute attack of porphyria and is considered unsafe in porphyria patients.

PHARMACOKINETICS

Clonidine is highly lipid soluble and hence rapidly absorbed after oral, intravenous and epidural administration. After epidural administration, Clonidine is rapidly and extensively absorbed into the spinal CSF compartment, with concentration peaking 30 to 60 min after injection. There is a powerful correlation between CSF concentration of Clonidine and analgesia following administration epidural Clonidine.

Epidurally administered Clonidine readily partitions into plasma via the epidural veins and attains systemic concentrations (0.5 – 2 ng / ml) that are associated with a hypotensive effect mediated by the central nervous system. After intravenous administration it is readily distributed into extravascular sites including the central nervous system.

Molecular mass 230.093 gm / ml

Bioavailability 75 – 95%

Protein binding 20 – 40%

Volume of distribution 2.1 + 0.4 L / Kg

Elimination T ½ 9 + 2 hours

Onset time 26 + 11 minutes

METABOLISM

In the liver Clonidine undergoes hydroxylation to form major metabolite p-hydroxy Clonidine.

Only 50% of the medication is metabolized in the liver and the rest is excreted as unchanged medication in the urine. Plasma albumin is the most important protein binding site for Clonidine and varies between 20 – 40% in vitro.

SIDE EFFECTS

The most common side effects produced by Clonidine are drowsiness, dry mouth, bradycardia and hypotension. Rebound hypertension can occur after abrupt discontinuation of Clonidine therapy (1.2 mg / day) as early as 8 hours and as late as 36 hours after the last dose. Rebound hypertension can usually be controlled by reinstituting Clonidine therapy or by administering a vasodilating drug such as Hydralazine or Sodium Nitroprusside.

CLINICAL USE

Usual daily adult dose is 0.2 to 0.3 mg orally. Transdermal Clonidine patch designed for weekly administration is useful for surgical patients who are unable to take oral medications.

Hypertension

Treatment of patients with severe hypertension or renin dependent disease. The Usual daily adult dose is 0.2 to 0.3 mg orally.

Anaesthetic use of Clonidine:

1. **Premedication:** The sedative effect can be useful when Clonidine is used as a premedicant. In addition it also has an anaesthesia-sparing effect. α2 adrenergic agonists reduce the dose of intravenous hypnotics and also reduce the MAC of the volatile anaesthetic agents.
2. **Control of hemodynamic response**: α2 adrenergic agonist's hemodynamic impacts are both central as well as peripheral. In addition α2 adrenergic agonists in the lateral horn of the thoracic spinal cord depress presynaptic sympathetic neurons. It should be observed here that the local administration of cholinesterase inhibitor neostigmine reverses this impact. Clonidine prevents hypertension and tachycardia during laryngoscopy and intubation as well as during surgical stimulation.

Postoperative analgesia and Regional anesthesia Clonidine interacts with cholinergic neurons to increase the analgesic impact of opiates. They increase the blockage of local anaesthetics and extends duration.

Central Neuraxial Block

a) **Epidural** It is used more commonly as a combination with opioids and or local anesthetics to provide good to excellent analgesia with minimal side effects.

b) **Spinal**: Clonidine generates short lived analgesia but without the related risk of respiratory depression or urinary retention. The maximum dose of Clonidine intrathecally is 1-2 mcg/kg. Giving Clonidine with local anaesthetics enhances the block quality and length, reduces the tourniquet pain during lower limb surgery and avoids shivering.

c) **Caudal:** The dosage recommended in the caudal route is 1-2 mcg / kg.

3. Peripheral Nerve Blocks:

Clonidine is frequently used in peripheral nerve blocks as an adjuvant to local anesthetics where it extends both the length of anaesthesia and analgesia. This effect is obtained at relatively small doses (1-2 mcg/kg) which obviously reduce the risks of side effects.

Other uses are:

1. Prevention of emergence agitation
2. Decreasing Minimum Alveolar Concentration (MAC) of sevoflurane
3. Postoperative nausea and vomiting (PONV)
4. Controlled hypotension
5. In cardiovascular surgery
6. Post-operative shivering- To prevent shivering a dose of 1.5mcg/kg.
7. Daycare Surgery
8. Attenuation of pressor response to intubation and extubation of trachea There was no increase in neuropeptide Y, a marker of significant adrenergic ac tivation

   during tracheal intubation, among children premedicated with rectal Clonidine 2.5mcg/kg Oral Clonidine 4 mcg/kg attenuated hemodynamic changes associated with tracheal extubation, when given 10 minutes before induction

9. Anaesthetic sparing effect- At a dose of 2-4mcg/kg, oral Clonidine premedication decreases the intravenous barbiturate dose required for anaesthesia induction.
10. Treatment of spasticity Clonidine is used in cerebral palsy or traumatic brain injury.

Precautions

Use cautiously in:

- Renal insufficiency, serious cardiac or cerebrovascular disease
- Elderly patients
- Pregnant or breastfeeding patients.

Interactions

- Drug-drug.

1. Amphetamines, beta-adrenergic blockers, MAO inhibitors, prazosin, tricyclic antidepressants: decreased antihypertensive effect.
2. Beta-adrenergic blockers :increased withdrawal phenomenon.
3. CNS depressants (including antihistamines, opioids, sedative hypnotics):additive sedation.
4. Epidurally administered local anaesthetics: prolonged Clonidine effects.
5. Levodopa: decreased levodopa efficacy
6. Myocardial depressants (including beta-adrenergic blockers): additive bradycardia
7. Other antihypertensives, nitrates: additive hypotension Verapamil: increased risk of adverse cardiovascular reactions

- Drug-herbs

Capsicum: reduced antihypertensive effect

- Drug-behaviors

Alcohol use: increased sedation

DOSAGE GUIDELINES: CLONIDINE DOSE

Oral - 3-5mcg/Kg

Intrathecal – 15mcg to 30mcg

Epidural – 1mcg/kg (or) 50mcg . 30 mcg /hr (for infusion)

Intravenous - 50 – 75 mcg (or) 1mcg/kg 15 minutes prior to induction for intubation response attenuation;150 – 300 mcg (or) 3 mcg / kg for hypertensive crisis; 30 mcg given slowly for shivering management.

PREPARATION:

Clonidine is available in 100 mcg, 150 mcg and 300 mcg tablets. Also it is available in injectable form as clear preservative free preparation in1 ml ampoules of 150 mcg.

PHARMACOLOGY OF PREGABALIN[32]

Pregabalin is structurally defined as (S)-3 aminoethyl-5-methylhexanoic acid, a compound of gabapentinoids. Pregabalin is structurally linked to, but not functionally linked to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).

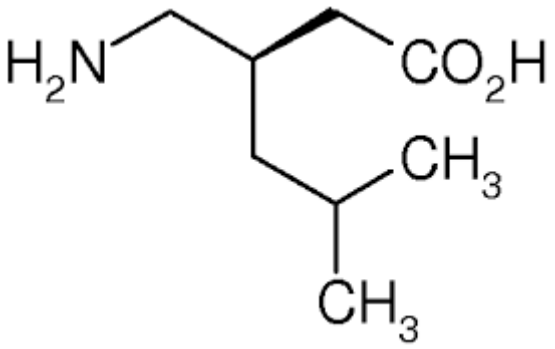

Fig no.6. Chemical structure of Pregabalin

It was originally introduced as an antiepileptic, and also has an analgesic, anticonvulsant and anxiolytic effects. This drug is well tolerated by patients and produce limited side effects. Pregabalin (S-[+]-3-isobutylgaba) was designed as a lipophilic GABA (γ-aminobutyric acid) analog substituted at the 3'-position to facilitate diffusion across the blood-brain barrier.

Mechanism of action:

Pregabalin binds to the α2-delta subunit of the neuronal voltage gated calcium channel, resulting in reduced depolarization induced calcium influx at the nerve terminals with a consequential decrease in the release of the excitatory neurotransmitters.

Its primary action site appears to be on the α2-delta subunit of presynaptic, voltage dependent calcium channels that are commonly spread across the peripheral and central nervous system.For the α2-delta subunit, binding and potency is six times greater than that of gabapentin.

By altering calcium currents, Pregabalin reduces or modulates the release of several excitatory neurotransmitters including glutamate, norepinephrine, substance P, and calcitonin gene-related peptide, producing inhibitory modulation of "overexcited" neurons and returning them to a "normal" state. Thus, Pregabalin appears to reduce the hyperexcitability of dorsal horn neurons that is induced by tissue damage. Pregabalin appears to produce on inhibitory modulation of neuronal excitability particularly in areas of CNS (neocortex, amygdala and hippocampus) and result in reduction of various neurotransmitter.

Voltage-dependent calcium channels were divided into six classes, based on their dependence on voltage, kinetics and sensitivity to a variety of drugs. It has been determined that the molecular structure of these functionally recognized calcium channels as P-, Q-, N-, L-, R-, and T-type. N-type calcium channels are believed to play a part in pain sensitization processes.

Pharmacokinetics:

Absorption of Pregabalin is not saturable, resulting in linear pharmacokinetic profi1e. Well absorbed after oral administration; bioavailability exceeds 90% and is dose independent, which can generate a more predictable patient response.

Pregabalin is rapidly absorbed with peak blood concentration within 1 hour. Study state is achieved within 24 to 48 hours.

The half life elimination of Pregabalin varies from 5.5 to 6.7 hrs, regardless of dose and repeated dose administration.

Pregabalin does not undergo hepatic metabolism and is not bound to plasma protein. It is renally excreted and 98% of the absorbed dose is excreted unchanged in urine Pregabalin elimination is nearly proportional to creatinine clearance.

In patients with creatinine clearance between 30and 60ml/min , 50% reduction in daily dose of Pregabalin is suggested compared to creatinine clearance >60ml/min. Pregabalin binding affinity for the alpha2-delta subunit and potency, is six times more than that of gabapentin.

Pregabalin is inactive to GABA A and GABA B receptor, is not converted metabolically into GABA or a GABA antagonist, and it does not alter GABA uptake and degradation.

Uses:

1) For preoperative anxiolysis
2) Prevention of chronic postsurgical pain.
3) As a pre-emptive analgesic
4) It has been tried to attenuate haemodynamic response to direct laryngoscopy and endotracheal intubation.
5) In psychiatric patients with anxiety and bipolar disorders.
6) In the treatment of neuropathic pain like diabetic neuropathy, the maximum recommended dose of Pregabalin is 100mg thrice a day. Dosing should begin at 50mg thrice a day and may be increased to 300mg/day within 1 week based on efficacy and tolerability.
7) In treatment HIV neuropathy.
8) Post herapeutic neuralgia – dosage should start twice daily at 75mg or at 50mg three times daily.
9) As an anti-epileptic: Gabapentin is used in the treatment of partial seizures as an adjunctive therapy in patients unresponsive to or intolerant of standard antiepileptic drugs.
10) Pregabalin is a drug that modulates sleep. Pregabalin raises non rapid eye

movement length and also reduces rapid eye movement sleep. Its noted that it increases slow-wave sleep in healthy volunteers. It has been shown that the time spent in stages III-IV sleep is considerably increased while night time awakening is reduced.

Adverse reactions:

They are dose dependent adverse effect and usually transient. Dizziness and somnolence is most commonly reported adverse events. Headache, confusion, trouble with memory are other common side effects. Serious side effects may include angioedema. When Pregabalin is taken at high doses over a period of time, addiction may occur, but if taken at usual doses the risk is low.

Drug interactions:

1) ACE inhibitors (eg. Captopril) : Co-administration of these agents may increase the risk of swelling and hives. The patient's health care provider should be contacted immediately, if these signs occur.
2) CNS depressants (eg. Alcohol, lorazepam, oxycodone) : Additive effects on cognitive and gross motor function have been seen. Alcohol should be avoided.
3) Thiazolidinediones (eg. Pioglitazone): Both Pregabalin and thiazolidinediones may cause weight gain and/or fluid retention, possibly exacerbating or leading to heart failure. It should be used with caution. Monitor the patient, if an interaction is suspected, it may be necessary to adjust the dose of one or both agents.

MATERIALS AND METHODS

SOURCE OF DATA:

This study was carried out in the Department of Anaesthesiology, from the December 2017 to August 2019.

METHOD OF COLLECTION OF DATA:

Study Design: Randomised, prospective study.

Study Period: One and half years from December 2017 to August2019.

Sample Size: With anticipated proportion of stress response between 2study groups as 29.9% and 12.7%[20] with 95% confidence level and 80 % power , minimum sample size per group is 44, using the formula,

$$n = \frac{(Z_\alpha + Z_\beta)^2 * p * q}{D^2}$$

where, Z_α = Z value at α level=95%

Z_β = Z value atβlevel=80%

D = Difference between two parameters

p = Proportion value

q = 100-p

Hence 45 cases was included in each group.

Statistical data:

1. Data was represented in the form of frequencies and diagrams
2. Association between qualitative variables were assessed by Chi-square test, fisher's exact test.

3. Analysis of Quantitative data between the two groups was done using unpaired t-Test if data passes 'Normality test' and by Mann- Whitney Test if data fails 'Normality test'.
4. pvalue was considered significant if<0.05 and highly significant if <0.001

Inclusion criteria

1. Patient belonging to ASA physical status Iand II.
2. Patient undergoing elective surgery under general anesthesia.
3. Age between18 to 60years.
4. BMI 18 to 25
5. Stable Hemodynamics
6. No history of allergy to study drugs

Exclusion criteria

1. Patientwith h/o severe hypertension, diabetes, cardiovascular , respiratory, cerebral , renal and liver disease.
2. Pregnant patient
3. Patient with difficult airway, obesity.
4. Patient's pulse rate less than 60bpm and systolic blood pressure less than 90mmhg at the time of study drug medication.

Preliminaries: Written informed consent

Study drugs : Tablet Clonidine 300mcg , Tablet Pregabalin 75mg.

Procedure:

- 90 patients posted for elective endotracheal intubation for general anaesthesia was assigned randomly to 2 groups containing 45 patients each. Randomization was done by computer generated random numbers.
- All patients were examined the day before surgery and thoroughly investigated according to institute protocol and were counselled with regards to anaesthesia as well as procedure.
- Patient's meeting the above criteria were asked to participate in the study and informed consent was taken. Patients were instructed to fast overnight.
- On the day of surgery, basal values of heart rate, systolic blood pressure ,diastolic blood pressure, mean arterial pressure were recorded.
- **Group C** (Clonidine group) pts were given Tablet Clonidine 300mcg orally 120 minutes before surgery as oral premedication and **Group P** (Pregabalin group) pts were given Tablet Pregabalin 75mg orally 120 minutes before surgery as oral premedication.
- In the operating room multipara monitors were applied to the patient. All cases were then premedicated with i.v.Inj Glycopyrrolate 0.004mg/kg, Inj Ondansetron4mg, Inj Midazolam 0.015mg/kg and after 5min of premedication Inj.Fentanyl 1-1.5mcg/kg was given as analgesic.
- All cases were preoxygenated with facemask and Bains circuit with 100% O2 for 3 mins.
- Anaesthesia was induced with i.v.Inj Propofol 2mg/kg. Neuromuscular blockade was achieved with i.v.Inj Succinyl choline1mg/kg. Laryngoscopy and intubation was performed after 90sec of injection of Succinyl choline.

- The endotracheal tube was secured firmly in place after confirming equal air entry bilaterally. oxygen, nitrous oxide and isoflurane were used maintaninance of anaesthesia using Bains circuit and intermittent dose of depolarizing neuromuscular blockers .
- Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure was noted at following intervals-
    1. Base line
    2. After study drug a) 30 min b) 60 min c) 90 min
    3. Before induction
    4. During laryngoscopy and at 1,5,10 and 15 mins after intubation
- The rate pressure product(RPP) calculated by formula

  RPP = HR X SBP

  Where, HR : Heart Rate

  SBP : Systolic Blood pressure

OBSERVATION AND RESULTS

1) AGE DISTRIBUTION

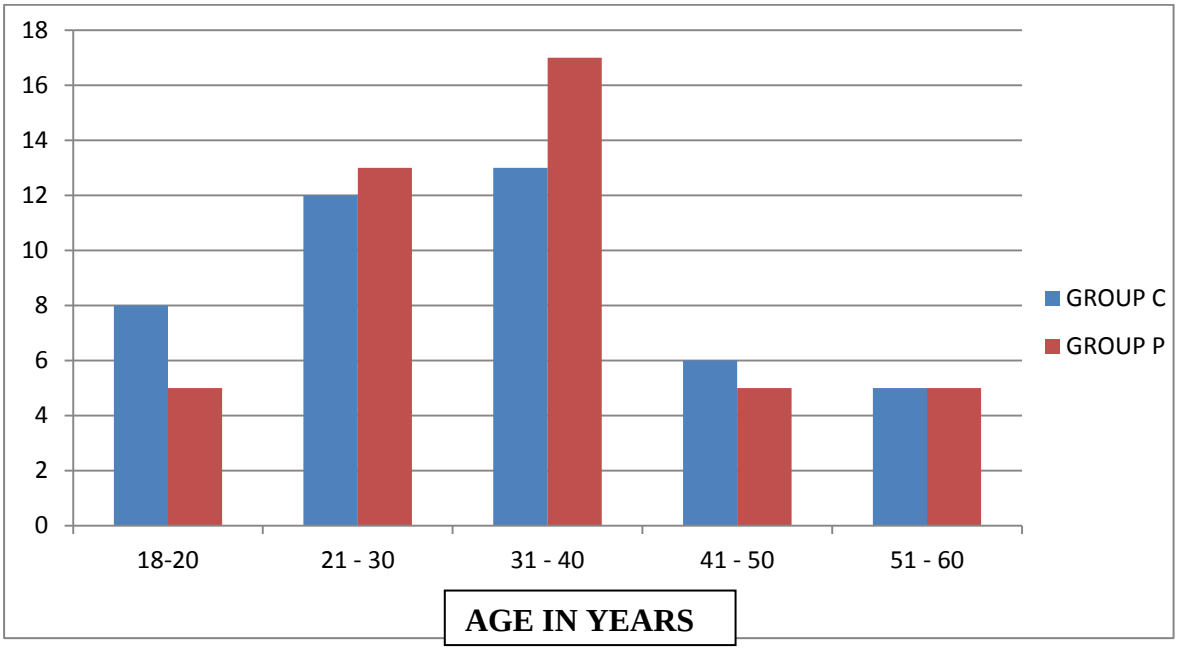

Fig no.7: SHOWING AGE DISTRIBUTION shows that the predominant age group in both groups was 31-40 years

Age(Years)	Group C		Group P	
	No. of patients	Percentage	No. of patients	Percentage
18 – 20	8	17.7	5	11.1
21 – 30	12	26.7	13	28.9
31 – 40	14	31.1	17	37.8
41 – 50	6	13.4	5	11.1
51 – 60	5	11.1	5	11.1
Total	45	100.0	45	100.0

TABLE NO.3: AGE DISTRIBUTION OF PATIENTS

In Group C the mean age was 33±13 and in Group P it was 34±11 years. There was no significant difference between the groups with respect to age as their p-value was 0.852 (NS).

2. GENDER DISTRIBUTION

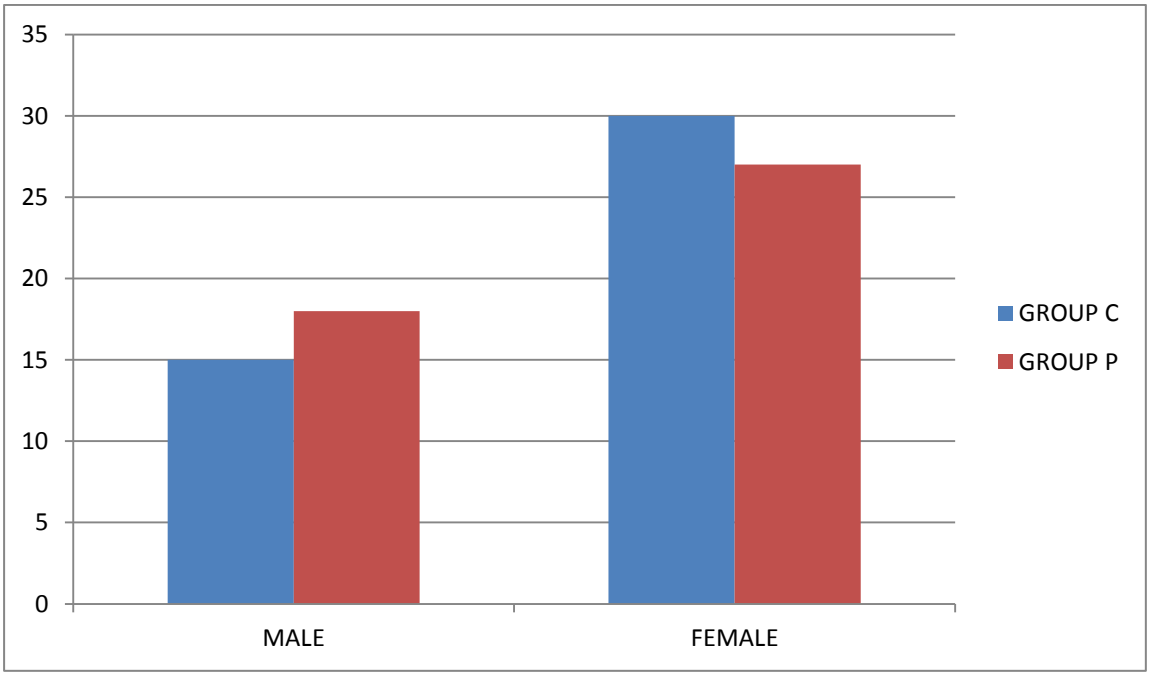

Fig no.8: SHOWING GENDER DISTRIBUTION

GENDER	GROUP C	GROUP G
MALE	15	18
FEMALE	30	27
TOTAL	45	45

TABLE NO.4: GENDER DISTRIBUTION OF PATIENTS

In Group C male 33.33%, female 66.66% In Group G, male 40%,female 60%.Gender wise both the groups were comparable but it was statistically non-significant.

3. Comparison of mean heart rate between Group C and GroupP

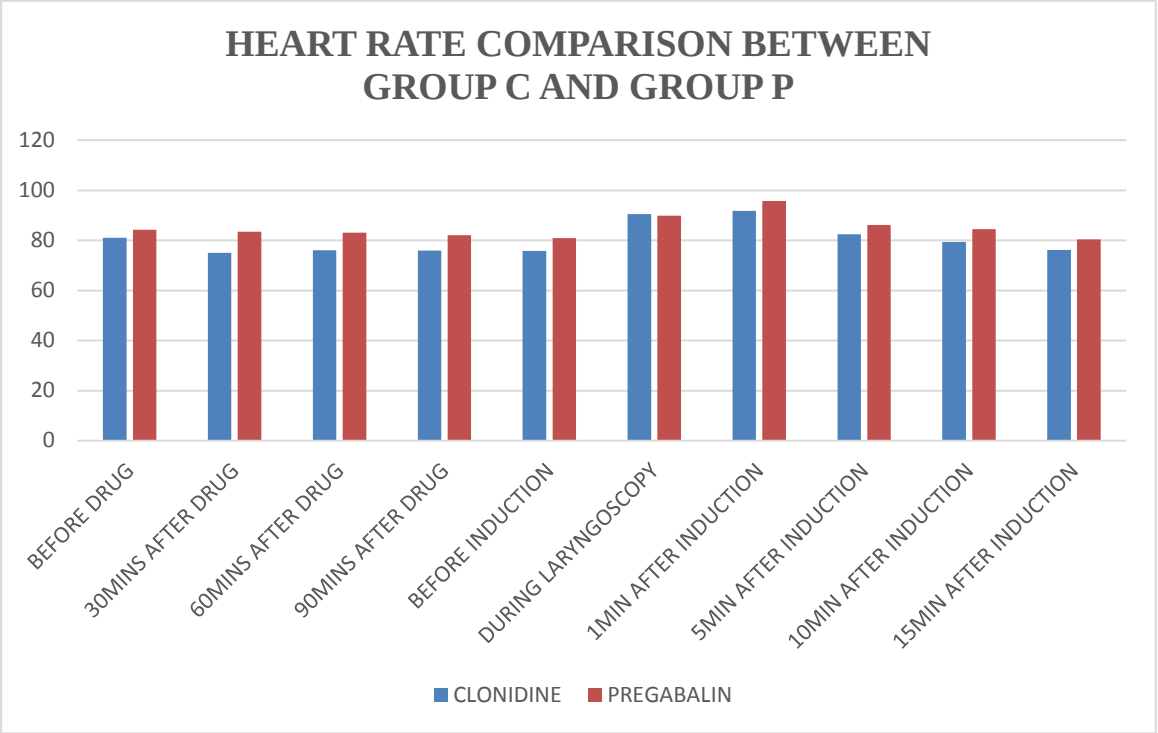

Fig no.9 SHOWING INTERGROUP COMPARISON OF HEART RATE

VARIABLES	GROUP C		GROUP P		Independent t test	p-value
	MEAN	SD	MEAN	SD		
BEFORE DRUG	81.07	9.161	84.27	10.426	1.547	0.126
30MINS AFTER DRUG	75.07	6.559	83.51	8.314	5.349	0.000*
60MINS AFTER DRUG	76.00	6.403	83.07	8.007	4.477	0.000*
90MINS AFTER DRUG	75.96	6.403	82.09	7.211	4.267	0.000*
BEFORE INDUCTION	75.78	5.530	80.87	6.373	4.046	0.001*
DURING LARYNGOSCOPY	90.53	12.759	89.80	9.764	0.306	0.760
1MIN AFTER INTUBATION	91.82	11.360	95.71	9.818	1.737	0.086
5MIN AFTER INTUBATION	82.40	7.563	86.20	10.954	1.915	0.059
10MIN AFTER INTUBATION	79.42	7.430	84.53	9.305	2.864	0.005*
15MIN AFTER INTUBATION	76.16	7.236	80.36	7.607	2.683	0.009*

***p value- significant**

TABLE NO.5: INTERGROUP COMPARISON OF HEART RATE

The mean baseline HR at before drug in Group C and Group P were 81.07±9.161/min, and 84.27±10.426/min respectively which were comparable.

On comparing mean HR in Group C and Group P, it was observed that there was a drop in the values in both the groups after administration of the drugs. However, the drop in heart rate in group C was statistically more significant than group P at 30min, 60min, 90min from the time of drug administration.

Before induction of the patient the drop in heart rate is statistically significant in group C when compared to group P.

During laryngoscopy, there is rise in heart rate due to the pressor effect of the intubation procedure. There is a drop in heart rate in both groups at 1min, 5min, 10min, 15min after intubation showing that both the drugs attenuate the pressor effect, however drop in values in group C is statistically more significant than group P.

4.Comparison of Mean systolic blood pressure changes between Group C and Group P

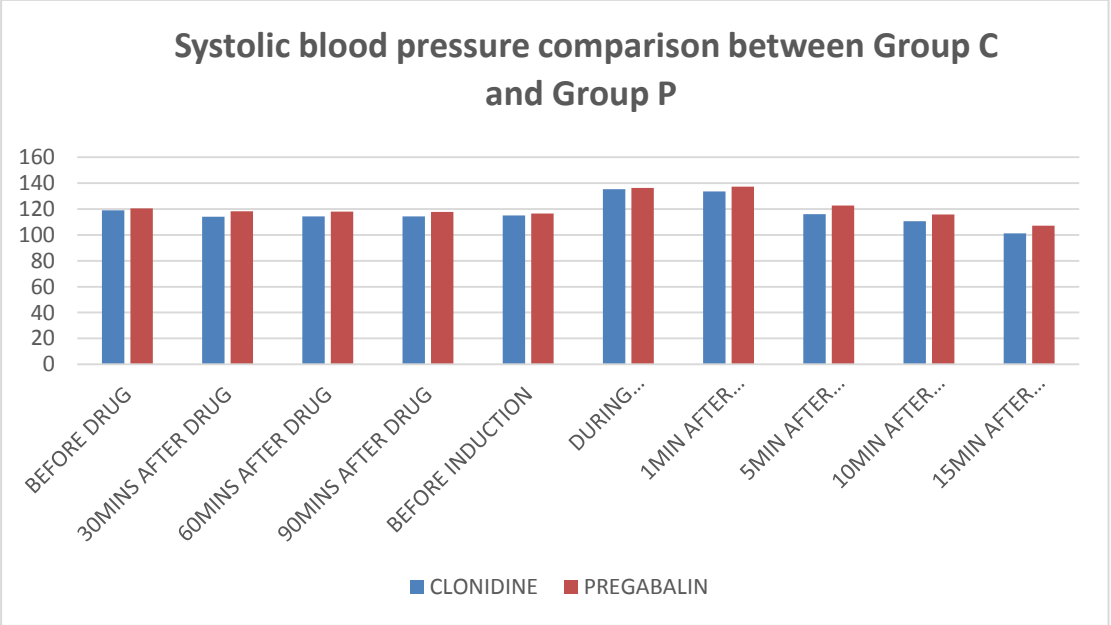

Fig no.10 SHOWING INTERGROUP COMPARISON OF SYSTOLIC BLOOD PRESSURE

VARIABLE	GROUP C		GROUP P		t-VALUE	p-VALUE
	MEAN	SD	MEAN	SD		
BEFORE DRUG	119	9.520	120.51	8.714	0.785	0.434
30MINS AFTER DRUG	113.96	5.901	118.22	8.762	2.710	0.008*
60MINS AFTER DRUG	114.18	6.117	118.09	7.236	2.769	0.007*
90MINS AFTER DRUG	114.40	4.525	117.69	5.861	2.980	0.004*
BEFORE INDUCTION	114.98	6.989	116.56	6.946	1.074	0.286
DURING LARYNGOSCOPY	135.20	13.249	136.29	7.771	0.476	0.636
1MIN AFTER INTUBATION	133.47	8.543	137.36	7.392	2.309	0.023
5MIN AFTER INTUBATION	115.96	6.138	122.62	9.252	4.028	0.000*
10MIN AFTER INTUBATION	110.51	8.176	115.69	10.446	2.618	0.010*
15MIN AFTER INTUBATION	101.18	6.138	107.18	10.478	3.290	0.001*

***p- Value significant**

TABLE NO.6: INTERGROUP COMPARISON OF SYSTOLIC BLOOD PRESSURE

The mean baseline systolic blood pressure at before administration of drug in Group C and Group P were 119±9.520 mm of hg, and 120±8.714 mm of hg respectively which were comparable.

On comparing mean systolic blood pressure in Group C and Group P, it was observed that there was a drop in the values in both the groups after administration of the drugs. However, the drop in systolic blood pressure in group C was statistically more significant than group P at 30min, 60min, 90min from the time of drug administration.

Before induction of the patient the drop in systolic blood pressure is statistically significant in group C when compared to group P.

During laryngoscopy, there is rise in heart rate due to the pressor effect of the intubation procedure. There is a drop in systolic blood pressure in both groups at 1min, 5min, 10min, 15min after intubation showing that both the drugs attenuate the pressor effect, however drop in values in group C is statistically more significant than group P.

5.Comparison of Mean diastolic blood pressure changes between Group C and Group P

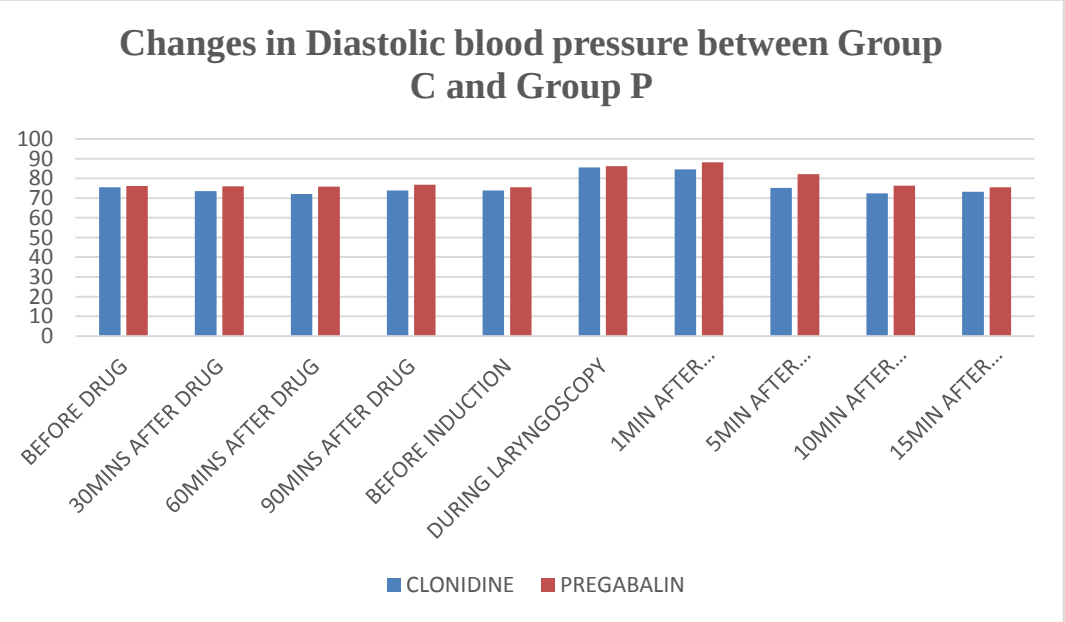

Fig no.11:SHOWING INTERGROUP COMPARISON OF DIASTOLIC BLOOD PRESSURE

VARIABLE	Group C		Group P		t-VALUE	p-VALUE
	MEAN	SD	MEAN	SD		
BEFORE DRUG	75.51	7.137	76.09	7.336	0.379	0.706
30MINS AFTER DRUG	73.51	6.370	75.96	6.172	1.849	0.068
60MINS AFTER DRUG	72.13	6.258	75.82	6.492	2.744	0.007*
90MINS AFTER DRUG	73.78	4.557	76.80	5.367	2.880	0.005*
BEFORE INDUCTION	73.91	5.308	75.56	5.007	2.884	0.005*
DURING LARYNGOSCOPY	85.49	7.876	86.18	4.914	0.498	0.620
1MIN AFTER INTUBATION	84.53	4.962	88.09	4.111	3.702	0.000*
5MIN AFTER INTUBATION	75.20	6.170	82.11	5.188	5.751	0.000*
10MIN AFTER INTUBATION	72.47	5.255	76.27	5.902	3.226	0.02*
15MIN AFTER INTUBATION	73.16	4.123	75.47	4.980	2.398	0.019*

***p value –significant**

TABLE NO.7: INTERGROUP COMPARISON OF DIASTOLIC BLOOD PRESSURE

The mean baseline diastolic blood pressure at before administration of drug in Group C and Group P were 75.51±7.137 mm of hg, and 76.09±7.336 mm of hg respectively which were comparable.

On comparing mean diastolic blood pressure in Group C and Group P, it was observed that there was a drop in the values in both the groups after administration of the drugs. However, the drop in diastolic blood pressure in group C was statistically more significant than group P at 30min, 60min, 90min from the time of drug administration.

Before induction of the patient the drop in diastolic blood pressure is statistically significant in group C when compared to group P.

During laryngoscopy, there is rise in heart rate due to the pressor effect of the intubation procedure. There is a drop in diastolic blood pressure in both groups at 1min, 5min, 10min, 15min after intubation showing that both the drugs attenuate the pressor effect, however drop in values in group C is statistically more significant than group P.

6.Comparison of mean arterial pressure between Group C and Group P

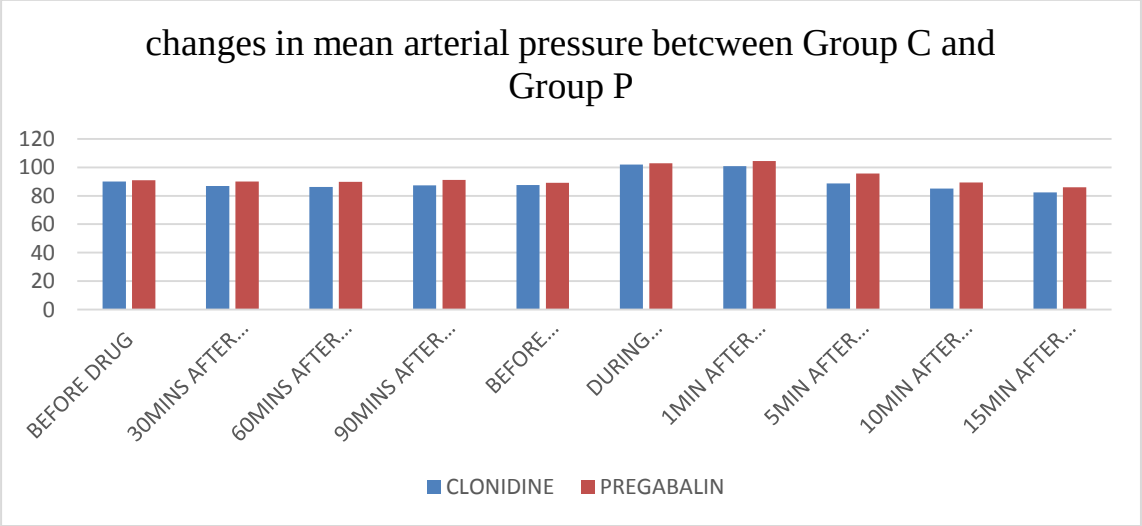

Fig no.12: SHOWING INTERGROUP COMPARISON OF MEAN ARTERIAL PRESSURE

VARIABLE	Group C		Group P		t-VALUE	p-VALUE
	MEAN	SD	MEAN	SD		
BEFORE DRUG	89.955	7.635	90.911	7.400	0.603	0.548
30MINS AFTER DRUG	86.992	5.914	90.044	6.597	2.311	0.023*
60MINS AFTER DRUG	86.148	5.872	89.911	6.371	2.913	0.005*
90MINS AFTER DRUG	87.318	3.974	91.259	5.023	4.127	0.000*
BEFORE INDUCTION	87.60	5.390	89.222	5.210	1.451	0.150
DURING LARYNGOSCOPY	102.059	9.307	102.881	5.226	0.517	0.607
1MIN AFTER INTUBATION	100.844	5.744	104.511	4.702	3.313	0.001*
5MIN AFTER INTUBATION	88.785	5.789	95.614	6.037	5.477	0.000*
10MIN AFTER INTUBATION	85.148	5.759	89.407	6.984	3.156	0.002*
15MIN AFTER INTUBATION	82.511	4.164	86.037	6.082	3.207	0.002*

***p value- significant**

TABLE NO.8: INTERGROUP COMPARISON OF MEAN ARTERIAL PRESSURE

On comparing mean MAP in Group C and Group P, the following results were obtained. The mean baseline MAP at before drug in Group C and Group P were 89.9550±7.635mmHg, and 90.911±7.4mmHg respectively which were comparable.

The mean MAP in both the groups, at 30mins, 60mins and 90mins and before induction were observed and there was significant change in Group C as compared to Group P.

There was rise in MAP in subsequent events from during laryngoscopy to 1min after endotracheal in Group C and Group P as compared to baseline. However, on comparing difference in mean MAP at respective events in each groups viz. during laryngoscopy, 1min, 5mins, 10mins and 15mins after intubation, it was observed that there was statistically significant difference at 1mins, 5mins, 10mins and 15mins after intubation where group C showed significant drop compared to group P ($p<0.05$).

6.Comparison of mean rate pressure product between Group C and Group P

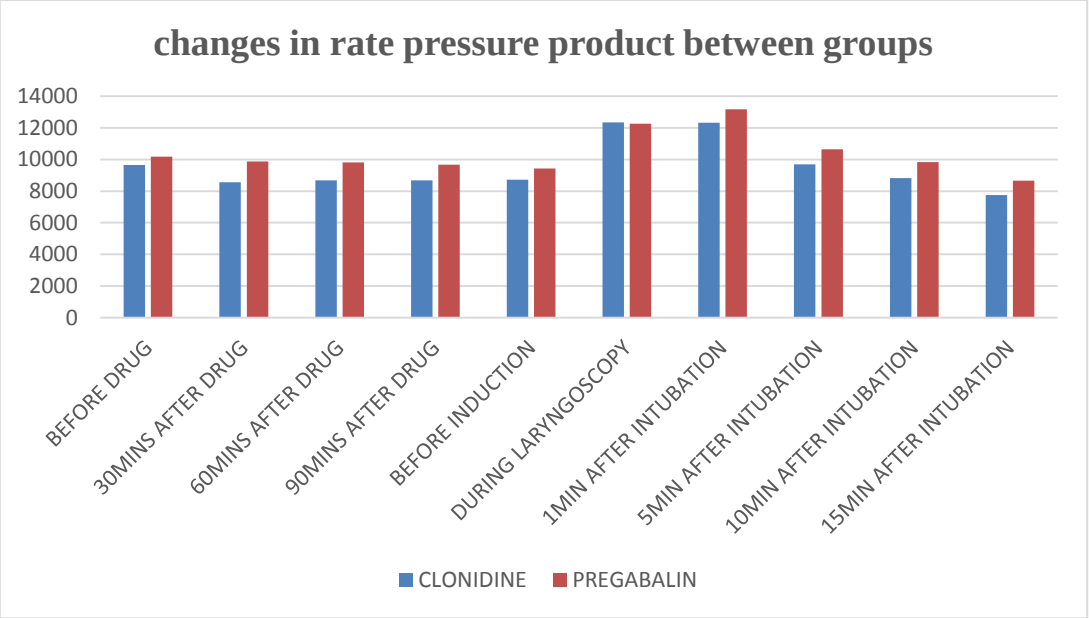

Fig no.13: SHOWING INTERGROUP COMPARISON OF RATE PRESSURE PRODUCT

VARIABLE	Group C		Group P		t-VALUE	p-VALUE
	MEAN	SD	MEAN	SD		
BEFORE DRUG	9640.36	1279.941	10181.96	1692.161	1.712	0.091
30MINS AFTER DRUG	8561.42	951.707	9878.40	1302.08	5.478	0.000*
60MINS AFTER DRUG	8670.49	849.358	9811.73	1156.502	5.335	0.000*
90MINS AFTER DRUG	8683.82	749.878	9663.73	1007.48	5.234	0.000*
BEFORE INDUCTION	8716.80	886.382	9423.84	932.111	3.687	0.000*
DURING LARYNGOSCOPY	12345.07	2788.635	12264.04	1735.68	0.165	0.869
1MIN AFTER INTUBATION	12319.64	2162.751	13175.86	1786.88	2.047	0.044*
5MIN AFTER INTUBATION	9688.49	1347.604	10641.24	2069.738	2.588	0.012*
10MIN AFTER INTUBATION	8812.09	1333.129	9831.38	1788.214	3.066	0.003*
15MIN AFTER INTUBATION	7739.02	1141.580	8648.71	1453.445	3.302	0.001*

*p value- significant

TABLE NO.9: INTERGROUP COMPARISON OF RATE PRESSURE PRODUCT

The mean baseline RPP at before drug in Group C and Group G were 9640.36±1279.941mmHg/min and 10181.96±1692.161mmHg/min respectively, which were comparable..

On comparing mean RPP in Group C and Group G, it was observed that there was statistical significant difference between the two groups from the point before drug, 30mins, 60mins, 90mins, before induction where group C showed a significantly lower values compared to group G. After induction, similarly the values were statistically significant after laryngoscopy at 1min, 5mins, 10min and 15min after intubation

DISCUSSION

This study was done to evaluate the efficacy of oral Clonidine and oral Pregabalin premedication in attenuating the hemodynamic stress response to laryngoscopy and endotracheal intubation. Pregabalin and Clonidine act as an anxiolytic , mild analgesic and sedative.

Tracheal intubation is a critical skill in anaesthetic practice. Direct laryngoscopy needs to be performed to view the vocal cords for insertion of the endotracheal tube. Both laryngoscopy and passage of a tracheal tube are noxious stimuli that can trigger adverse events in the respiratory, cardiovascular and other physiologic systems.

Shribman et al[29] reported that laryngoscopy and tracheal intubation has been noted to increase blood pressure, HR and catecholamine levels, whereas Hassan et al[33] reported increased incidence of cardiac arrhythmias, myocardial ischemia, and acute left ventricular failure during laryngoscopy and tracheal intubation.

Reid and Brace[26] in their study noted that there was a hemodynamic response to laryngoscopy and intubation, probably owing it to intense sympathetic release triggered by epipharynx and larynx stimulation. Many pharmacological methods were tested either in the premedication or during induction to attenuate the response of hemodynamic stress to intubation, but the findings were controversial. During laryngoscopy and tracheal intubation , more attention was paid to the selective beta-adrenergic blockers to avoid the reflex sympatho-adrenal discharge mediated tachycardia and hypertension. Hypotensive agents including Sodium Nitroprusside, Nitroglycerin, Adrenoreceptor blockers, Calcium channel blockers and Opioids have been used efficiently to attenuate these hemodynamic reactions but they are linked with bradycardia, hypotension, and post-operative respiratory depression and are

therefore not used as a premedication.

Pregabalin's analgesic effect has been researched over the last few years and is used in post-operative pain management due to its excellent analgesic and opioid sparing effect. Both Pregabalin and Clonidine effectively blunts the sympathetic response and maintain hemodynamic stability during laryngoscopy .

Elderly patients were excluded due to the possibility of taking drugs such as antidepressants, hypnotics, and antihypertensives with enhanced sensitivity to anaesthetic drugs. Pregabalin's safety and efficacy in patients younger than 18 years have not been established.

The hemodynamic stability action of oral Clonidine group during the present study may be explained by several mechanisms, such as activation of central α2‑adrenoceptors, which causes both a decrease in peripheral sympathetic tone and an increase in vagally induced reflex bradycardia. Moreover, stimulation of peripheral presynaptic adrenoceptors leads to a diminished release of norepinephrine from the nerve endings toward the vasculature and thereby reduces the peripheral sympathetic tone.

Pregabalin, an antiepileptic drug, is efficient in regulating the neuropathic element of acute nociceptive surgical pain by inhibiting the membrane voltage-gated calcium channels. It does not interact with receptors of GABA. Its analgesic, anticonvulsant, and anxiolytic properties makeas it a beneficial oral premedicant.

Several mechanisms may contribute to the attenuation of pressor response by Pregabalin, which include the modulation of visceral pain and central nervous system sensitization. Pregabalin inhibits membrane voltage‑dependent Calcium channels acting in a manner similar to calcium channel blockers in controlling the hemodynamic response . Memis and colleagues[34] reported that the inhibitions of

Calcium efflux from muscle cells with a consequent smooth muscle relaxation which might explain the effectiveness of gabapentinoids in the relaxation of laryngoscopy.

In our study, without any significant respiratory depression , we observed the anxiolytic and sedative effects of oral premedication. Laryngoscopy and endotracheal intubation's hemodynamic responses were better attenuated by oral Clonidine than oral Pregabalin as premedication. The rise in hemodynamic factors in Pregabalin may be due to insufficient sedation and analgesia. Near stable hemodynamic factors and lack of any sympatho-somatic response with oral Clonidine in this study indicated of adequate analgesia and sedation.

Gupta K et al[16] concluded that Oral premedication with Pregabalin 150 mg or Clonidine 200mcg resulted in a clear increase in sedation and a moderate reduction in anxiety compared to control. According to them Clonidine was found superior to Pregabalin for attenuation of the haemodynamic stress responses to laryngoscopy and tracheal intubation but with increased incidence of intra-and postoperative bradycardia. Postoperative side effects in premedicated patients were not noted. In our study , we found Clonidine to be superior to Pregabalin in attenuating both heart rate and blood pressure thereby reducing the pressor effect during laryngoscopy and intubation, however did not encounter any cases with intra or postoperative bradycardia in both the groups.

Archana et al[19] in there study compared Pregabalin with Clonidine , which showed Clonidine was better in attenuation of heart rate response. Pregabalin attenuates haemodynamic response to laryngoscopy and endotracheal intubation in a dose response manner. Pregabalin in a dose of 150 mg administered 60 to 90 minutes prior to surgery and it was found to effectively attenuate the rise in SBP, DBP and MAP at 1, 3, 5 and 10 minutes after laryngoscopy and intubation, similarly in our

study Clonidine showed a better response than Pregabalin at 1, 3, 5 and 10 minutes after laryngoscopy and tracheal intubation.

In our study, 1min after tracheal intubation HR in the Pregabalin group was (95.71±9.818) while in the Clonidine group was (91.82±11.360) which shows there was a significant difference between two groups which showed Clonidine had a better hemodynamic attenuating capacity than Pregabalin. There was good surgical and post extubation control on HR in both groups. 1 min after laryngoscopy MAP was 104.51±4.702 in the Pregabalin group and 100.84±5.744 in the Clonidine group which shows both drugs are excellent for hemodynamic stability during laryngoscopy, however Clonidine had a stronger attenuating effect. Both drugs had sedative and analgesic action. There were no obvious side effecs in any group in post-operative ward such as respiratory depression, hypotension or bradycardia.

The present study showed that the preoperative administration of oral Pregabalin 75 mg or oral Clonidine 300 mcg has significantly reduced the intraoperative heart rate, mean arterial blood pressure values during direct laryngoscopy, and endotracheal intubation.

Similar to our study, Khan AA et al [20] ,Saini V et al and Ahmed B A et al[36] have used oral Clonidine and oral Pregabalin for premedication in the dose of 300mcg & 75mg respectively 120min before intubation and the results showed that Clonidine attenuated the hemodynamic stress better than Pregabalin.

Our study results are also in agreement with the studies by Rastogi et al[17] , Parveen.S et al[23] who demonstrated that hemodynamic pressor response of tracheal intubation attenuated by the use of premedication with oral Pregabalin or Clonidine. Greater hemodynamic stability was found with the use of Clonidine and this as well is in agreement with our work.

LIMITATIONS OF THE PRESENT STUDY

The limitations of the present study include

1) Stress mediators such as endogenous plasma catecholamines or cortisol were not measured. As they are the mediators of hemodynamic response, measuring their plasma levels would give greater credibility to this study and would help in understanding the exact mechanism of action of Pregabalin in attenuating hemodynamic stress
2) our study did not consider to evaluate the adverse effects of both drugs Clonidine and Pregabalin
3) The interactions of Clonidine and Pregabalin with other drugs and anaesthetic agents have not been considered.

SUMMARY

This study entitled **"A STUDY OF THE EFFECTIVENESS OF ORAL CLONIDINE AND ORAL PREGABALIN IN ATTENUATING THE HEMODYNAMIC PRESSOR RESPONSE DURING LARYNGOSCOPY AND TRACHEAL INTUBATION"** was conducted to compare the attenuation of hemodynamic response to laryngoscopy and intubation 90 patients of ASA grade 1 and 2 in the age group of 18 to 60 years of both gender were included in the study and were randomly divided into two groups of 45 each.

Group C received Clonidine 300mcg and Group P received Pregabalin 75mg orally with sips of water 120min before induction. Both groups were managed with same anaesthetic protocol. Hemodynamic variables like HR, SBP, DBP, MAP and RPP were recorded Base line, After study drug at 30 min, at 60 min,at 90 min, Before induction, during laryngoscopy and at 1,5,10 and 15 mins after intubation. Any undesirable effects of the drug were looked for.

In this study it was observed that oral Clonidine significantly attenuated the HR, SBP, DBP, MAP and RPP than oral Pregabalin due to laryngoscopy and endotracheal intubation

It was concluded that the hemodynamic response to laryngoscopy and endotracheal intubation are potentially harmful and methods to attenuate these responses have been sought particularly in high risk patients. The advantages of using Pregabalin or Clonidine premedication for attenuation of cardiovascular responses to the laryngoscopy are easy administration and availability with low price. Thus in our study, oral Clonidine 300 mcg 120min before anaesthesia, provided good attenuation of haemodynamic response to laryngoscopy and intubation as compared to oral Pregabalin 75mg.

CONCLUSION

Clonidine and Pregabalin is emerging as an efficient, safe and cheap drug to attenuate the hemodynamic pressor response during laryngoscopy and tracheal intubation From the present study it can be concluded that a single ,oral dose of Clonidine (300mcg) compared to single, oral dose of Pregabalin(75mg) given 120min preoperatively successfully attenuates the hemodynamic response associated with direct laryngoscopy and tracheal intubation.

BIBLIOGRAPHY

1. Kovac AL, et al. controlling the hemodynamic response to laryngoscopy and endotracheal intubation. J Clin Anesth 1996; 8: 63–79
2. Wycoff, C.O.: Endotracheal intubation: Effects on blood pressure and pulse rate. Anesthesiology, 1960, 21:153.
3. Fassoulaki A, Kaniasis P. Intranasal administration of nitroglycerine attenuatesthe pressor response to laryngoscopy & intubation of trachea. BJA 1983;55:49-52.
4. Mikawa K et al. The effect of diltiazem on the cardiovascular response to tracheal intubation. Anaesthesia 1990; 45:289-93.
5. Stoelting RK: Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation: influence of duration of laryngoscopy with or without prior lignocaine. Anesthesiology, 1977, 47:381-384.
6. Stoelting RK: Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lignocaine. Anaesthesia and analgesia, 1978, 57: 197-199.
7. Ghignone M, Quintin L, Duke PC, Kehler CH, Calvillo O. Effects of Clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology. 1986 Jan;64(1):36-42
8. Thompson JP, Hall AP, Russell J, Cagney B, Rowbotham DJ. Effect of remifentanil on the haemodynamic response to orotracheal intubation. Br J Anaesth 1998; 80: 467–9.
9. Vucevic M, Durdy G M, Ellis F R. Esmolol hydrochloride for management of thecardiovascular stress responses to laryngoscopy & tracheal

intubation. BJA1992; 68:529-30.

10. Coleman, K.S., Jordan,C.: Cardiovascular response to anesthesia: Influence of beta- adrenergic receptor blockade with metoprolol. Anesthesia, 35:972, 1980.
11. Zalunardo MP, Zollinger A, Spahn DR, et al. Effect of intravenous and oral Clonidine on hemodynamic and plasmacatecholamine response due toendotracheal intubation. J Clin Anesth 1997;9:143–7.
12. Burstein C. L., Lopinto F. J., Newman, W.: Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine techniques. Anesthesiology, 11: 224, 1950
13. King BD, Harris LC, Greifenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology: The Journal of the American Society of Anesthesiologists.1951Sep1;12(5):556-66.
14. Laurito CE, Baughman VL, Becker GL, Cunningham F, Pygon BH, Citron GM. Oral Clonidine blunts the hemodynamic responses to brief but not prolonged laryngoscopy. Journal of clinical anesthesia. 1993 Jan 1;5(1):54-7.
15. Gupta K, Bansal P, Gupta PK, Singh YP. Pregabalin premedication-A new treatment option for hemodynamic stability during general anesthesia: A prospective study. Anesthesia, essays and researches. 2011 Jan;5(1):57.
16. Gupta K, Sharma D, Gupta PK. Oral premedication with Pregabalin or Clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy: A comparative evaluation. Saudi journal of anaesthesia. 2011 Apr;5(2):179.
17. Rastogi B, Gupta K, Gupta PK, Agarwal S, Jain M, Chauhan H. Oral

Pregabalin premedication for attenuation of haemodynamic pressor response of airway instrumentation during general anaesthesia: A dose response study. Indian journal of anaesthesia. 2012 Jan;56(1):49.

18. Sundar AS, Kodali R, Sulaiman S, Ravullapalli H, Karthekeyan R, Vakamudi M. The effects of preemptive Pregabalin on attenuation of stress response to endotracheal intubation and opioid-sparing effect in patients undergoing off-pump coronary artery bypass grafting. Annals of cardiac anaesthesia. 2012 Jan 1;15(1):18.
19. Raichurkar A, Dinesh K, Ravi M, Talikoti AT, Somasekharam P. A comparative study of oral Pregabalin and Clonidine for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation. J Clin Biomed Sci. 2015;5:25-9.
20. Khan AA, Gani S, Munshi FA, Saleem B, Hameed S, Rather MA. A comparative trial studying the effectiveness of oral Clonidine and Pregabalin premedication in attenuation of haemodynamic response following laryngoscopy and endotracheal intubation. Journal of evolution of medical science2015. 2015 May 21:7134-43.
21. Chaudhary A, Sanghvi K, Parikh H. Oral premedication with Pregabalin and Clonidine for haemodynamic stability during laryngoscopy: A comparative study. Int J Basic Clin Pharmacol. 2015;4:294-9.
22. Bahgat NM, Sadik SA, Mahdy WR, El-Sharkawy OA, Metwally AA, El-Shafey MK. The effects of using Pregabalin versus Clonidine premedication in laparoscopic cholecystectomy. Menoufia Medical Journal. 2016 Jul 1;29(3):530.
23. Parveen S, Negi DS, Kumar R, Bagwan MC. Oral Clonidine vs oral

Pregabalin premedication to attenuate pressor response to direct laryngoscopy in patients undergoing laparoscopic cholecystectomy: a randomized double blind study. Journal of clinical and diagnostic research: JCDR. 2016 Sep;10(9):UC21.

24. Waikar C, Singh J, Gupta D, Agrawal A. Comparative study of oral gabapentin, Pregabalin, and Clonidine as premedication for anxiolysis, sedation, and attenuation of pressor response to endotracheal intubation. Anesthesia, essays and researches. 2017 Jul;11(3):558.
25. Williams, Warwick. Gray's anatomy. 36th ed, Edinburgh Churchill Livingstone 2000
26. Reid LC, Brace DE. Irritation of the respiratory tract and its reflex effect upon the heart. Surg Gynecol Obstet. 1940 Feb;70:157-62.
27. Russell WJ, DREW S, MORRIS R, FREWIN D. Changes in plasma catecholamine concentrations during endotracheal intubation. British Journal of Anaesthesia. 1981 Aug 1;53(8):837-9.
28. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. BJA: British Journal of Anaesthesia. 1970 Jul 1;42(7):618-24.
29. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. British journal of anaesthesia. 1987 Mar 1;59(3):295-9.
30. Emilio B. Lobato, Nikolaus Gravenstein, Robert R. Kirby Complications in Anaesthesiology April 2008; 55 (4) pp 258-258.
31. Robert K stoeting, Simon C Hiller Pharmacology and Physiology in anaesthesia practice 4th edition chapter 15 antihypertensivedrugs page no 340-

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32. Ben-Menachem E. Pregabalin pharmacology and its relevance to clinical practice. Epilepsia. 2004:45:13-8.
33. Hassan HG, El-Sharkawy TY, Renck H, Mansour G, Fouda A. Hemodynamic and catecholamine responses to laryngoscopy with vs. without endotracheal intubation. Acta anaesthesiologica scandinavica. 1991 Jul;35(5):442-7.
34. .Memiş D, Turan A, Karamanlıoğlu B, Şeker Ş, Türe M. Gabapentin reduces cardiovascular responses to laryngoscopy and tracheal intubation. European journal of anaesthesiology. 2006 Aug;23(8):686-90.
35. Laisalmi M, Koivusalo AM, Valta P, Tikkanen I, Lindgren L. Clonidine provides opioid-sparing effect, stable hemodynamics, and renal integrity during laparoscopic cholecystectomy. Surgical endoscopy. 2001 Nov 1;15(11):1331-5.
36. Rathore P, Saini V, Ahmed F, Chatterjee R, Rathore M. A COMPARATIVE STUDY OF ORAL CLONIDINE VERSUS ORAL PREGABALIN ON HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION UNDER GENERAL ANAESTESIA. International Journal of Medical and Biomedical Studies. 2019 May 1;3(4).

ANNEXURE – I

ETHICAL CLEARANCE CERTIFICATE

ANNEXURE – II

INFORMED CONSENT FORM

TITLE OF THE PROJECT: "A STUDY OF THE EFFECTIVENESS OF ORAL CLONIDINE AND ORAL PREGABALIN IN ATTENUATING THE HEMODYNAMIC PRESSOR RESPONSE DURING LARYNGOSCOPY AND TRACHEAL INTUBATION"

PRINCIPAL INVESTIGATOR :

PG GUIDE :

I have been informed that this study is **"A STUDY OF THE EFFECTIVENESS OF ORAL CLONIDINE AND ORAL PREGABALIN IN ATTENUATING THE HEMODYNAMIC PRESSOR RESPONSE DURING LARYNGOSCOPY AND TRACHEAL INTUBATION"** . 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 audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time and 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 WITHDRAWL 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 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 :

(Guide) (Investigator)

ANNEXURE – III

PROFORMA

STUDY:**"A STUDY OF THE EFFECTIVENESS OF ORAL CLONIDINE AND ORAL PREGABALIN IN ATTENUATING THE HEMODYNAMIC PRESSOR RESPONSE DURING LARYNGOSCOPY AND TRACHEAL INTUBATION."**

Name of the patient : I.P. No.:

Age : sex:

M	F

Weight : Date of Admission:

Diagnosis& Planned surgery:

Consent for study taken:

Y	N

Group

C	P

allocated

Pre anaesthetic evaluation :

Chief complaints :

Past History :

a) Presence of any comorbid condition - Diabetes/ Hypertension/ Ischemic heart disease/ Cerebrovascular accident / Asthma/ Epilepsy/ Bleeding disorder/ Drug allergy/ any other .

b) Drug Therapy

c) H/o previous anaesthetic exposure :

Family History :

General Physical Examination:

- General condition :
- Pallor / Icterus / Cyanosis / Clubbing / Lympadenopathy / Pedal edema.
- Temperature:
- Pulse rate:
- Respiratory rate:
- Blood Pressure :

AIRWAY ASSESSMENT:

- Mallampati grade

Systemic Examination :

- CVS
- RS
- CNS
- Others

Investigations :

- Complete blood picture
- Total Leucocyte count :
- Differential count :
    - Neutrophils :
    - Lymphocytes :
    - Basophils :
    - Eosinophils :
    - Monocytes :
- Platelet count :
- Random Blood sugar :
- Urine routine:
- ECG:
- Chest X ray(if needed) :
- Any other :

ASA GRADING

Diagnosis:

ANAESTHESIA PROTOCOL:

- PREMEDICATION
- INDUCTION
- LARYNGOCOPY DURATION

Hemodynamic Variables:

	HR	**SBP**	**DBP**	**MAP**	**RPP**
BEFORE STUDY DRUG					
AT 30 MIN					
AT 60 MIN					
AT 90 MIN					
BEFORE INDUCTION					
DURING LARYNGOSCOPY					
1 MIN AFTER INTUBATION					
5 MIN AFTER INTUBATION					
10 MIN AFTER INTUBATION					
15 MIN AFTER INTUBATION					

Signature of Anaesthesiologist

Name:

Designation:

KEY WORDS TO MASTERCHART

Wt	:	weight
ASA	:	American Society of Anaesthesiologist
HR	:	Heart Rate
SBP	:	Systolic Blood Pressure
DBP	:	Diastolic Blood Pressure
MAP	:	Mean Arterial Pressure
RPP	:	Rate Pressure Product

MASTER CHART

Group C					PAC					BEFORE STUDY DRUG					AT 30 MIN of DRUG					AT 60 MIN of DRUG					AT 90 MIN OF DRUG					BEFORE INDUCTION				
SR.NO	AGE (Yr)	GENDER	WT (KG)	ASA GRADE	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
1	17	F	49	I	82	130	80	96.67	10660	80	124	78	93.333	9920	72	118	74	88.67	8496	76	118	76	90.00	8968	74	120	78	92.00	8880	78	118	80	92.667	9204
2	58	M	60	I	80	120	80	93.33	9600	84	132	82	98.667	11088	78	120	78	92.00	9360	78	120	80	93.33	9360	78	118	70	86.00	9204	76	108	68	81.333	8208
3	20	M	52	II	84	116	70	85.33	9744	80	114	70	84.667	9120	76	114	68	83.33	8664	76	116	70	85.33	8816	76	116	74	88.00	8816	76	114	76	88.667	8664
4	27	M	62	I	82	130	82	98	10660	88	116	72	86.667	10208	82	120	78	92.00	9840	80	120	78	92.00	9600	76	120	70	86.67	9120	74	118	80	92.667	8732
5	30	M	50	I	78	108	66	80	8424	90	120	80	93.333	10800	84	106	64	78.00	8904	84	108	60	76.00	9072	78	108	78	88.00	8424	80	108	78	88.000	8640
6	58	F	65	I	72	122	74	90	8784	92	124	78	93.333	11408	86	120	72	88.00	10320	86	118	72	87.33	10148	80	114	78	90.00	9120	80	116	78	90.667	9280
7	32	F	60	II	72	110	70	83.33	7920	70	124	82	96.000	8680	64	120	78	92.00	7680	66	114	78	90.00	7524	62	120	80	93.33	7440	68	118	80	92.667	8024
8	38	F	55	I	82	100	62	74.67	8200	80	112	68	82.667	8960	74	100	64	76.00	7400	76	100	60	73.33	7600	76	110	74	86.00	8360	74	110	64	79.333	8140
9	53	F	62	I	78	120	80	93.33	9360	76	118	70	86.000	8968	70	118	80	92.67	8260	72	120	80	93.33	8640	76	110	78	88.67	8360	72	110	80	90.000	7920
10	29	M	86	I	76	112	78	89.33	8512	80	122	78	92.667	9760	74	112	74	86.67	8288	72	114	76	88.67	8208	74	116	76	89.33	8584	74	112	80	90.667	8288
11	28	F	65	I	86	130	80	96.67	11180	90	132	80	97.333	11880	84	120	78	92.00	10080	80	114	78	90.00	9120	80	114	70	84.67	9120	78	114	68	83.333	8892
12	18	F	50	I	92	114	76	88.67	10488	94	116	74	88.000	10904	88	114	68	83.33	10032	84	112	70	84.00	9408	84	112	70	84.00	9408	84	112	70	84.000	9408
13	40	F	60	I	68	120	80	93.33	8160	72	124	82	96.000	8928	64	116	78	90.67	7424	66	116	78	90.67	7656	62	120	78	92.00	7440	66	118	78	91.333	7788
14	28	F	42	I	72	117	72	87	8424	72	120	80	93.333	8640	68	114	76	88.67	7752	70	114	74	87.33	7980	72	114	78	90.00	8208	70	114	76	88.667	7980
15	30	F	55	I	88	120	80	93.33	10560	82	116	68	84.000	9512	74	114	68	83.33	8436	76	112	66	81.33	8512	74	112	62	78.67	8288	74	112	68	82.667	8288
16	29	F	55	I	78	110	62	78	8580	72	116	68	84.000	8352	76	114	68	83.33	8664	76	110	66	80.67	8360	72	114	74	87.33	8208	74	100	68	78.667	7400
17	45	F	50	I	66	96	60	72	6336	78	100	60	73.333	7800	72	100	60	73.33	7200	74	112	60	77.33	8288	74	110	70	83.33	8140	78	110	70	83.333	8580
18	45	F	54	I	60	98	64	75.33	5880	74	100	62	74.667	7400	68	100	60	73.33	6800	68	110	60	76.67	7480	70	110	68	82.00	7700	74	110	70	83.333	8140
19	47	M	64	I	88	112	62	78.67	9856	86	110	60	76.667	9460	80	110	62	78.00	8800	84	110	62	78.00	9240	78	114	74	87.33	8892	76	108	70	82.667	8208
20	37	F	70	I	70	114	70	84.67	7980	78	112	72	85.333	8736	72	114	70	84.67	8208	74	112	70	84.00	8288	74	110	70	83.33	8140	72	108	68	81.333	7776
21	25	F	54	I	84	102	72	82	8568	78	100	70	80.000	7800	74	112	72	85.33	8288	76	114	68	83.33	8664	78	112	74	86.67	8736	74	110	70	83.333	8140
22	49	F	56	I	72	124	82	96	8928	70	118	76	90.000	8260	64	118	78	91.33	7552	64	118	78	91.33	7552	66	118	78	91.33	7788	62	118	74	88.667	7316
23	35	F	74	I	66	126	84	98	8316	82	118	74	88.667	9676	78	114	72	86.00	8892	76	110	68	82.00	8360	76	114	72	86.00	8664	90	114	72	86.000	10260
24	60	M	55	II	80	140	90	106.7	11200	86	140	90	106.667	12040	80	126	84	98.00	10080	80	124	80	94.67	9920	78	126	80	95.33	9828	84	130	82	98.000	10920
25	41	F	40	I	78	110	70	83.33	8580	82	120	74	89.000	9840	76	116	72	86.67	8816	76	116	68	84.00	8816	78	114	70	84.67	8892	82	116	72	86.667	9512

Group C					PAC					BEFORE STUDY DRUG					AT 30 MIN of DRUG					AT 60 MIN of DRUG					AT 90 MIN OF DRUG					BEFORE INDUCTION				
SR.NO	AGE (Yr)	GENDER	WT (KG)	ASA GRADE	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
26	18	F	60	II	78	100	70	80	7800	82	110	70	83.000	9020	74	110	70	83.33	8140	76	108	68	81.33	8208	76	106	68	80.67	8056	76	112	68	82.667	8512
27	33	F	52	i	78	110	70	83.33	8580	100	132	84	100.000	13200	90	124	80	94.67	11160	88	124	78	93.33	10912	88	120	78	92.00	10560	80	124	78	93.333	9920
28	24	F	48	I	100	114	68	83.33	11400	112	100	70	80.000	11200	80	110	72	84.67	8800	94	100	68	78.67	9400	88	116	78	90.67	10208	78	118	76	90.000	9204
29	36	F	55	I	90	123	74	90.33	11070	88	119	80	93.000	10472	82	116	78	90.67	9512	84	120	80	93.33	10080	82	112	72	85.33	9184	60	120	80	93.333	7200
30	35	F	63	I	70	118	72	87.33	8260	76	118	70	86.000	8968	72	114	70	84.67	8208	74	112	68	82.67	8288	78	116	74	88.00	9048	78	116	72	86.667	9048
31	18	M	60	I	66	114	76	89	7524	70	118	74	87.000	8260	64	110	72	84.67	7040	64	108	70	82.67	6912	64	108	70	82.67	6912	66	114	70	84.667	7524
32	25	M	64	II	78	118	78	91.33	9204	80	108	72	84.000	8640	74	110	70	83.33	8140	76	100	70	80.00	7600	88	110	74	86.00	9680	76	118	78	91.333	8968
33	45	F	52	I	62	124	80	94.67	7688	68	122	80	94.000	8296	60	116	78	90.67	6960	60	120	76	90.67	7200	64	114	60	78.00	7296	78	110	70	83.333	8580
34	40	F	48	I	82	126	82	96.67	10332	80	120	86	97.333	9600	76	118	84	95.33	8968	78	118	80	92.67	9204	80	112	74	86.67	8960	74	112	70	84.000	8288
35	18	M	60	I	72	118	78	91.33	8496	70	116	76	89.333	8120	70	110	68	82.00	7700	70	110	70	83.33	7700	74	110	72	84.67	8140	72	108	68	81.333	7776
36	23	F	50	I	94	116	76	89.33	10904	98	112	70	84.000	10976	80	106	70	82.00	8480	90	108	68	81.33	9720	88	110	72	84.67	9680	78	118	72	87.333	9204
37	24	F	50	I	90	120	80	93.33	10800	90	124	84	97.333	11160	78	112	78	89.33	8736	74	118	74	88.67	8732	76	112	78	89.33	8512	82	126	80	95.333	10332
38	60	F	75	II	66	140	90	106.7	9240	68	140	90	106.667	9520	76	126	88	100.67	9576	70	126	82	96.67	8820	66	124	80	94.67	8184	78	136	88	104.000	10608
39	38	M	78	I	76	144	90	108	10944	80	138	84	102.000	11040	78	120	78	92.00	9360	70	122	78	92.67	8540	74	118	74	88.67	8732	74	128	80	96.000	9472
40	40	F	52	I	84	116	70	85	9744	80	122	78	92.667	9760	78	114	80	91.33	8892	78	118	78	91.33	9204	82	114	74	87.33	9348	78	116	70	85.333	9048
41	34	M	63	I	86	122	78	93	10492	84	120	80	93.333	10080	76	112	78	89.33	8512	80	118	76	90.00	9440	76	114	72	86.00	8664	78	100	70	80.000	7800
42	20	M	55	II	76	136	82	100	10336	78	130	82	98.000	10140	72	110	80	90.00	7920	74	122	78	92.67	9028	76	124	80	94.67	9424	78	112	72	85.333	8736
43	18	F	60	I	88	122	80	94	10736	80	122	80	94.000	9760	74	114	78	90.00	8436	78	108	68	81.33	8424	76	118	78	91.33	8968	78	120	78	92.000	9360
44	26	M	64	I	68	110	70	83	7480	68	118	72	87.333	8024	68	114	72	86.00	7752	74	112	70	84.00	8288	74	114	70	84.67	8436	80	124	68	86.667	9920
45	32	M	62	I	82	100	60	73	8200	80	118	68	84.667	9440	78	112	68	82.67	8736	78	114	70	84.67	8892	82	110	78	88.67	9020	78	116	78	90.667	9048

	DURING LARYNGOSCOPY (GROUP C)					AFTER INTUBATION (GROUP C)																		
SR.NO	0 MIN					1 MIN					5 MIN					10 MIN					15 MIN				
	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
1	90	134	86	102.000	12060	88	130	82	98.00	11440	78	116	74	88.00	9048	78	108	74	85.33	8424	74	98	76	83.333	7252
2	88	136	86	102.667	11968	88	134	88	103.33	11792	82	114	74	87.33	9348	80	108	72	84.00	8640	76	102	74	83.333	7752
3	90	120	80	93.333	10800	90	124	84	97.33	11160	80	110	76	87.33	8800	78	106	74	84.67	8268	74	100	78	85.333	7400
4	88	122	82	95.333	10736	90	124	84	97.33	11160	82	118	72	87.33	9676	80	110	70	83.33	8800	76	100	74	82.667	7600
5	80	128	84	98.667	10240	82	128	84	98.67	10496	78	110	70	83.33	8580	76	102	68	79.33	7752	74	93	78	83	6882
6	84	136	90	105.333	11424	94	140	84	102.67	13160	84	114	70	84.67	9576	82	108	66	80.00	8856	78	100	76	84	7800
7	84	128	78	94.667	10752	78	124	78	93.33	9672	80	110	68	82.00	8800	72	104	65	78.00	7488	75	102	54	70	7650
8	88	120	80	93.333	10560	82	128	80	96.00	10496	76	110	74	86.00	8360	72	104	66	78.67	7488	70	98	74	82	6860
9	86	136	82	100.000	11696	90	130	88	102.00	11700	82	114	74	87.33	9348	80	108	68	81.33	8640	74	100	78	85.333	7400
10	78	122	84	96.667	9516	82	120	84	96.00	9840	76	114	74	87.33	8664	74	104	68	80.00	7696	70	98	74	82	6860
11	100	128	86	100.000	12800	98	130	84	99.33	12740	90	112	70	84.00	10080	88	104	68	80.00	9152	80	96	76	82.667	7680
12	80	142	88	106.000	11360	82	134	88	103.33	10988	76	110	74	86.00	8360	72	100	68	78.67	7200	70	94	78	83.333	6580
13	76	128	78	94.667	9728	78	130	78	95.33	10140	74	108	70	82.67	7992	72	102	66	78.00	7344	68	100	76	84	6800
14	78	140	90	106.667	10920	82	140	88	105.33	11480	74	114	78	90.00	8436	72	108	68	81.33	7776	70	102	76	84.667	7140
15	80	130	82	98.000	10400	84	128	82	97.33	10752	76	114	72	86.00	8664	74	106	70	82.00	7844	70	98	78	84.667	6860
16	82	134	86	102.000	10988	82	134	86	102.00	10988	74	116	72	86.67	8584	72	104	74	84.00	7488	70	96	76	82.667	6720
17	78	124	82	96.000	9672	80	130	80	96.67	10400	72	118	70	86.00	8496	72	110	72	84.67	7920	68	100	74	82.667	6800
18	70	126	80	95.333	8820	72	120	80	93.33	8640	72	112	72	85.33	8064	70	104	72	82.67	7280	66	94	72	79.333	6204
19	100	138	90	106.000	13800	104	134	80	98.00	13936	90	110	72	84.67	9900	88	106	78	87.33	9328	78	96	80	85.333	7488
20	88	120	68	85.333	10560	94	128	78	94.67	12032	82	114	70	84.67	9348	78	106	70	82.00	8268	78	98	70	79.333	7644
21	80	142	90	107.333	11360	82	140	88	105.33	11480	76	114	72	86.00	8664	74	108	78	88.00	7992	72	100	80	86.667	7200
22	78	124	82	96.000	9672	78	128	84	98.67	9984	74	108	70	82.67	7992	72	104	74	84.00	7488	68	98	76	83.333	6664
23	102	138	90	106.000	14076	106	140	90	106.67	14840	90	116	72	86.67	10440	88	106	78	87.33	9328	80	100	78	85.333	8000
24	98	138	90	106.000	13524	100	140	88	105.33	14000	84	120	78	92.00	10080	78	118	74	88.67	9204	78	100	74	89	7800
25	110	136	80	98.667	14960	106	136	78	97.33	14416	94	122	74	90.00	13000	86	120	72	88.00	10320	86	102	74	89	10800

	DURING LARYNGOSCOPY (GROUP C)					AFTER INTUBATION (GROUP C)																			
SR.NO	0 MIN					1 MIN					5 MIN					10 MIN					15 MIN				
	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
26	96	132	84	100.000	12672	98	136	88	104.00	13328	82	124	76	92.00	10920	74	120	74	89.33	8880	76	106	74	89	9360
27	98	140	90	106.667	13720	100	140	90	106.67	14000	86	125	76	92.33	11880	88	118	70	86.00	10384	80	108	76	89	9348
28	70	122	80	94.000	8540	78	126	82	96.67	9828	70	109	74	85.67	7630	70	100	70	80.00	7000	66	90	78	82	5940
29	100	120	80	93.333	12000	98	124	82	96.00	12152	86	112	72	85.33	9632	84	109	70	83.00	9156	80	100	74	82.667	8000
30	70	130	70	90.000	9100	72	124	72	89.33	8928	70	112	68	82.67	7840	68	102	68	79.33	6936	66	94	70	78	6204
31	80	120	76	90.667	9600	84	124	78	93.33	10416	72	114	70	84.67	8584	68	108	68	81.33	7344	66	100	70	80.6	7140
32	90	128	84	98.667	11520	98	128	88	101.33	12544	82	112	78	89.33	10320	78	112	70	84.00	8736	72	102	70	84	8288
33	114	138	86	103.333	15732	110	138	88	104.67	15180	90	114	74	87.33	10260	92	106	70	82.00	9752	86	98	74	82	8428
34	90	148	92	110.667	13320	94	140	90	106.67	13160	86	118	76	90.00	10148	86	108	68	81.33	9288	80	100	78	85.333	8000
35	78	128	82	97.333	9984	80	126	78	94.00	10080	82	108	74	85.33	8856	72	102	70	80.67	7344	70	94	76	82	6580
36	90	120	76	90.667	10800	94	126	78	94.00	11844	86	110	72	84.67	9460	84	106	72	83.33	8904	78	98	72	80.667	7644
37	94	130	84	99.333	12220	96	132	84	100.00	12672	88	118	78	91.33	10384	84	120	70	86.67	10080	78	104	74	84	8112
38	90	148	88	108.000	13320	94	142	82	102.00	13348	82	128	78	94.67	10496	78	124	74	90.67	9672	78	110	80	90	8580
39	96	142	96	111.333	13632	94	140	90	106.67	13160	84	130	84	99.33	10920	78	122	80	94.00	9516	74	110	80	90	8140
40	102	156	100	118.667	15912	106	144	90	108.00	15264	94	124	84	97.33	11656	88	124	82	96.00	10912	88	108	80	89.333	9504
41	116	168	102	124.000	19488	110	150	90	110.00	16500	96	126	90	102.00	12096	90	128	84	98.67	11520	90	114	84	94	10260
42	100	158	96	116.667	15800	98	144	90	108.00	14112	90	124	82	96.00	11160	88	122	84	96.67	10736	82	112	76	88	9184
43	116	176	112	133.333	20416	110	160	96	117.33	17600	94	130	100	110.00	12220	90	128	86	100.00	11520	88	116	86	96	10208
44	116	160	90	113.333	18560	112	148	90	109.33	16576	98	118	78	91.33	11564	92	122	78	92.67	11224	92	110	78	88.667	10120
45	112	150	85	106.667	16800	118	140	90	106.67	15960	94	124	88	100.00	11656	94	124	84	94.67	11656	94	116	80	92	10904

Group G					PAC					BEFORE STUDY DRUG					AT 30 MIN of DRUG					AT 60 MIN of DRUG					At 90 MIN of DRUG					BEFORE INDUCTION				
SR.NO	AGE (Yr)	GENDER	WT (KG)	ASA GRADE	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
1	28	F	60	I	72	122	78	92.667	8784	70	116	76	89.333	8120	70	114	70	84.667	7980	72	112	72	85.333	8064	76	112	72	85.333	8512	74	108	68	81.3	7992
2	20	F	55	I	86	112	62	78.667	9632	86	110	60	76.667	9460	86	110	62	78	9460	88	110	62	78	9680	82	114	76	88.667	9348	78	110	70	83.3	8580
3	35	F	62	l	78	110	72	84.667	8580	72	110	70	83.333	7920	72	110	72	84.667	7920	72	122	70	87.333	8784	76	116	76	89.333	8816	78	100	70	80	7800
4	44	F	45	I	76	116	68	84	8816	80	116	68	84	9280	80	118	68	84.667	9440	80	114	66	82	9120	78	116	64	81.333	9048	76	114	68	83.3	8664
5	33	M	40	I	82	108	62	77.333	8856	78	112	68	82.667	8736	78	100	64	76	7800	78	100	62	74.667	7800	78	112	64	80	8736	78	110	64	79.3	8580
6	57	M	62	I	78	120	80	93.333	9360	74	118	70	86	8732	74	120	82	94.667	8880	76	122	84	96.667	9272	76	114	80	91.333	8664	76	114	80	91.3	8664
7	21	F	65	I	76	116	78	90.667	8816	78	122	78	92.667	9516	78	114	76	88.667	8892	76	116	78	90.667	8816	80	120	82	94.667	9600	78	116	80	92	9048
8	37	F	50	I	86	130	80	96.667	11180	90	132	80	97.333	11880	88	124	80	94.667	10912	86	124	80	94.667	10664	84	120	86	97.333	10080	80	118	68	84.7	9440
9	33	F	50	I	90	110	70	83.333	9900	100	116	74	88	11600	98	100	70	80	9800	98	110	70	83	10780	96	110	70	83.3	10560	90	108	70	83	9720
10	22	F	45	I	92	114	76	88.667	10488	94	116	74	88	10904	94	116	70	85.333	10904	92	118	72	87.333	10856	90	118	70	86	10620	88	116	70	85.3	10208
11	37	M	48	I	68	120	80	93.333	8160	66	124	82	96	8184	66	122	80	94	8052	66	120	80	93.333	7920	62	124	82	96	7688	68	120	80	93.3	8160
12	37	F	52	I	72	117	72	87	8424	70	120	80	93.333	8400	70	118	78	91.333	8260	72	116	76	89.333	8352	74	118	80	92.667	8732	72	116	78	90.7	8352
13	29	M	75	I	90	130	80	96.667	11700	76	128	78	94.667	9728	80	120	76	90.667	9600	84	126	80	95.333	10584	84	128	82	97.333	10752	77	113	68	83	8701
14	30	F	50	I	82	126	82	96.667	10332	80	120	86	97.333	9600	80	122	86	98	9760	80	120	84	96	9600	82	116	78	90.667	9512	76	112	72	85.3	8512
15	25	M	60	I	76	116	70	85.333	8816	78	120	70	86.667	9360	78	116	72	86.667	9048	80	112	70	84	8960	76	118	70	86	8968	78	120	70	86.7	9360
16	30	F	52	I	78	120	80	93.333	9360	80	118	82	94	9440	78	118	80	92.667	9204	76	118	80	92.667	8968	82	116	76	89.333	9512	82	116	76	89.3	9512
17	42	F	55	I	76	118	74	88.667	8968	74	118	72	87.333	8732	74	116	70	85.333	8584	76	114	70	84.667	8664	80	120	80	93.333	9600	80	116	72	86.7	9280
18	35	F	55	I	82	132	80	97.333	10824	96	124	78	93.333	11904	76	122	76	91.333	9272	76	122	78	92.667	9272	78	122	78	92.667	9516	78	120	80	93.3	9360
19	22	M	75	I	82	130	82	98	10660	88	116	72	86.667	10208	86	128	80	96	11008	86	128	80	96	11008	80	128	82	97.333	10240	76	120	80	93.3	9120
20	40	F	54	I	78	108	70	82.667	8424	90	120	80	93.333	10800	88	106	64	78	9328	88	108	60	76	9504	82	108	80	89.333	8856	82	110	78	88.7	9020
21	58	F	53	I	78	140	80	100	10920	72	120	70	86.667	8640	70	116	68	84	8120	72	110	62	78	7920	74	110	70	83.333	8140	76	112	70	84	8512
22	19	M	56	I	64	110	70	83.333	7040	76	110	60	76.667	8360	76	108	60	76	8208	78	112	62	78.667	8736	78	112	72	85.333	8736	80	112	70	84	8960
23	60	F	55	I	74	140	90	106.67	10360	76	112	72	85.333	8512	76	114	70	84.667	8664	74	114	72	86	8436	74	110	72	84.667	8140	74	108	70	82.7	7992
24	18	F	50	I	94	116	76	89.333	10904	98	112	70	84	10976	96	110	70	83.333	10560	94	110	70	83.333	10340	92	112	72	85.333	10304	88	118	72	87.3	10384
25	35	M	60	I	88	122	84	96.667	10736	80	118	74	88.667	9440	82	116	72	86.667	9512	80	112	70	84	8960	80	118	74	88.667	9440	94	116	72	86.7	10904

Group G					PAC					BEFORE STUDY DRUG					AT 30 MIN of DRUG					AT 60 MIN of DRUG					At 90 MIN of DRUG					BEFORE INDUCTION				
SR.NO	AGE (Yr)	GENDER	WT (KG)	ASA GRADE	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
26	35	M	57	I	62	124	80	94.667	7688	58	122	80	94	7076	58	120	80	93.333	6960	56	122	82	95.333	6832	60	118	60	79.333	7080	82	110	70	83.3	9020
27	23	F	65	I	96	120	80	93.333	11520	98	130	70	90	12740	98	132	70	90.667	12936	92	128	70	89.333	11776	90	126	70	88.667	11340	86	134	78	96.7	11524
28	35	F	50	I	90	110	70	83.333	9900	80	110	70	83.333	8800	80	108	66	80	8640	82	108	66	80	8856	80	110	68	82	8800	84	116	74	88	9744
29	25	F	65	I	72	130	70	90	9360	88	140	90	107	12320	88	138	88	104.67	12144	86	136	84	101.33	11696	88	134	82	99	11792	90	130	80	96.7	11700
30	50	M	60	II	78	110	70	83.333	8580	68	120	70	87	8160	66	116	68	84	7656	66	116	64	81.333	7656	64	114	62	79	7296	68	116	66	82.7	7888
31	32	F	41	I	92	130	80	96.667	11960	112	140	90	106.67	15680	100	130	84	99.333	13000	98	128	80	96	12544	96	120	80	93.333	11520	80	118	78	91.3	9440
32	38	M	50	I	90	123	82	95.667	11070	88	119	80	93	10472	86	120	80	93.333	10320	88	122	82	95.333	10736	82	116	74	88	9512	60	120	80	93.3	7200
33	38	M	55	I	84	116	70	85.333	9744	80	114	70	84.667	9120	80	116	70	85.333	9280	82	118	72	87.333	9676	80	118	78	91.333	9440	78	118	76	90	9204
34	18	M	53	I	72	122	78	92.667	8784	92	124	78	93.333	11408	90	122	74	90	10980	90	122	74	90	10980	86	120	80	93.333	10320	84	118	78	91.3	9912
35	57	F	50	I	90	110	68	82	9900	100	116	74	88	11600	98	100	70	80	9800	98	110	70	83.333	10780	96	110	70	83.333	10560	90	108	70	82.7	9720
36	46	M	70	I	84	102	72	82	8568	77	100	70	80	7700	77	112	72	85.333	8624	78	116	70	85.333	9048	80	114	76	88.667	9120	78	112	70	84	8736
37	49	M	66	II	72	124	82	96	8928	68	118	78	91.333	8024	66	120	80	93.333	7920	64	122	82	95.333	7808	66	122	80	94	8052	62	120	78	92	7440
38	52	F	60	I	62	130	90	103.33	8060	75	140	90	106.67	10500	72	136	84	101.33	9792	72	132	80	97.333	9504	70	130	80	96.667	9100	72	132	86	101	9504
39	30	F	55	I	90	110	70	83.333	9900	100	120	80	93.333	12000	98	120	78	92	11760	94	116	78	90.667	10904	90	116	78	90.667	10440	90	114	80	91.3	10260
40	36	M	55	I	76	110	70	83.333	8360	88	130	90	103.33	11440	85	126	84	98	10710	84	122	80	94	10248	80	120	80	93.333	9600	84	128	86	100	10752
41	24	F	56		88	130	80	96.667	11440	106	140	88	105.33	14840	98	134	84	100.67	13132	94	130	82	98	12220	90	126	82	96.667	11340	90	128	80	96	11520
42	27	F	70	II	74	110	70	83.333	8140	88	128	82	97.333	11264	86	124	82	96	10664	80	120	82	94.667	9600	80	120	80	93.333	9600	86	124	86	98.7	10664
43	35	F	60	I	94	120	74	89.333	11280	92	116	72	86.667	10672	90	116	70	85.333	10440	86	116	72	86.667	9976	80	112	72	85.333	8960	82	110	70	83.3	9020
44	18	M	50	I	72	128	88	101.33	9216	72	128	82	97.333	9216	68	124	80	94.667	8432	66	124	80	94.667	8184	66	120	80	93.333	7920	74	126	82	96.7	9324
45	32	M	56	I	80	120	80	93.333	9600	82	120	76	90.667	9840	76	116	76	89.333	8816	74	116	72	86.667	8584	72	118	70	86	8496	80	120	74	89.3	9600

SR.NO	DURING LARYNGOSCOPY(GROUP P)					AFTER INTUBATION (GROUP P)																			
	0 MIN					1 MIN					5 MIN					10 MIN					15 MIN				
	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
1	98	128	82	102.667	12544	80	126	80	95.3	10080	80	108	70	82.7	8640	72	104	60	74.7	7488	88	100	58	72	8800
2	100	140	90	104	14000	108	138	90	106	14904	94	117	68	84.3	10998	92	107	56	73	9844	84	109	60	76.3	9156
3	82	134	86	99.3333	10988	82	138	90	106	11316	76	114	72	86	8664	74	108	58	74.7	7992	72	99	62	74.3	7128
4	80	130	82	#REF!	10400	84	130	84	99.3	10920	74	116	78	90.7	8584	76	110	60	76.7	8360	84	100	56	70.7	8400
5	88	120	80	93.3333	10560	86	130	82	98	11180	76	114	77	89.3	8664	74	106	66	79.3	7844	70	100	62	74.7	7000
6	86	138	82	100.667	11868	90	140	90	107	12600	84	122	80	94	10248	82	114	64	80.7	9348	78	102	70	80.7	7956
7	78	122	84	96.6667	9516	82	124	86	98.7	10168	78	119	76	90.3	9282	76	112	66	81.3	8512	72	100	56	70.7	7200
8	100	130	86	100.667	13000	106	134	88	103	14204	96	116	80	92	11136	94	106	65	78.7	9964	84	96	60	72	8064
9	92	126	88	101	11776	94	128	86	100	12032	88	119	79	92	10472	86	109	78	88	9374	82	99	78	85	8118
10	80	146	88	107.333	11680	82	140	90	107	11480	78	114	72	86	8892	76	104	62	76	7904	74	94	50	64.7	6956
11	84	128	78	94.6667	10752	78	130	80	96.7	10140	82	116	70	85.3	9512	74	106	65	78.7	7844	77	104	54	70.7	8008
12	78	142	90	107.333	11076	82	146	92	110	11972	76	125	76	92.3	9500	74	115	74	87.7	8510	70	105	70	81.7	7350
13	100	150	90	110	15000	109	140	79	99.3	15260	95	120	80	93.3	11400	110	120	84	96	13200	100	113	78	89.7	11300
14	99	148	92	104	14652	94	150	94	113	14100	86	125	80	95	10750	86	115	76	89	9890	82	105	60	75	8610
15	110	160	88	112	17600	108	155	83	107	16740	100	132	74	93.3	13200	96	130	72	91.3	12480	92	124	72	89.3	11408
16	90	155	90	111.667	13950	94	150	86	107	14100	84	124	76	92	10416	82	120	78	92	9840	84	120	76	90.7	10080
17	70	130	70	90	9100	72	124	72	89.3	8928	70	114	70	84.7	7980	68	104	70	81.3	7072	66	94	70	78	6204
18	90	134	86	102	12060	88	134	80	98	11792	80	120	76	90.7	9600	78	110	78	88.7	8580	76	100	76	84	7600
19	88	124	82	96	10912	92	128	80	96	11776	84	122	74	90	10248	82	112	68	82.7	9184	78	102	74	83.3	7956
20	80	128	84	98.6667	10240	84	130	86	101	10920	78	114	79	90.7	8892	80	110	70	83.3	8800	74	110	78	88.7	8140
21	70	126	80	96.6667	8820	92	122	82	95.3	11224	72	116	74	88	8352	70	106	60	75.3	7420	66	96	60	72	6336
22	90	124	82	98.6667	11160	80	130	80	96.7	10400	74	122	77	92	9028	72	117	68	84.3	8424	68	102	74	83.3	6936
23	88	120	68	85.3333	10560	94	130	84	99.3	12220	86	120	74	89.3	10320	84	110	72	84.7	9240	80	100	70	80	8000
24	90	120	76	90.6667	10800	94	126	80	95.3	11844	88	116	74	88	10208	86	106	68	80.7	9116	80	100	72	81.3	8000
25	102	140	90	106.667	14280	110	142	92	109	15620	94	121	82	95	11374	92	111	50	70.3	10212	84	102	68	79.3	8568

SR.NO	DURING LARYNGOSCOPY(GROUP P)					AFTER INTUBATION (GROUP P)																			
	0 MIN					1 MIN					5 MIN					10 MIN					15 MIN				
	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP	HR	SYS BP	DIAST BP	MEAN BP	RPP
26	114	138	86	107.333	15732	114	140	90	107	15960	100	121	74	89.7	12100	94	116	70	85.3	10904	90	102	68	79.3	9180
27	96	146	80	102	14016	100	148	86	107	14800	82	132	80	97.3	10824	78	124	76	92	9672	70	118	70	86	8260
28	90	124	80	95	11160	91	136	86	103	12376	90	130	78	95.3	11700	86	126	74	91	10836	78	120	72	88	9360
29	110	140	90	107	15400	112	142	94	110	15904	100	136	84	101	13600	92	130	82	98	11960	88	122	80	94	10736
30	88	138	90	106	12144	86	140	92	108	12040	74	132	86	101	9768	72	124	80	95	8928	70	112	76	88	7840
31	88	122	80	94	10736	88	133	82	99	11704	72	109	78	88.3	7848	70	100	56	70.7	7000	66	90	78	82	5940
32	82	120	80	93.3333	9840	100	128	82	97.3	12800	90	119	74	89	10710	88	109	60	76.3	9592	84	104	74	84	8736
33	90	130	80	96.6667	11700	98	135	82	99.7	13230	82	110	78	88.7	9020	80	110	70	83.3	8800	76	104	78	86.7	7904
34	84	140	90	106.667	11760	96	146	90	109	14016	88	123	80	94.3	10824	86	113	74	87	9718	80	103	76	85	8240
35	92	128	88	101.333	11776	94	126	86	99.3	11844	88	119	79	92.3	10472	86	109	66	80.3	9374	82	99	72	81	8118
36	80	144	90	108	11520	82	142	90	107	11644	78	121	82	95	9438	76	111	60	77	8436	72	101	80	87	7272
37	78	124	82	96	9672	78	130	90	103	10140	74	112	78	89.3	8288	72	108	68	81.3	7776	68	98	76	83.3	6664
38	88	140	90	106.667	12320	96	144	92	109	13824	90	142	88	106	12780	80	136	82	100	10880	74	136	78	97.3	10064
39	102	130	88	102	13260	110	138	94	109	15180	98	134	90	105	13132	82	130	84	99.3	10660	76	122	78	92.7	9272
40	96	136	90	105.333	13056	100	140	90	107	14000	96	136	84	101	13056	90	128	80	96	11520	82	120	74	89.3	9840
41	94	130	88	102	12220	120	148	96	113	17760	116	140	94	109	16240	110	136	90	105	14960	94	130	82	98	12220
42	98	138	90	106	13524	114	146	94	111	16644	120	150	98	115	18000	104	142	90	107	14768	98	136	88	104	13328
43	84	114	74	87.3333	9576	90	124	80	94.7	11160	96	132	84	100	12672	96	136	88	104	13056	90	126	80	95.3	11340
44	86	134	88	103.333	11524	96	138	90	106	13248	88	130	82	98	11440	82	126	80	95.3	10332	76	124	78	93.3	9424
45	88	132	80	97.3333	11616	90	130	86	101	11700	84	126	80	95.3	10584	80	120	78	92	9600	76	110	70	83.3	8360