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Oral Clonidine vs Oral Gabapentin for Obtunding Hemodynamic Response to Laryngoscopy and Tracheal Intubation

Dr. Aravinthan Mamallan, Dr. U. G. Thirumaaran

Abstract: ***Introduction: The sequence of induction of anaesthesia, laryngoscopy and tracheal intubation are highly noxious stimuli associated with marked haemodynamic changes consisting of increase in circulating catecholamines and autonomic reflex activity which involves activation of adrenocortical system. There is an increase in myocardial oxygen demand and dysrhythmias may occur as well.These changes are transient in nature and do not affect healthy individuals however in patients with co morbidities like hypertension, raised intracranial pressure or coronary artery disease. The cardiovascular response is also directly related to the force and duration of laryngoscopy. Both Clonidine, an α2 adrenergic agonist and gabapentin which is a GABA-B receptors agonist causes obtunding of hemodynamic response during laryngoscopy and endotracheal intubation. Aim: The aim of conducting this study was to compare the effects of 100mcg oral Clonidine given 90 min prior to time of surgery with 300mg oral gabapentin given 90 min before surgery in blunting the haemodynamic response to laryngoscopy and intubation. Methodology: A prospective randomized study was done in 60 patients undergoing elective surgeries general anaesthesia in Meenakshi medical college hospital and research institute was selected randomly and the patients were randomly split into two groups of 30 each. One group C received 100mcg of orral clonidine and the other group G received 300 mg of Gabapentin orally 90 minutes before surgery. ECG monitoring, systolic blood pressure, diastolic blood pressure, mean arterial pressure(MAP) with noninvasive monitoring and pulse oximetry (SpO2) and ETCO2 monitoring was done and recorded after premedication, after induction, before and during intubation at different time intervals (T0, T1, T3, T5 T10 and T15 minutes). Other adverse effects of this oral premedication with 100mcg Clonidine and 300mg Gabapentin like bradycardia, hypotension, sedation and dryness of mouth were recorded post operatively also. Result: In both group the heart rate (HR), systolic blood pressure (SBP),diastolic blood pressure (DBP),mean arterial pressure (MAP) were increased atT0,T1,T3,T5 and T15.The 1 minute post induction values of SBP, DBP, MAP were significantly less in Clonidine group (P<0.001) and significance persisted upto 5 minutes. Increase in HR was less in Clonidine group than in the Gabapentin group. Conclusion: Premedication with oral Clonidine 100mcg 90 minutes before laryngoscopy and intubation superior to oral gabapentin 300mg in obtunding the hemodynamic response to endotracheal intubation and laryngoscopy***

Keywords: 100mcg oral Clonidine, 300mg oral Gabapentin, direct laryngoscopy, endotracheal intubation, attenuation of hemodynamic response, heart rate systolic blood pressure; diastolic blood pressure, mean arterial pressure**.**

1. Introduction

Many strategies have been employed to minimize the adverse hemodynamic response to laryngoscopy and intubation like reducing the duration of laryngoscopy to less than 15 seconds and administration of drugs like volatile anaesthetics, topical and intravenous lidocaine, opioids, vasodilators, calcium channel blockers, β- lockers, and alpha-2 adrenergic agonist before laryngoscopy. No single agent has been established as the most appropriate for Laryngoscopy and intubation is a day to day routine in the practice of anaesthesiology.

It is not only performed for general anaesthesia during elective and emergency surgeries as indicated, we are also called upon for securing airway in critical care. However both laryngoscopy and intubation are noxious stimuli and are associated with stress response in the form of laryngo sympathetic stimulation which is manifested as hypertension, tachycardia and cardiac arrhythmias.

The hemodynamic response to laryngoscopy and intubation is dependent of multiple factorslike adequate premedication, dose of induction agent, depth of anaesthesia, topicalization of the airway, the duration and number of attempts of laryngoscopy and endotracheal intubation.

In young and healthy individuals such a haemodynamic response does not pose any threat, however in patients with comorbidities like hypertension, coronary artery disease, cerebrovascular disease and intracranial aneurysms hemodynamic changes due to laryngoscopy may lead to complications such as left heart failure, intracranial haemorrhage, acute myocardial ischemia, and cardiac arrythmias.

Clonidine is an alpha-2 adrenergic agonist used for many years as an antihypertensive agent. Pharmacological action of clonidine has been used in attenuating stress response to laryngoscopy and intubation. Gabapentin, 1-(amino methyl) cyclohexane acetic acid, is a structural analogue of the neurotransmitter γ–aminobutyric acid. The mechanism of gabapentin in controlling this hemodynamic response remains unknown. Since, gabapentin inhibits membrane voltage gated calcium channels (VGCCs), it is possible that it may have a similar action to calcium channel blockers.

Gabapentin acts on the voltage gated calcium channels and it has also been proven that for Gabapentin to be effective the intergrity of the alpha-2 receptors in the spinal cord, noradrenergic descending pathway and spino bulbo spinal circuit.

The aim of conducting this study was to compare the effects of 100mcg oral Clonidine given 90 min prior to time of surgery with 300mg oral gabapentin given 90 min before surgery in blunting the haemodynamic response to laryngoscopy and intubation.

2. Objectives

Primary Objectives

- To observe the efficacy of oral pre medication with Clonidine 100 mcg with Gabapentin 300 mg given 90 minutes prior to surgery, in attenuating the adverse hemodynamic responses to laryngoscopy and intubation of the trachea.
- To compare the efficacy of oral pre medication with Clonidine 100 mcg with Gabapentin 300 mg given 90 minutes prior to surgery and conclude which of the above two drugs is suoerior in attenuating the adverse hemodynamic responses to laryngoscopy and intubation of the trachea.

Secondary Objectives

To observe and compare if there are any untoward effects like excessive sedation of such pre medication Clonidine 100 mcg with Gabapentin 300 mg given 90 minutes prior to surgery.

Physiology of Sympathetic Response to Laryngoscopy and Tracheal Intubation

Direct laryngoscopy (1) and endotracheal intubation (2) stimulate a sympatheticoadrenal response. Suctioning of the airway and laryngoscopy itself can cause sudden increase in blood pressure, heart rate, increase in intraoccular pressure and increase in intracranial tension

Supraglottic traction (3) during laryngoscopy or superficial stimulation of airway(4)or passage of tracheal tube into trachea(5) may be associated with reflex sympathetic changes.

After the induction of anesthesia other factors like anxiety and baroreceptor mediated reflexes do not cause hypertension and tachycardia unlike laryngoscopy as the MAC value of intubation is approximately 30% higher than the mac value of a given agent. The tracheal intubation following laryngoscopy is not only accompanied by increased sympathetic activity but also increased sympathoadrenal activity (6). Increased hypothalamic adrenal axis activity and traffic in sympathetic efferent tracts are observed. Release of trophic hormones from hypothalamus stimulate release of ACTH, TSH, GH, FSH, luteinizing hormone and prolactin in addition to ADH from the pituitary.

Autonomic afferent impulses are transmitted by cranial nerves V, IX, X and sympathetic nerves from the airway. The afferents are relayed to cranial nerve nuclei, vasomotor and autonomic regulatory areas.

Key areas that integrate CVS responses and maintain CVS homeostasis are nucleus solitarius, dorsal vagal nucleus, nucleus ambiguus and parabranchial nucleus. The primary central synapse for baroreceptor mediated reflexes is nucleus solitarius and acts as relay station to hypothalamic sympathetic control centers peripheral information. It projects directly to interomediolateral nucleus of the spinal cord, the common pathway for preganglionic sympathetic outflow. Nucleus solitariusandh nucleus ambiguous regulate the secretion of vasopressin (7).

Increase in sympathetic and hypothalamo-pitutary adrenal activity is responsible for cardiovascular changes seen with laryngoscopy and tracheal intubation.

Norepinephrine levels are doubled from 160pg/ml to 300pg/ml &last for 4-8 minutes. Epinephrine levels are increased from 70 to 280 pg/ml.

Surprisingly increase in plasma noradrenaline concentration and mean arterial pressures of upto 100% and 50% respectively can be correlated but correlation does not exist in postoperative period where noradrenaline concentration can increase upto 200% of the basal value.

The areas in the central nervous system which regulate the haemodynamic response have Mu receptors. Neurons in this area contain an endogenous opioid enkephalin. Opioids can modulate the afferent impulses at spinal cord and brain stem. It can also modulate the activity of hypothalamo pituitary adrenal axis (7).

Pharmacology of Clonidine

History and Chemistry

Clonidine hydrochloride, an imidazoline derivative was originally developed as a nasal decongestant and vasoconstrictor (8). Its hypotensive and bradycardic effects were first appreciated in 1962. It is a centrally acting adrenergic agonist that lowers blood pressure by decreasing basal sympathetic nervous system activity. It was introduced first in Europe in 1966 and subsequently in the U.S. for use as an antihypertensive agent.

Structure:

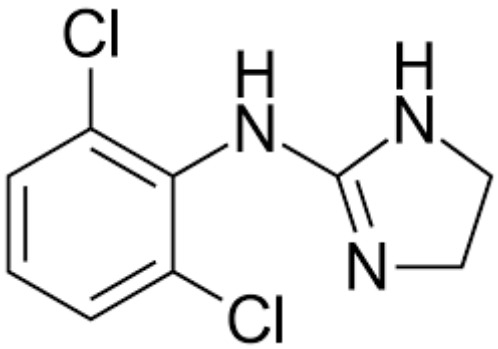

Figure 1

Clonidine

Pharmacokinetics:

Clonidine is rapidly absorbed from the G.I. tract. The onset of action occurs within 30-60 minutes with peak effect occurring 2-4 hours after oral administration.

Peak plasma levels occur at 90 minutes and the plasma half life is 6 – 15 hours(8,9).

Clonidine is metabolized mainly by the liver. Approximately 40% - 60% of an oral dose is excreted unchanged in the urine within 24 hours.

Clonidine is also well absorbed through the skin as a result of its low molecular weight and high lipid solubility. It is released from a transdermal preparation at a constant rate for a day period(10).

Mechanism of Action

It is thought to act by selective stimulation of Post-synaptic adrenergic receptors in the central nervous system, more specifically the nucleus tractus solitarii of the medulla oblongata and therefore reduction in catecholamine levels. This causes inhibition of basal efferent sympathetic vasoconstrictor effects on the peripheral and renal vasculature (11).

The role of the sympathetic nervous system as one of a number of important blood pressure regulating factors is well established (12). A direct relationship between blood pressure and plasma catecholamine levels has been demonstrated in hypertensive patients. Hypertensive patients have been shown to have an exaggerated sympathetic nervous system response to stress. Additionally, it has been suggested that sympathetic mechanisms may contribute to elevations in blood pressure by blunting the sensitivity of the carotid baroreceptors. Clonidine may restore baroreceptor sensitivity by its central action. The frequently observed decrease in heart rate during clonidine therapy reflects vagal stimulation or sinoatrial nodal inhibition. This comes about as a result of reciprocal relationship between the sympathetic vasomotor centre and the dorsal motor nucleus of the vagus nerve. Stimulation of the inhibitory sympathetic nerves results in increased vagal tone.

In addition, clonidine also has pre-synaptic agonist activity. This may inhibit neurotransmitter release and contribute to the decrease in plasma norepinephrine concentrations found during clonidine therapy.

Haemodynamic Effects:

Oral administration of clonidine causes a reduction in blood pressure, heart rate, cardiac output and stroke volume without any consistent change in calculated total peripheral resistance. The reduction in cardiac output is due primarily to the reduction in heart rate and venous return (due to venodilation) with no change in myocardial contractility. Incremental increases in cardiac output and heart rate in response to exercise are preserved probably because the central sympathetic inhibitory action of clonidine is more prominent than the peripheral constrictor action allowing peripheral effector mechanisms to remain intact. Reduction in resting heart rate is seen in both supine and upright position. Orthostatic hypotension is unusually less frequent than with ganglionic blockers and peripherally acting vasodilators.

Cardiac Effects:

Regression of left ventricular hypertrophy has been observed with clonidine with and without a low-dose diuretic. Diastolic left ventricular filling which reflects diastolic ventricular function has been found to be abnormal in hypertensive patients and may improve during short term (12 weeks) clonidine therapy.

Effects on Renin and Aldosterone:

Clonidine reduces plasma renin activity probably as a result of reduced sympathetic stimulation at the renal adrenergic receptors. This contributes to the antihypertensive effect. Clonidine causes suppression of aldosterone production which may also contribute to its blood pressure lowering effect. The notable lack of salt and water retention seen with clonidine therapy is probably a result of the inhibition of the renin-aldosterone axis.

Dosage and Administration:

Usual starting dose of oral clonidine is 0.1 mg twice a day which may gradually be increased by 0.1mg per week. In elderly once daily administration at bedtime is a very effective and convenient way of lowering blood pressure and avoiding unpleasant side-effects. Transdermal clonidine greatly reduces the incidence of sedation, and causes a dry mouth.

Different sizes of the patch are programmed to yield 0.1 mg, 0.2 mg or 0.3 mg of clonidine per day for 7 days.

Side Effects:

Dry mouth and sedation occur during therapy particularly at high doses. However these effects wear off with time. Impotence and postural hypotension are less of a problem. The side effect of clonidine which has received most attention and is of particular concern to anesthesiologist is the so called clonidine withdrawal syndrome which has been described following abrupt cessation of the drug. It hasfeatures of a hyperadrenergic state resembling pheochromocytoma with increase in blood pressures, pulse rate and catecholamine concentrations. Best treatment is to reinstitute clonidine therapy. Blockers such as phentolamine are also effective. Care should be taken if clonidine is discontinued prior to anaesthesia when the dose should be slowly tapered, while other antihypertensives are substituted. `

Clinical Uses

- Antihypertensive
- Treatment for opioid, nicotine and alcohol addiction
- Treatment of anxiety attacks
- Treatment for chronic pain
- As a premedicant for its sedative and anxiolytic effect
- Attenuation of haemodynamic response to intubation
- Reduces requirement of opioids, intravenous and general anaesthetics
- Reduces post operative shivering
- Reduces intraocular pressure
- To reduce perioperative ischemia

Clonidine may be used in treating all forms of hypertension.38 It is still more useful in combination with a diuretic. Of late clonidine has been used increasingly in the field of anesthesiology. Oral dose of clonidine (about 5µg/kg) as a premedicant has been useful in many ways. Studies have shown that it can attenuate the tachycardia and hypertensive responses to laryngoscopy and intubation. It is also effective as an anxiolytic and a sedative. Moreover it has been seen that clonidine can decrease the MAC value inhaled anaesthetics intraoperatively

Gabapentin

Gabapentin or 1, Aminomethyl,cyclohexane aceticacid is structurally similiar to gamma amino butyric acid is freely water soluble. It is used for its anticonvulsant, antihyperalgesic and antinociceptive properties(13).

Structure

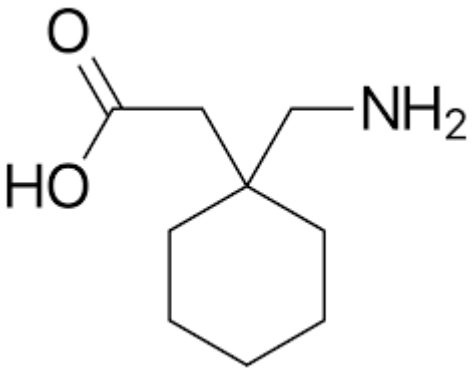

Figure 2

Mechanism of Action

Although structurally similar to GABA it does not act through GABA receptors. The proposed mechanism of action is through their effect on voltage gated calcium channels (alpha 2 delta subunit) (14). Although this may seem to have similar effects like calcium channel blockers there is no proof regarding its other anticonvulsant, antihyperalgesic and nociceptive properties. Other proposed actions include agonositc action on GABA-B receptors, augments the current flow in NMDA and spinal cord level AMPA mediated inhibition of neurotramission (15).

Pharmacokinetics

Gabapentin, is absorbed from gutby diffusion and facilitated transport mediated mechanish and currently only oral preparations are available. It is transported by binding to a receptor linked to a saturable L-amino acid transport mechanism Due to the saturable nature of the transport mechanism the bioavailability of gabapentin decreases with increasing dose.

The bioavailability of a 300-mg doseis 60%,whereas that of a600mg dose is 40% , and this decreases to 35% at steady state with doses of 1600 mg three times daily. Peak plasma levels (Cmax) of gabapentin of 2.7±2.99 mg.l) are achieved 3±3.2 h after ingestion of a single 300-mg capsule

As a result of the dose-dependent saturable absorption of gabapentin, Cmax increases less than threefold when the dose is tripled from 300 to 900 mg.

Metabolism

Gabapentin is not metabolized in humans and is excreted unchanged in urine.The unmetabolized drug is excreted through faeces.It is not a microsomal enzyme inducer. Due to renal excretion plasma clearance and elimination rate are dependent on creatinine clearance.

Therapeutic Uses

1) Used in the treatment of partial seizures as a adjunt of standard therapy with antiepileptic's (16).
2) Used to treat neuropathic pain, post-herptic neuralgia, diabetic neuropathy, HIV neuropathy (16).
3) Used as adjunct with in anxiety and bipolar disorder (16).
4) Used in treatment of hot flushes (16).
5) Used as preamptive analgesic and resuces post-operative opiod consumption.
6) Used to attenuate hemodynamic response to direct laryngoscopy and endotracheal tube intubation.
7) Used as pre-medication for anxiolysis.
8) Used in prevention of postoperative nausea, vomiting.
9) Used in prevention of chronic post -surgical pain.

Adverse Effects:

- Dizziness 11%
- Somnolence 15%
- Nausea 3%
- Ataxia 2%
- Esthenia 6%
- Weight gain 2%
- Withdrawal symptoms appear after abrupt discontinuation of long term gabapentin therapy.

Drug Interactions:

Gabapentin does not have significant drug interaction with othr drugs undergoing renal excretion.
Antacids when administered together with gabapentin reduce the bioavailability of gabapentin by 15%.

3. Review of Literature

A study (Raval et al) was conducted in 100 patients of ASA 1 & 2 undergoing elective surgeries with endotracheal intubation between oral diazepam and oral clonidine.Two groups of 40 each received oral clonidine and oral diazepam respectively with a control group of 20 patients receiving placebo.Oral colnidine had higher sedation, more antisialagogue and anxiolysis. Oral clonidine was also superior in obtunding haemodynamic response to laryngoscopy (17).

A study (Millar Forbes et al) conducted to evaluate the effects of hypertension on response to endotracheal intubation it was concluded both treated and untreated patients were equally at risk to deliterious haemodynamic response to laryngoscopy and intubation.However uncontrolled and untreated patients had a higher incidence of myocardial infarction (18).

A study (Shribman et al) conducted to find any increase in to detect the levels of plasma catecholamines in response to laryngoscopy and endotracheal intubation found that significant rise in plasma noradrenaline levels with corresponding rise in arterial blood pressure. However there were no changes in adrenaline levels (19).

A study (Derbyshire et al) was conducted to compare plasma adrenaline and plasma nor adrenaline levels in patients undergoing general anesthesia with endotracheal intubation using thiopentone. The patients were split into two groups one receiving suxamethonium and the other receiving pancuronium. Pancuronium group showed significantly lower noradrenaline levels (20).

In a study (Derbyshire et al) conducted to observe the sypatheticoadrenal stimulation at variousstages of anesthesia by measuring plasma noradrenaline levels. It showed significant sympathetico adrenal stimulation with corresponding increase in nor adrenaline levels (21).

A study (Wright et al) was conducted in 69 patients on the effects of 300mcg of clonidine as premedication. Normotensive patients were chosen and the study was conducted with randomized double blinding and showed clonidine was effective in attenuating the tachycardia and hypertensive response to laryngoscopy and intubation (22).

A study (Carabine et al) was conducted with 80 patients in ASA1 group to observe the effects of clonidine at oral doses of 100mcg, 200mcg, 300mcg. They were split into groups of 20 each with a control group of 20 receiving regular benzodiazepine premedication. It concluded that oral clonidine of upto 200mcg is ideal as 300mcg clonidine premedication causes excessivesedation postoperatively (23).

Clonidine augments the effect of other anesthetic drugs thereby reducing requirement of opiods and induction agents.Oral clonidine at 5µg/kg reduces dose of fentanyl to 55% and obtunds haemodynamic response to intubation with reduced plasma catecholamine levels (24).

Administratin of oral clonidine 30 to 90 mins before surgery reduces the dose of anesthetic agents and opiods and also obtunds the haemodynamic response to endotracheal intubation (25).

A study (Tanaka et al) was conducted measuring plasma catecholamine levels in response to two subsequent doses of ephedrine in two groups of patients with one receiving receiving clonidine premedication. The group receiving clonidine showed significantly lower noradrenaline levels (26).

A study (Adriana et al) was conducted to study the effects of clonidine for fibreoptic bronchoscopy at an intravenous dose of 3mcg/kg and it proved to be effective in reducing the sypatheticoadrenal stimulation to bronchoscopy with a lower incidence of arrhythmias (27).

A study (Martina et al) was conducted with clonidine administered intramuscularly at 4.5mcg/kg to obtund the haemodynamic response to laryngoscopy and endotracheal intubation proved effective and was confirmed by plasma beta endorphin responses (28).

A study (Goyaji et al) was done using oral clonidine at 2.5-5mcg/kg as premedication to observe decrease in the awakening concentration of Isoflurane and showed delayed awakening in patients receiving oral clonidine (29).

A study(Batra et al)in patients receiving oral clonidine as premedication showed attenuation of increase to heart rate and blood pressure in response to laryngoscopy and endotracheal intubation (30).

Using α2 adrenergic agonist is one of the modalities of obtunding the haemodynamic response to laryngoscopy and endotracheal intubation. Oral clonidine as premedication is effective (31).

A study (Stuhmeier et al) conducted in patients undergoing vascular surgery showed reduced incidence of postoperative myocardial infarction at a oral dose of 2 mcg/kg (32).

A study (Chadha et al) in patients undergoing craniotomy, with oral premedication with clonidine showed obtunding of haemodynamic response to laryngoscopy and also showed reduction in dose of thiopentone (33).

A study was conducted in 75 patients divided into 3 groups of 25 each each receiving 300mcg oral clonidine,900mg oral gabapentin and placebo 120 min before surgery. The study concluded both clonidine and gabapentin were effective when given orally as premedication (34).

A study conducted in 75 patients of ASA 1 & 2 undergoing elective surgeries with endotracheal intubation were given 900mg oral gabapentin 90 mins prior to surgery showed it was effective in obtunding the haemodynamic response to laryngoscopy (35).

A study was conducted in 50 ASA1 patients divided into 2 groups of 25 each with one received in 1200mg oral Gabapentin and other receiving a placebo 120 min before surgery. There was significant blunting of haemodynamic response to intubation but there was no difference in plasma catecholamine levels (36).

A study concluded in 100 patients undergoing elective surgery in groups of 50 each, with one group receiving 800mg oral gabapentin and another receiving a placebo. The study concluded Gabapentin was effective in obtunding the rise in blood pressure but was not effective in obtunding the rise in heart rate (37).

4. Methodology

A total of 60 patients posted for elective surgery under general anaesthesia were chosen for the study randomly.They were divided into 2 groups by double blinding.Written and informed consent in their native language was obtained regarding their participation in the study along with consent for general anesthesia.The study was conducted in Meenakshi medical college and research institute, Enathur, Kanchipuram in patients undergoing elective surgeries under general anesthesia with endotracheal intubation.

Patients undergoing various Urologic, Orthopaedic,E NT, Gynecological and General surgical procedures were selected.

Inclusion Criteria:

1) Patients between age of 18-55 years of both the sexes.
2) Patients of ASA Grade I or II status.
3) Patients undergoing elective surgical procedures under General anaesthesia.

Exclusion criteria:

1) Unwilling Patients.
2) Emergency Surgeries.
3) Age >55years or <18 years
4) Difficult airway

5) Patients with congestive heart failure, Valvular heart disease, Hypotension, IHD, diabetes mellitus.
6) Patients on Psychotropic drugs or history of drug allergies.

60 cases were divided into two groups with 30 each in every group.

Group – C: Patients in this group received oral tablet clonidine 100mcg 90 minutes prior to surgery.
Group –G: Patients in this group received oral tablet gabapentin 300mg 90 minutes prior to surgery.

On the day of surgery, systolic and diastolic blood pressures, heart rate and respiratory rate were measured before premedication and 90 minutes later before induction, scoring was done for sedation, and pain postoperatively.
Other unwanted effects like hypotension, bradycardia, vomiting was evaluated.

Ramsay sedation scale system was used to assess sedation**:**

Ramsay Sedation Scale

Score	Level of Sedation
1	Patient is anxious and agitated or restless or both
2	Patient is Co-operative, oriented and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light tactile stimuli or loud auditory stimulus
5	Patient exhibits sluggish response to light tactile stimuli or loud auditory stimulus
6	Patient exhibits no response

Figure 3

5. Technique

After the was shifted to OT 90min after oral premedication patients were connected to the cardiac monitor for ECG monitoring of lead II. Pulse oximeter was connected and blood pressure was measured non-invasively. Baseline recording of heart rate and arterial pressure was done. An 18G intravenous line was secured and Ringer lactate was started. Inj Glycopyrrolate. 0.2 mg i.v and Inj Midazolam 1mg was given prior to induction. All the patients were pre-oxygenated with 100% oxygen for 3 minutes before induction with a tight fitting face mask. Anaesthesia was induced with Inj Propofol 1.5-2mg/kg body weight and administered slowly till the loss of verbal contact. Inj. vecuronium was administered at a dose of 0.1 mg/kg body weight i.v. Direct laryngoscopy was performed with rigid laryngoscope with appropriare sized curved Macintosh blade. Patients were intubated under vision with appropriate sized cuffed endotracheal tube and cuff was inflated with adequate volume of air.POsitioning was confirmed with ETCO2 trace and 5 point auscultation. The patients were then ventilated with 50% nitrous oxide and 50% oxygen with appropriate tidal volume of 7-8 ml/kg and a respiratory rate of 12 to 14 breaths per minute. For maintenance of relaxation, Inj. vecuronium bromide was administered accordingly to body weight. Systolic, diastolic blood pressures and heart rate were monitored before induction,after induction and at one, three, five, ten, fifteen minutes after laryngoscopy and endotracheal intubation

At the end of the surgery, reversal was done with Inj Neostigmine 0.05mg/kg to 0.03mg/kg and Inj Glycopyrrolate 0.01mg/kg i.v. Patients were extubated after complete recovery from non depolarizing muscle relaxant.

The adverse effects of these drugs were monitored intraoperatively and postoperatively. All necessary precautions were taken to ensure patient safety.

6. Statistical Analysis

Descriptive data presented as mean with SD in percentage. Pair wise comparison between the groups was done using repeated measures ANOVA test, Bonferroni test and student unpaired t test. For all tests a p value of less than or equal to 0.05 and was considered significant. Chi square test is also used for some pair wise comparison.

Note: The following list of formulae can be added in the analysis part

1. Arithmetic mean = Sum of all the values =ΣX
   No. of values n

2. Standard deviation, 1)(2−−=Σ*nXXSD*
3. One-way ANOVA
F = Between sample variance

Within sample variance

1. Student's unpaired t test
   T = Difference of means

S.E of difference of means

1. Paired t test

t= Mean of paired differences

S.E of paired differences

1. Chi square test

X2 = Σ (O-E)2

E

O= Observed value, E= Expected value

7. Results

The mean age of the study participants was 40 (1.6) years. 50% (n=30) participants were males and 50% (n=30) were females.

Table 1

Surgical procedure	n (%)
Appendicectomy	3 (5)
Myringoplasty	3 (5)
Antrostomy	4 (6.7)
Rhinoplasty	1 (1.7)
Diagnostic laproscopy	2 (3.3)
Septal correction	3 (5)
Nasal bone reduction	1 (1.7)
Pyramidal lobe excision	1 (1.7)
Intrarenal surgery	1 (1.7)
Cholecystectomy	8 (13.3)
Sinus tract excision	1 (1.7)
Websters procedure	1 (1.7)
MRM	3 (5)
Modified radical mastectomy	5 (8.3)
PCNL	9 (15)

Meshplasty	2 (3.3)
Septoplasty	5 (8.3)
Thyroidectomy	5 (8.3)
Tonsillectomy	3 (5)

Table 2

Preoperative parameter	Treatment	N	Mean (SEM)	p
Heart rate (beats/ min)	Clonidine	30	73.8 (0.9)	0.4
	Gabapentin	30	74.9 (0.8)	
Systolic Blood Pressure (mm Hg)	Clonidine	30	122.5 (1.6)	0.008*
	Gabapentin	30	127.8 (1)	
Diastolic Blood Pressure (mm Hg)	Clonidine	30	76.6 (1)	0.004**
	Gabapentin	30	80.5 (0.8)	
Mean arterial pressure (mm Hg)	Clonidine	30	92.3 (1.2)	0.008╫
	Gabapentin	30	96.2 (0.8)	

*indicates significantly lower preoperative systolic blood pressure in patients who received clonidine using independent sample t test. **indicates significantly lower diastolic blood pressure in patients who received clonidine using independent sample t test

╫ indicates significantly lower baseline mean arterial pressure in patients receiving clonidine using independent sample t test

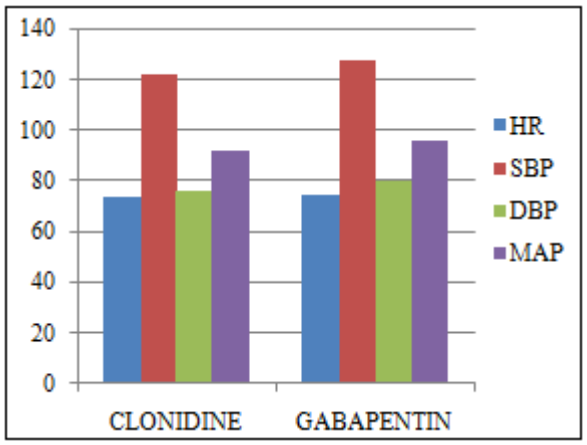

Figure 4: Cardiovascular parameters at various time intervals between treatment groups

Table 3

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
0 minutes	Heart rate (beats/ min)	Clonidine	30	73.8 (0.9)	0.08
		Gabapentin	30	74.9 (0.8)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	109.6 (1.6)	0.013*
		Gabapentin	30	115.5 (1.6)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	71.5 (1.5)	0.08
		Gabapentin	30	75.1 (1.4)	
	Mean arterial pressure (mm Hg)	Clonidine	30	84.3 (1.3)	0.02**
		Gabapentin		88.6(1.3)	

*indicates significantly lower systolic blood pressure in patients who received clonidine using independent sample t test. **indicates significantly lower mean arterial pressure in patients who received clonidine using independent sample t test

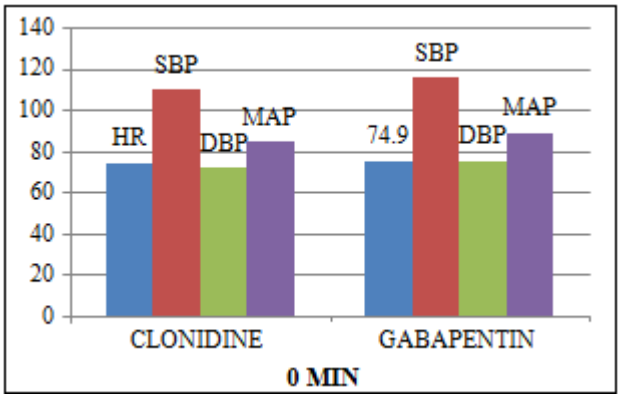

Figure 5

Table 4

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
1 minute	Heart rate (beats/ min)	Clonidine	30	80.0 (1)	<0.001*
		Gabapentin	30	85.8 (1.1)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	129.8(1.3)	<0.001*
		Gabapentin	30	138.7(1.2)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	81.3 (1)	<0.001*
		Gabapentin	30	87.1 (0.8)	
	Mean arterial pressure (mm Hg)	Clonidine	30	97.5 (1)	<0.001*
		Gabapentin	30	104.2(0.9)	

*indicates significantly lower heart rate, systolic blood pressure, diastolic blood pressure mean arterial pressure in patients who received clonidine at 1 min after laryngoscopy using independent sample t test.

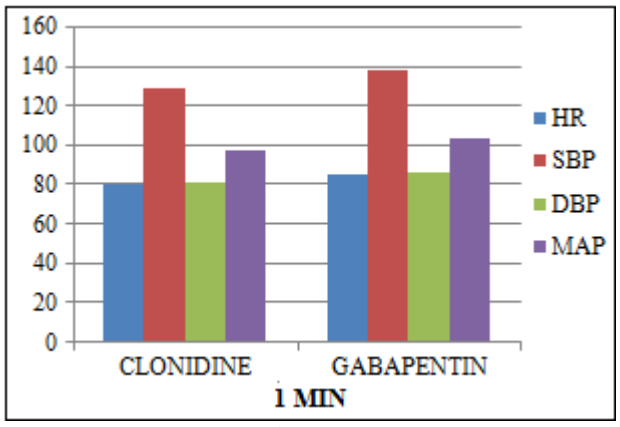

Figure 6

Table 5

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
3 minute	Heart rate (beats/ min)	Clonidine	30	76.5 (1)	<0.001*
		Gabapentin	30	82.2 (1)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	124.9 (1.4)	<0.001*
		Gabapentin	30	134.5 (1.2)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	78 (0.9)	<0.001*
		Gabapentin	30	84.1 (0.7)	
	Mean arterial pressure (mm Hg)	Clonidine	30	93.6 (1)	<0.001*
		Gabapentin	30	100.9 (0.8)	

*indicates significantly lower heart rate,systolic blood pressure, diastolic blood pressure, mean arterial pressure in

patients who received clonidine at 3 min after laryngoscopy using independent sample t test.

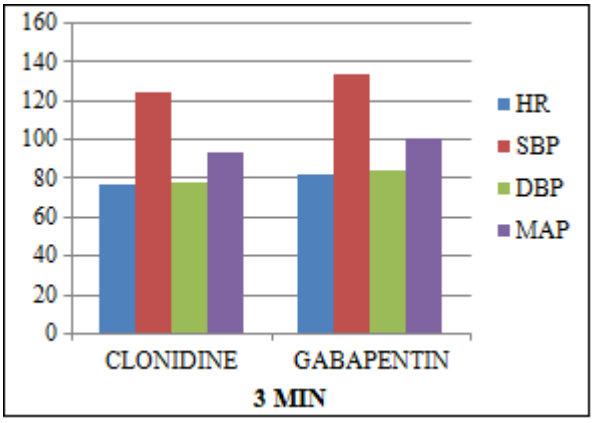

Figure 7

Table 6

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
5 minutes	Heart rate (beats/ min)	Clonidine	30	73.7 (0.9)	<0.001*
		Gabapentin	30	79.7 (1)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	119.7 (1.3)	<0.001*
		Gabapentin	30	132 (1.3)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	75.5 (1)	<0.001*
		Gabapentin	30	82 (0.7)	
	Mean arterial pressure (mm Hg)	Clonidine	30	90.3 (1)	<0.001*
		Gabapentin	30	98.7(0.9)	

*indicates significantly lower heart rate,systolic blood pressure, diastolic blood pressure, mean arterial pressure in patients who received clonidine at 5 min after laryngoscopy using independent sample t test.

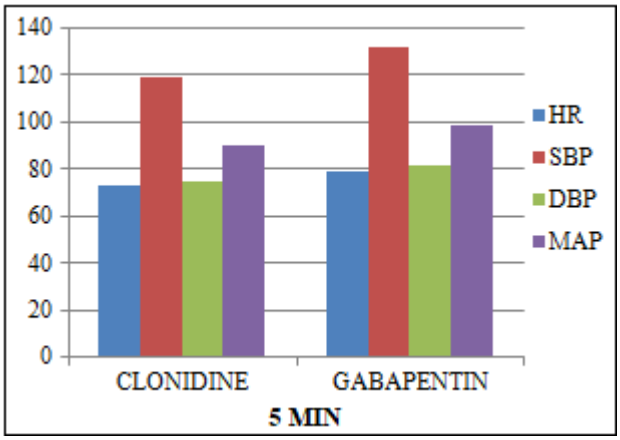

Figure 8

Table 7

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
10 minutes	Heart rate (beats/ min)	Clonidine	30	69.3 (0.6)	<0.001*
		Gabapentin	30	76.5 (1)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	112.9 (1.5)	<0.001*
		Gabapentin	30	127.4 (1.2)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	70.8 (0.9)	<0.001*
		Gabapentin	30	79.1 (0.8)	
	Mean arterial pressure (mm Hg)	Clonidine	30	84.5 (1.1)	<0.001*
		Gabapentin	30	95.2(0.9)	<0.001*

*indicates significantly lower heart rate, systolic blood pressure, diastolic blood pressure,mean arterial pressure in patients who received clonidine at 10 min after laryngoscopy using independent sample t test.

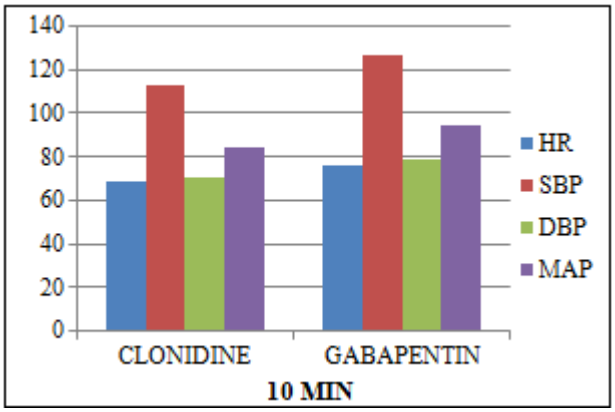

Figure 9

Table 8

Time of measurement	Parameter	Treatment	n	Mean (SEM)	P
15 minutes	Heart rate (beats/ min)	Clonidine	30	66.9 (0.6)	<0.001*
		Gabapentin	30	73.9 (0.9)	
	Systolic Blood Pressure (mm Hg)	Clonidine	30	111.3 (1.6)	0.04*
		Gabapentin	30	120.4 (3.9)	
	Diastolic Blood Pressure (mm Hg)	Clonidine	30	68.5 (0.9)	<0.001*
		Gabapentin	30	76.5 (0.8)	
	Mean arterial pressure (mm Hg)	Clonidine	30	82.8 (1.1)	<0.001*
		Gabapentin	30	91.2 (1.6)	

*indicates significantly lower heart rate,systolic blood pressure, diastolic blood pressure, mean arterial pressure in patients who received clonidine at 3 min after laryngoscopy using independent sample t test.
**indicates significantly lower values with clonidine compared to gabapentin using independent sample t test.

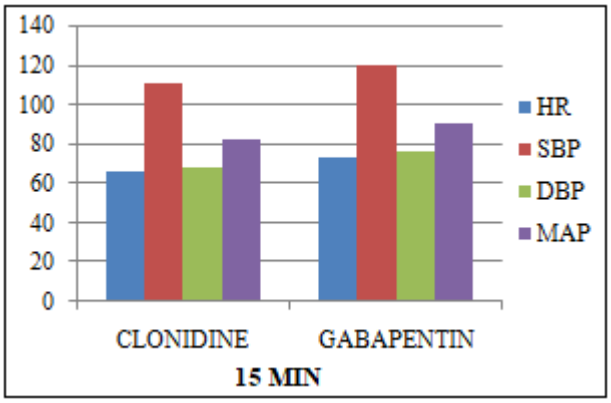

Figure 10

8. Discussion

Laryngoscopy and endotracheal intubation are frequently associated with sympathetic oadrenal response characterized

by tachycardia, hypertension, rise in ICT, IOP. This study has been undertaken to observe and compare the effectiveness of oral Clonidine with oral Gabapentin as a premedication in attenuating the hemodynamic response during laryngoscopy and tracheal intubation.

The present study was done in 60 patients under ASA Grade I and II aged 18-55 years undergoing elective surgeries. The adverse effects pertaining to both Clonidine and Gabapentin were observed and recorded. Sedation occurred in almost 60% of patients. Hypotension and bradycardia were less common side effect. Dryness of mouth (63%) was reported in patients administered oral clonidine which is mediated by the alpha-2 agonistic action presynaptically in the brainstem and parasympathetic nervous system, which innervates the salivary gands. No patients in gabapentin group hadbradycardia or hypotension but in clonidine group the overall incidence of bradycardia was 5% and 10% patients had hypotension. Episode of bradycardia was treated by injection Atropine 0.6mg.Overall the incidence of side effects is significantly less in gabapentin group.

There are few limitations of this study. Patients with ASA physical status I and II were enrolled in the study, so the results cannot be generalized to the patients with higher ASA status. The study was conducted in a single centre. A multi-centered larger study may be more informative. Another limitation of our study was that we did not measure the stress mediators, i.e. endogenous plasma catecholamines or cortisol values perioperatively

9. Conclusion

1) Oral clonidine 100mcg given 90 minutes prior to surgery wassuperior to oral gabapentin 300mg in attenuation of hemodynamic response to laryngoscopy and intubation.
2) There was no significant hypotension and bradycardia inclonidine group as compared to gabapentin group.
3) Ramsay sedation score was more in clonidine group as comparedto gabapentin group but the patients were not deeply sedated and were arousable.
4) Post-operative pain using visual analougue score was lower in clonidine group.

10. Summary

The study entitled " ORAL CLONIDINE VS ORAL GABAPENTIN FOR OBTUNDING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION" was conducted in Meenakshi medical college hospital and research institute. The study was done in 60 patients undergoing elective surgeries general anaesthesia with endotracheal intubation and were divided into two groups consisting of 30 patients in each group. Group C received 100mcg oral clonidine and Group G received 300 mg oral gabapentin orally 90 minutes prior to surgery with double blinding.. Parameters such as ECG monitoring, systolic blood pressure, diastolic blood pressure, mean arterial pressure(MAP) with noninvasive monitoring and pulse oximetry (SpO2) and ETCO2 monitoring was done and recorded after premedication, after induction, before and during intubation at different time intervals (T0, T1, T3, T5 T10 and T15 minutes. Other adverse effects of this oral premedication with 100mcg Clonidine and 300mg Gabapentin like bradycardia, hypotension, sedation and dryness of mouth were recorded post operatively also. This study was conducted with an objective to compare the effect of 100 mcg oral Clonidine administered 90 minutes before surgery with 300mg oral gabapentin administered 90 minutes before surgery on the haemodynamic response to laryngoscopy and intubation.

In both the groups the reflex changes in heart rate , systolic blood pressure ,diastolic blood pressure ,mean arterial pressure were obtunded in response to laryngoscopy and endotracheal intubation at 0,1,3,5,10 and 15min.The 1 minute post induction values of SBP, DBP, MAP were significantly less in Clonidine group ($P<0.001$) and significance persisted upto 5 minutes. Increase in HR was less in Clonidine group than in the Gabapentin group.

With the above findings we conclude that premedication with oral Clonidine 100mcg 90 minutes before laryngoscopy and intubation superior to oral gabapentin 300mg in attenuation of hemodynamic response to laryngoscopy and endotracheal intubation.

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Abbreviations

GABA-gamma amino butyric acid
ASA – American Society of Anesthesiologist
BP- Blood pressure
SBP- systolic blood pressure
DBP-diastolic bloop pressure
MAP- mean arterial pressure
HR- Heart Rate
LA- Local Anesthesia
MPC –Mallampatti Class
min– Minutes
PD- Pharmacodynamics
PK-Pharmacokinetics
RR- Respiratory rate
Spo2- Saturation of oxygen
VGCC-voltage gated calcium channels

COMPARATIVE STUDY BETWEEN "ORAL CLONIDINE VERSUS ORAL GABAPENTIN AS PERMEDICATION FOR OBTUNDING HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION"

PROFORMA

CODE:

NAME: AGE/SEX: DATE:
MRD NO:
PROCEDURE:
ANAESTHESIA TIME:
ASA: HEIGHT: ;WEIGHT-

BASELINE VITALS:
PR- ;BP- ;RR- ; TEMP-
CVS- RS-

AIRWAY
MOUTH OPENING- ;MPC- ;TMD-
NECK MOVEMENT- ;DENTITION- ;SPINE-
SMD- MANDIBULAR PROTRUSION-

LARYNGOSCOPY

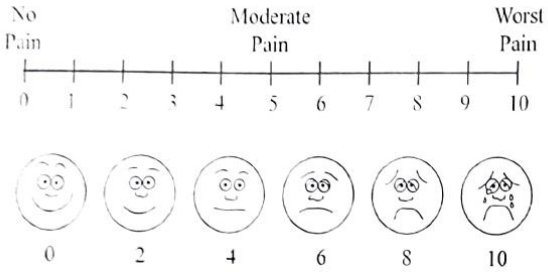
TIME	HR	BP(mean)	SPO2	RR	REMARKS
0 MIN					
1 MIN					
3 MIN					
5 MIN					
10 MIN					
15 MIN					

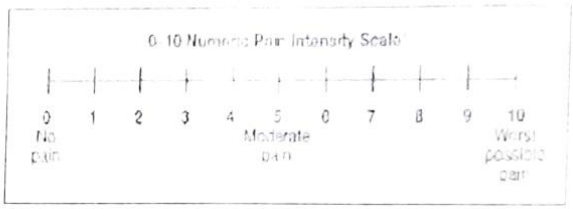
EXTUBATION

TIME	BP(mean)	PR	SPO2
0 MIN			
5 MIN			
15 MIN			
30 MIN			
45 MIN			
60 MIN			

POST -OP PAIN

TIME	NUMERIC RATING SCALE	VISUAL ANALOGUE SCALE
30min		
60min		
120min		
240min		





POST OP SEDATION

TIME	SCORE
0min	
30min	
60min	
120min	
240min	

RAMSAY SEDATION SCALE

Score	Level of Sedation
1	Patient is anxious and agitated or restless, or both
2	Patient is co-operative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light tactile stimuli or loud auditory stimulus
5	Patient exhibits sluggish response to light tactile stimuli or loud auditory stimulus
6	Patient exhibits no response

Signature of Candidate

Master Chart

GROUP C

S No.	Date	Name	Age	Sex	MRD no:	Surgery	Heart rate							Systolic BP							Diastolic BP							Mean arterial pressure[MAP]						
							Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min
1	23/01/2020	Ponnarasan	28	M	2718580	Laproscopic appendicectomy	76	68	80	86	79	74	66	124	108	128	132	118	124	120	76	68	84	82	78	74	72	92	81.33333	98.6	98.6	91.3	90.66667	88
2	28/01/2020	Padmanaban	41	M	2726250	Laproscopic cholecystectomy	82	66	88	78	72	68	64	110	104	132	134	128	122	128	70	66	82	86	80	74	72	83.33333	81.33333	98.66667	102	96	78.66667	90.66667
3	29/01/2020	Venkatesh	21	M	2485955	Modified radical mastoidectomy	68	62	74	72	70	68	66	118	102	124	118	114	104	106	72	66	78	74	74	66	64	87.33333	78	93.33333	88.66667	87.33333	78.66667	78
4	32/01/2020	Perumal	35	M	2712531	Right PCNL	78	68	88	84	80	74	70	138	122	134	130	128	122	118	82	76	82	78	74	72	76	100.6667	91.33333	99.33333	95.33333	92	88.66667	90
5	31/01/2020	Vignesh	20	M	2716976	Right modified radical mastoidectomy	70	66	78	74	70	68	72	126	110	128	122	114	110	112	74	70	76	72	70	68	66	91.33333	83.33333	93.33333	88.66667	84.66667	82	81.33333
6	05/02/2020	Banumathy	50	F	2689449	Retrograde intrarenal surgery	78	72	90	84	84	78	76	132	118	134	130	126	118	114	84	78	86	82	82	78	76	100	91.33333	102	98	96.66667	91.33333	88.66667
7	12/02/2020	Neelakandan	28	M	2796275	Left PCNL	70	62	76	74	70	66	64	116	104	128	126	118	110	106	72	68	67	72	70	68	66	86.66667	80	87.33333	90	86	82	79.33333
8	14/02/2020	Jayanthi	29	F	2749363	Left PCNL	76	68	86	84	76	68	64	118	102	128	122	116	108	106	70	62	82	76	70	67	64	86	75.33333	97.33333	91.33333	85.33333	80.66667	78
9	19/02/2020	Subramaniam	18	M	2386352	Septal correction	70	64	78	70	68	66	65	110	104	122	118	116	106	104	72	84	76	72	68	66	64	84.66667	90.66667	91.33333	87.33333	84	79.33333	77.33333
10	22/02/2020	Nagarajan	60	M	2733950	Laproscopic cholecystectomy	82	70	88	84	82	76	70	134	114	138	130	128	126	128	78	88	86	84	80	78	76	96.66667	96.66667	103.3333	99.33333	96	94	93.33333
11	23/02/2020	Adimoolam	52	M	2760333	Laproscopic cholecystectomy	76	68	80	76	74	68	64	126	108	134	130	126	124	122	82	76	88	86	82	80	74	96.66667	86.66667	103.3333	100.6667	96.66667	94.66667	90
12	25/02/2020	Lavanya	22	F	2760349	Right PCNL	66	62	72	72	69	66	64	108	98	128	122	120	108	104	68	60	70	68	66	64	64	81.33333	72.66667	89.33333	86	84	78.66667	77.33333
13	26/02/2020	Angamuthu	60	F	2757255	Laproscopic cholecystectomy	78	70	88	82	78	74	76	130	118	142	134	128	120	122	80	76	86	82	82	78	78	96.66667	90	104.6667	99.33333	97.33333	92	92.66667
14	26/02/2020	Laija	55	F	1108129	Pyramidal lobe excision	80	72	84	82	78	72	70	128	114	134	126	122	118	114	82	76	84	80	78	68	66	97.33333	88.66667	100.6667	95.33333	92.66667	84.66667	82
15	27/02/2020	Sudha	35	F	2765040	Total thyroidectomy	70	64	76	74	72	68	66	118	106	128	120	116	106	100	68	62	74	70	68	66	62	97.33333	76.66667	92	86.66667	84	79.33333	74.66667
16	27/02/2020	Kuppu	55	F	2758667	Total thyroidectomy	78	68	82	80	78	70	68	130	118	138	136	128	116	114	78	88	84	80	80	76	72	95.33333	98	102	98.66667	96	89.33333	86
17	28/02/2020	Subash	20	M	2737076	Superficial parotidectomy	68	60	70	72	68	66	66	110	100	120	110	106	100	94	70	62	74	72	70	68	66	83.33333	74.66667	89.33333	84.66667	82	78.66667	75.33333
18	01/03/2020	Velu	53	M	2768244	Right superficial parotidetomy	70	66	78	74	70	66	64	122	108	134	128	122	108	100	80	86	82	78	74	66	64	94	93.33333	99.33333	94.66667	90	80	76
19	01/03/2020	Arjun	44	M	2768134	Nasal bone reduction	78	64	74	72	70	68	68	130	142	134	130	128	120	118	82	74	86	82	80	76	72	98	96.66667	102	98	96	90.66667	87.33333
20	03/03/2020	Kala	32	F	2771217	Total thyroidectomy	68	62	72	70	68	66	66	110	102	118	110	108	106	104	68	58	76	72	68	62	60	82	72.66667	90	84.66667	81.33333	76.66667	74.66667
21	03/03/2020	Meghanathan	30	M	2771107	Rhinoplasty	74	62	76	72	70	66	64	122	108	120	114	110	108	108	80	70	84	82	80	72	66	94	82.66667	96	92.66667	90	84	80
22	04/03/2020	Saradha	28	F	2776121	Septoplasty	70	62	74	72	72	68	66	108	98	118	114	108	98	102	72	66	78	72	70	66	64	84	76.66667	91.33333	86	82.66667	76.66667	76.66667
23	04/03/2020	Rajathi	40	F	2772943	Right modified radical mastoidectomy	78	68	84	80	78	68	64	130	118	134	132	128	116	114	82	74	88	84	80	74	72	98	88.66667	103.3333	100	96	88	86
24	05/03/2020	Thameen	27	M	2775660	Websters procedure	68	60	76	72	70	66	64	110	102	118	116	108	100	102	70	62	76	72	70	66	62	83.33333	75.33333	90	86.66667	82.66667	77.33333	75.33333
25	06/03/2020	Saradha	28	F	2776121	Tonsillectomy	72	66	78	72	70	66	62	128	108	130	128	126	112	110	80	70	82	78	76	68	64	96	82.66667	98	94.66667	92.66667	82.66667	79.33333
26	06/03/2020	Karpagam	55	F	2776163	Total thyroidectomy	78	70	88	86	84	72	70	130	116	138	132	122	118	116	82	70	86	82	78	70	72	98	85.33333	103.3333	98.66667	92.66667	86	86.66667
27	12/03/2020	Manoramani	55	F	2746946	Left mastectomy	72	66	78	72	70	68	66	128	112	132	126	124	116	112	84	74	86	82	82	72	68	98.66667	86.66667	101.3333	96.66667	96	86.66667	82.66667
28	13/03/2020	Arunagiri	38	M	2774165	Septoplasty	78	70	78	74	72	74	68	122	108	132	124	118	106	106	76	68	84	78	76	70	68	91.33333	81.33333	100	93.33333	90	82	80.66667
29	15/03/2020	Amudha	58	F	2625693	Laproscopic cholecystectomy	72	66	84	76	74	70	68	130	108	142	134	124	128	126	82	74	88	82	78	80	76	98	85.33333	106	99.33333	93.33333	96	92.66667
30	18/03/2020	Manikandan	40	M	2792695	Right PCNL	70	62	82	76	74	70	66	128	108	124	118	114	108	110	82	72	84	80	82	72	68	97.33333	84	97.33333	92.66667	92.66667	84	82

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S.No.	Date	Name	Age	Sex	MRD no:	Surgery	GROUP G	Heart rate						Systolic BP						Diastolic BP						Mean arterial pressure(MAP)					
							Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min	Pre-OP	0min	1min	3min	5min	10min	15min
1	01/01/2020	Devi	45	F	2695738	TESS	78	70	88	84	80	74	72	132	120	138	132	130	134	128	82	94	90	86	84	82	78	98.66667	102.6667	106	101.3333	99.33333	99.33333	94.66667
2	10/01/2020	Naveena	22	F	2703367	Laproscopic appendectomy	68	62	78	74	72	72	70	134	110	132	130	128	134	132	82	86	82	78	78	74	72	96	94.66667	95.33333	94.66667	90.66667	90.66667	92
3	20/01/2020	Durai	55	M	1008031	TURBOT	74	68	86	82	82	78	76	128	118	132	130	124	132	118	82	74	86	82	84	82	76	70	97.33333	88.66667	101.3333	98.33333	96	91.33333	86
4	24/01/2020	Rajendran	46	M	2723160	Laproscopic cholecystectomy	76	70	92	88	84	80	78	132	108	142	136	134	134	122	84	72	88	82	82	80	76	72	100	84	106	100	98	92	88.66667
5	28/01/2020	Poovizhi	50	F	2717334	Mastillectomy	80	70	94	90	88	86	76	134	122	144	140	138	130	128	84	76	88	82	82	82	78	78	100.6667	91.33333	106.6667	101.3333	100.6667	95.33333	94.66667
6	31/01/2020	Vaniaveeni	34	F	2721704	TURBOT	70	66	88	84	82	78	70	124	108	138	132	130	132	122	70	62	92	86	84	82	70	88	77.33333	108.6667	97.33333	99.33333	90	87.33333
7	01/02/2020	Mahabubnisi	36	F	2701797	Modified Radical Mastectomy	75	68	86	84	80	74	70	132	118	138	134	132	124	122	84	68	86	84	84	82	78	72	100	84.66667	103.3333	100.6667	98.66667	93.33333	88.66667
8	11/02/2020	Purushothaman	45	M	2740284	Left PCNL	78	70	84	82	78	78	76	128	116	138	134	132	128	124	78	74	86	82	80	76	72	94.66667	86.66667	103.3333	98.33333	97.33333	93.33333	90.66667
9	11/02/2020	Prabhakaran	24	M	2722716	Right PCNL	68	60	74	70	68	66	62	128	110	134	124	122	118	114	74	68	84	74	72	72	68	88.66667	80	97.33333	94	91.33333	86	82.66667
10	15/02/2020	Velmurugan	55	M	2747042	Laproscopic cholecystectomy	78	72	86	82	78	76	74	128	110	138	132	128	124	120	80	72	82	78	74	74	72	96	84.66667	100.6667	96	92	90.66667	88
11	18/02/2020	Vel	26	M	2755522	Bil Laproscopic meriplasty	64	62	82	80	76	72	70	118	102	132	128	128	122	120	74	64	84	82	80	78	78	88.66667	76.66667	100	97.33333	96	92.66667	92
12	20/02/2020	Mala	37	F	2755855	Middle meatal antrostomy	78	68	86	82	80	76	74	128	108	138	134	130	128	128	84	72	90	86	84	84	78	98.66667	84	106	102	99.33333	96	94.66667
13	21/02/2020	Aalis	60	F	2738615	Laproscopic meriplasty	76	68	82	80	76	74	74	132	112	142	140	138	130	122	82	88	86	84	76	74	74	98.66667	96	104.6667	104	102	92.66667	90
14	26/02/2020	Lakshmi	45	F	2765229	Laproscopic cholecystectomy	74	68	88	84	84	84	82	78	132	118	144	140	136	130	126	84	74	74	78	74	78	100	88.66667	108.3333	105.3333	102.6667	99.33333	94
15	26/02/2020	Prema	28	F	2659473	Tonsillectomy	68	60	72	70	68	66	62	110	104	122	114	110	108	104	72	70	74	70	70	70	68	84.66667	86.66667	90	87.33333	83.33333	82	80
16	27/02/2020	Rajesh	42	M	2765238	Sinus tract excision	76	64	82	78	76	70	68	126	134	130	126	126	124	122	82	86	82	80	80	78	78	96.66667	102	96	96.66667	96	93.33333	92.66667
17	27/02/2020	Vijaya	30	F	2765018	Modified Radical Mastectomy	80	68	86	82	80	78	78	132	140	144	142	140	134	130	84	92	88	86	84	82	80	100	118.6667	108	106	105.3333	100.6667	98
18	01/02/2020	Priya	25	F	2768463	Septoplasty	74	64	84	82	80	80	78	132	114	138	136	130	126	126	78	70	86	84	82	82	80	94.66667	84.66667	103.3333	101.3333	98	95.33333	95.33333
19	01/03/2020	Jeyakumar	42	M	2768255	Tonsillectomy	72	64	88	84	82	80	78	128	114	142	136	134	134	124	84	74	88	84	82	80	78	98.66667	87.33333	106	101.3333	99.33333	98	93.33333
20	03/03/2020	Pachiammal	60	F	2771281	Modified Radical Mastectomy	80	70	94	86	84	80	78	134	118	144	140	138	134	130	84	78	94	88	84	82	82	100.6667	91.33333	112.6576	106.6667	104.6667	100.6667	98
21	04/03/2020	Logeshwaran	43	M	2777701	Left myringoplasty	74	68	86	84	80	76	74	134	118	142	138	136	132	126	78	70	88	84	82	80	80	96.66667	86	106	102	101.3333	98.66667	95.33333
22	04/03/2020	Kamala	52	F	2777745	Middle meatal antrostomy	78	70	92	88	88	82	74	128	128	148	144	138	134	128	80	74	88	86	84	84	80	96	88.66667	110.6667	106.6667	103.3333	100.6667	96
23	04/03/2020	Suresh	38	M	2694726	Left myringoplasty	76	70	82	78	76	72	68	132	116	144	138	130	128	128	84	76	92	88	86	84	82	100	85.33333	103.3333	104.6667	103.3333	99.33333	97.33333
24	05/03/2020	Manonani	55	M	2764946	Left modified radical mastectomy	76	72	96	88	88	88	84	128	120	148	144	144	134	132	86	78	98	88	84	84	80	100	92	108	105.3333	104	100.6667	97.33333
25	06/03/2020	Balakrishnan	38	M	2728252	Right PCNL	72	68	86	82	82	80	74	124	112	138	132	130	128	124	78	70	88	84	84	80	76	93.33333	84	108	100	96.66667	96	92
26	11/03/2020	Selvarani	32	F	2335599	Right hemithyroidectomy	68	62	78	76	76	72	72	118	108	132	128	124	122	116	72	66	84	82	80	78	78	87.33333	80	100	97.33333	94.66667	92.66667	90.66667
27	12/03/2020	Veeramayil	38	F	2775704	Diagnostic laproscopy	74	68	80	78	72	70	70	132	122	138	136	134	132	128	84	74	88	86	84	82	82	98.66667	90	104.6667	102.6667	98.66667	98.66667	100
28	13/03/2020	Kanithan	38	M	2785332	Septoplasty	82	70	84	82	80	82	78	134	125	138	134	132	130	122	78	72	86	84	82	80	76	94	86.66667	103.3333	100.6667	98.66667	96.66667	91.33333
29	13/03/2020	Saravanan	48	M	2785311	Right superficial parotidectomy	84	74	92	88	84	84	78	134	112	146	140	138	132	128	82	78	94	88	86	84	82	102	89.33333	111.3333	105.3333	103.3333	100	97.33333
30	21/03/2020	Shanthi	54	F	2788008	Left Modified Radical Mastectomy	76	68	98	94	88	84	82	130	118	148	144	142	134	132	82	74	94	92	88	84	80	98	88.66667	112	108.3333	106	100.6667	97.33333