

**“COMPARISON OF TWO DOSES OF PREGABALIN FOR
PREVENTING SUCCINYLMCHOLINE INDUCED FASCICULATIONS
AND MYALGIA IN PATIENTS UNDERGOING SURGERY UNDER
GENERAL ANAESTHESIA : A RANDOMISED CONTROLLED
STUDY”**

By

DR. MALAVIKA SASIDHARAN

Dissertation submitted to the

B.L.D.E (DU)

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CENTRE VIJAYAPURA, KARNATAKA**



In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

Under the guidance of

DR. RENUKA HOLYACHI

PROFESSOR AND HOD

DEPARTMENT OF ANAESTHESIOLOGY

B.L.D.E. (DU)

**SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH
CENTRE,**

VIJAYAPURA, KARNATAKA

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HOLYACHI, Professor and HOD, Department of Anaesthesiology, B.L.D.E.
(DU), Shri B.M. Patil Medical College Hospital and Research Centre,
Vijayapura**

Date: 28-06-2024

Place: VIJAYAPURA



DR. MALAVIKA SASIDHARAN

B.L.D.E. (DU)

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Place: VIJAYAPURA



DR. RENUKA HOLYACHI

PROFESSOR AND HOD

DEPARTMENT OF ANAESTHESIOLOGY

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RENUKA HOLYACHI, Professor and HOD, Department of
Anaesthesiology, B.L.D.E (DU) Shri B.M. Patil Medical College Hospital
and Research Centre, Vijayapura.**

Date: 28-06-2024

Place: VIJAYAPURA



DR. RENUKA HOLYACHI

PROFESSOR AND HOD

DEPARTMENT OF ANAESTHESIOLOGY

B.L.D.E. (DU)

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Anaesthesiology, B.L.D.E (DU) Shri B.M. Patil Medical College Hospital
and Research Centre, Vijayapura.**

Date: 28-06-2024

Place: VIJAYAPURA



DR ARAVIND V PATIL

PRINCIPAL

B.L.D.E. (DU)

**SHRI B.M. PATIL MEDICAL COLLEGE
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DR MALAVIKA SASIDHARAN

ABBREVIATIONS

Ach	-	Acetylcholine
BBB	-	Blood Brain Barrier
BMI	-	Body Mass Index
Ca	-	Calcium
Cap	-	Capsule
CTRI	-	Clinical Trials Registry India
DBP	-	Diastolic Blood Pressure
GA	-	General Anaesthesia
GABA	-	Gamma aminobutyric acid
HR	-	Heart Rate
Kg	-	Kilogram
ICP	-	Intracranial Pressure
IOP	-	Intraocular Pressure
LRP 1	-	Low density Lipoprotein 1
MAP	-	Mean Arterial Pressure
mcg	-	Microgram
mg	-	Milligram
Mins	-	Minutes
NMDA	-	N methyl D aspartic acid
NMJ	-	Neuromuscular Junction
NSAID	-	Nonsteroidal anti inflammatory drug
p value	-	probability value
SBP	-	Systolic Blood Pressure
SCh	-	Succinylcholine
SL No	-	Serial Number

ABSTRACT

AIM

To compare the efficacy of two doses of Pregabalin for preventing succinylcholine induced fasciculations and myalgia.

BACKGROUND

Succinylcholine is the most commonly used muscle relaxant during endotracheal intubation in patients undergoing surgery under GA due to its rapid onset of action and shorter duration of action. It has been known to cause side effects, of which most commonly encountered are fasciculations and postoperative myalgia. Many drugs, such as magnesium sulphate, benzodiazepines, phenytoin, ketorolac, diclofenac, etc., have been studied to prevent postoperative myalgia and fasciculations. Gabapentin, an analog of Pregabalin, have been studied to prevent fasciculations and postoperative myalgia but requires a larger dose of the drug to produce significant results. Compared to gabapentin, Pregabalin is known to be more effective even at a lower dose, thereby decreasing side effects. But similar studies are done less using Pregabalin. Pregabalin is a structural analogue of neurotransmitter GABA and is an $\alpha_2\delta$ calcium channel antagonist which inhibits presynaptic neurotransmitter release like glutamate and substance P.

MATERIALS AND METHODS

This study was carried out on patients undergoing Surgery under General Anaesthesia in B.L.D.E. DU's Shri B.M. Patil Medical College, Hospital and

Research Centre, Vijayapura. Study Design: Prospective randomized, double-blind Study, Study Period: One and a half year, Sample Size: 201 patients of both genders are randomly divided into three groups of 67 each as:- Group A : Cap Pregabalin 75mg, Group B : Cap Pregabalin 150mg, Group C : Saccharine pill 10mg 2 hours prior to surgery.

RESULTS

Both incidence and severity of fasciculations and myalgia was reduced in patients who received pregabalin compared to placebo group (Group B>A>C).

It was observed that as severity of fasciculations increased, severity of myalgia also increased.

Time of 1st analgesic dose was prolonged in pregabalin group (Group B>A>C).

Attenuation of pressor response and hemodynamic stability was more in pregabalin group (Group B>A>C).

Sedation levels were insignificant among groups.

Incidence of adverse effects were also insignificant among groups.

CONCLUSION

We conclude that preoperative prophylactic administration of oral pregabalin at 75 mg and 150 mg reduced incidence and severity of succinylcholine induced fasciculations and myalgia. A dose of 150 mg was found to be more effective than 75 mg. Side effects were not significant at a dose of 150 mg. Pressor response attenuation was found to be more effective at a dose of 150 mg

compared to 75 mg. Hemodynamic stability was maintained at both pregabalin doses .

Hence it is concluded that preoperative oral Pregabalin is an effective and safe method for prevention of Succinylcholine induced fasciculations and myalgia.

KEYWORDS: Succinylcholine, Pregabalin, Fasciculation, Myalgia

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INTRODUCTION

- Succinylcholine is the most commonly used muscle relaxant during endotracheal intubation in patients undergoing surgery under GA due to its rapid onset of action and shorter duration of action. Although western countries are using other muscle relaxants more , developing countries like India use Sch more often.¹ Since the drug provides better relaxation and intubation conditions, it is better to consider Sch during laryngoscopy and intubation. It has been known to cause side effects like fasciculations, myalgia, bradycardia, hyperkalemia, malignant hyperthermia, etc of which most commonly encountered are fasciculations and postoperative myalgia.³ The resultant myalgia due to this shear stress on the muscle fibres as a result of fasciculations can stay for days to weeks. Typically seen in areas like neck, shoulder and upper abdominal muscles.²
- Several factors like age, gender, weight, extent of surgery, etc can influence both occurrence and duration of myalgia. Moreover these side effects like myalgia causes a lot of discomfort or it can be very much distressing for the patients and can prolong duration of stay in hospital ,especially for those patients who are posted for day care procedures for whom an early discharge from the hospital is expected. ⁷

- Many drugs, such as atracurium, dexmedetomidine magnesium sulphate, opioids, benzodiazepines, phenytoin, ketorolac, diclofenac, etc., have been studied to prevent postoperative myalgia and fasciculations. Gabapentin, an analog of Pregabalin, has been studied to prevent fasciculations and postoperative myalgia but requires a larger dose of the drug to produce significant results. Pregabalin is a structural analogue of neurotransmitter GABA and is an $\alpha 2\delta$ calcium channel antagonist which inhibits presynaptic neurotransmitter release like glutamate and substance P. ^{18,19}
- Compared to gabapentin, Pregabalin is known to be more effective even at a lower dose, thereby decreasing side effects like drowsiness, myalgia, etc. But similar studies with lower doses are done less using Pregabalin. Also, pregabalin has almost nil drug-drug interactions and enzyme inhibitory properties, thereby not interfering with metabolism and excretion of other drugs. ⁵
- In this study we are comparing both higher dose and lower dose of pregabalin with a control group, to find out whether low dose is enough to suppress the occurrence of Succinylcholine induced fasciculations and myalgia or higher dose is better for the same. Also we are assessing the severity of drowsiness or sedation in all three groups using Ramsay sedation score. ⁶ Additionally vital parameters are also being assessed to know action of different doses of pregabalin to pressor response due to endotracheal intubation. ³⁵

- In addition to prevention of fasciculations and myalgia, pregabalin is a drug being used to attenuate pressor response during laryngoscopy and intubation. Pressor response is generally characterized by an increased blood pressure and heart rate and studies previous studies were conducted for the same. In our study, we assess action of pregabalin on pressor response also both with lower dose and higher dose. ^{6,35}
- As increased somnolence is told to be a common side effect of gabapentinoid group of drugs, especially for gabapentin, in our study we will be assessing any significant sedation is caused by pregabalin using Ramsay sedation score. ⁶

AIM AND OBJECTIVES OF THE STUDY

- **Primary objective:** To study the efficacy of two doses of Pregabalin in reducing the incidence and severity of succinylcholine-induced fasciculations and myalgia.
- **Secondary objective:** To compare the efficacy of attenuating pressor response during laryngoscopy and intubation.

REVIEW OF LITERATURE

- **VELEZ et al, 2022** conducted a study on gabapentinoids (Pregabalin or Gabapentin) vs placebo group for preventing succinylcholine induced fasciculations and myalgia in 481 patients (241 patients in gabapentinoid group and 240 patients in placebo group). They observed that incidence of myalgia was reduced in gabapentinoid group compared to placebo group when drug was administered 30 minutes to 1 hour prior to surgery.

- **RASHMI et al, 2018** conducted a study on efficacy of low dose pregabalin in preventing succinylcholine induced fasciculations and myalgia using two groups, one supplemented with low dose 75mg pregabalin and other with placebo one hour prior to surgery. Their study observed no significant changes in incidence of fasciculations and myalgia but severity was significantly reduced in pregabalin group compared to placebo group. Also there was only mild myalgia after 24 hours in pregabalin group whereas moderate in placebo group.

- **KHAN et al, 2017** conducted a study in patients undergoing laparoscopic cholecystectomy on succinylcholine induced fasciculations and myalgia using two groups, one supplemented with 150mg pregabalin and other with placebo two hours prior to surgery. They observed that incidence of fasciculations were not reduced in pregabalin whereas severity was significantly reduced. Both incidence and severity for myalgia was significantly reduced in pregabalin group.

- **IQBAL et al, 2018** conducted a study on the preventing fasciculations, myalgia and hyperkalemia due to succinylcholine in patients posted for spine surgery. One group received oral pregabalin 150mg and other group received placebo one hour prior to surgery. It was observed that severity of fasciculations, incidence and severity of myalgia, serum potassium levels were reduced by pregabalin. Total opioid consumption was also found to be reduced in pregabalin group.

- **JAIN et al, 2019** conducted a study by randomly allocating patients to control and test groups to study the efficacy and safety of pregabalin and gabapentin for preemptive analgesia when given 30 minutes prior

induction. Their study observed that pain scores were significantly lower in pregabalin group at 6, 12, 24 hours and required less post operative analgesia for myalgia compared to gabapentin and placebo.

- **SHRIVASTAVA et al, 2014** conducted a study in two groups, one group received pregabalin 150mg and other group received placebo one hour prior to induction of anaesthesia. It was observed that incidence of fasciculations was not significant in both groups whereas severity was moderate to severe in placebo group. Both incidence and severity of myalgia was low in pregabalin group.

- **JAIN et al, 2012** conducted a study on post-operative patients of total knee arthroplasty where one group was given pregabalin 75mg and other group placebo twice a day where first given just before surgery and continued for 2 days after surgery. The group who received pregabalin had less post-operative pain and lesser requirement of morphine and Patient controlled epidural analgesia.

- **HASHEMIAN et al, 2017** conducted a study on efficacy of clonidine, pregabalin and Vitamin C in patients who underwent laparoscopic cholecystectomy and found that there was no much significant changes in pain level till patients left recovery and both clonidine and pregabalin group showed lower pain levels after 24 hour of surgery.
- **GHAI et al, 2011** conducted a study using pregabalin 300mg, gabapentin 900mg or placebo on 90 patients posted for total abdominal hysterectomy one to two hours prior to surgery assess efficacy on postoperative pain and observed that consumption of other analgesics like diclofenac and tramadol where significant in all groups but the time to first dose of rescue analgesia was more in pregabalin group compared to other groups.
- **PARVEEN et al, 2016** conducted a study with Oral Clonidine 0.3mg and Pregabalin 150mg administered 60 minutes prior surgery for attenuation of pressor response in 80 patients posted for laparoscopic cholecystectomy. It was observed that both clonidine and pregabalin reduced pressor response to laryngoscopy and intubation where clonidine was better but showed more bradycardia.

- **RASTOGI et al, 2012** conducted a study on oral pregabalin for attenuating pressor response. The study consisted of three groups (30 patients in each), where one group received placebo, one received pregabalin 75mg and one received pregabalin 150mg one hour prior to surgery. The study observed Statistically significant attenuation of Mean arterial pressure with pregabalin 150mg whereas no significant reduction in heart rate in any group.

GENERAL ANAESTHESIA

General anaesthesia is the procedure of putting a patient in a reversible state of unconsciousness characterized by amnesia, analgesia and muscle relaxation. ¹⁴

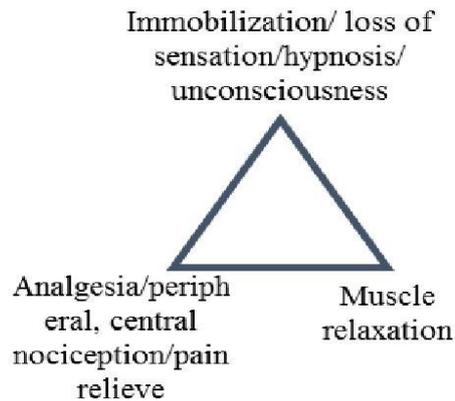


Figure 1: Triad of General Anaesthesia ³⁶

GA depresses the CNS adequate enough to perform surgeries and other procedures which involves noxious stimuli. ¹⁶

Benefits of GA:-

- A. Anxiolysis and Sedation
- B. Amnesia and Lack of awareness
- C. Suppression of Reflexes
- D. Analgesia
- E. Skeletal muscle relaxation

In order to provide all these benefits, different category of drugs are employed involving premedication, analgesics, intravenous induction agents, inhalation agents, muscle relaxants, etc to provide a **BALANCED ANAESTHESIA**.¹⁴

NEUROMUSCULAR TRANSMISSION

The area where motor neuron terminal meets a muscle cell is termed as Neuromuscular junction (NMJ). A narrow 20 nm gap exists between the muscle fiber and nerve terminal called as the synaptic cleft. A depolarized action potential results in influx of calcium ions through Ca^{2+} channels facilitating the vesicles to fuse to the cell membrane thereby releasing Ach. These Ach will cross the synaptic cleft and will bind to the cholinergic nicotinic receptors at the motor end plate. This leads to skeletal muscle contraction.¹⁵

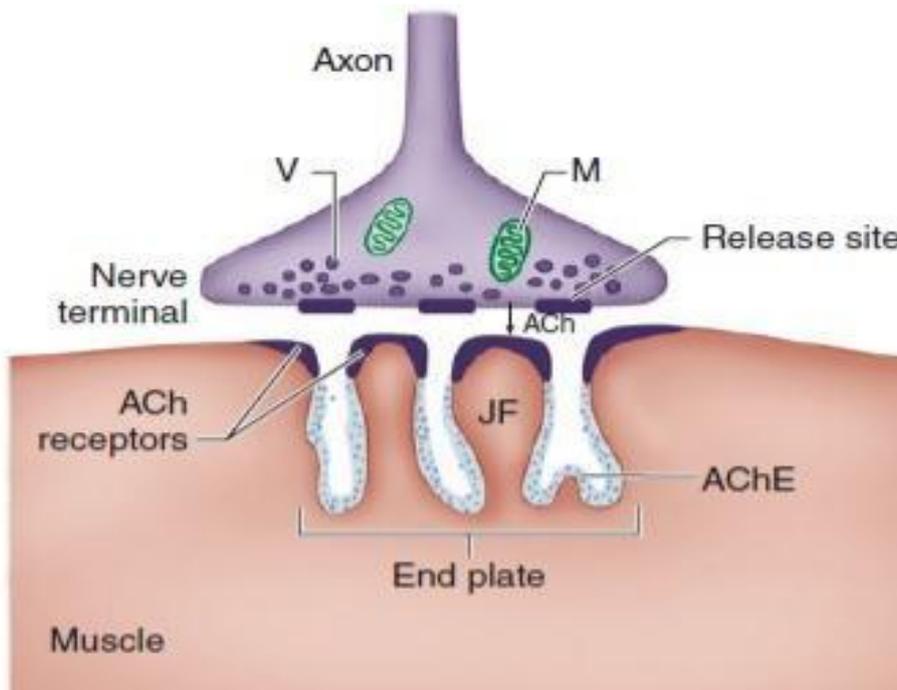
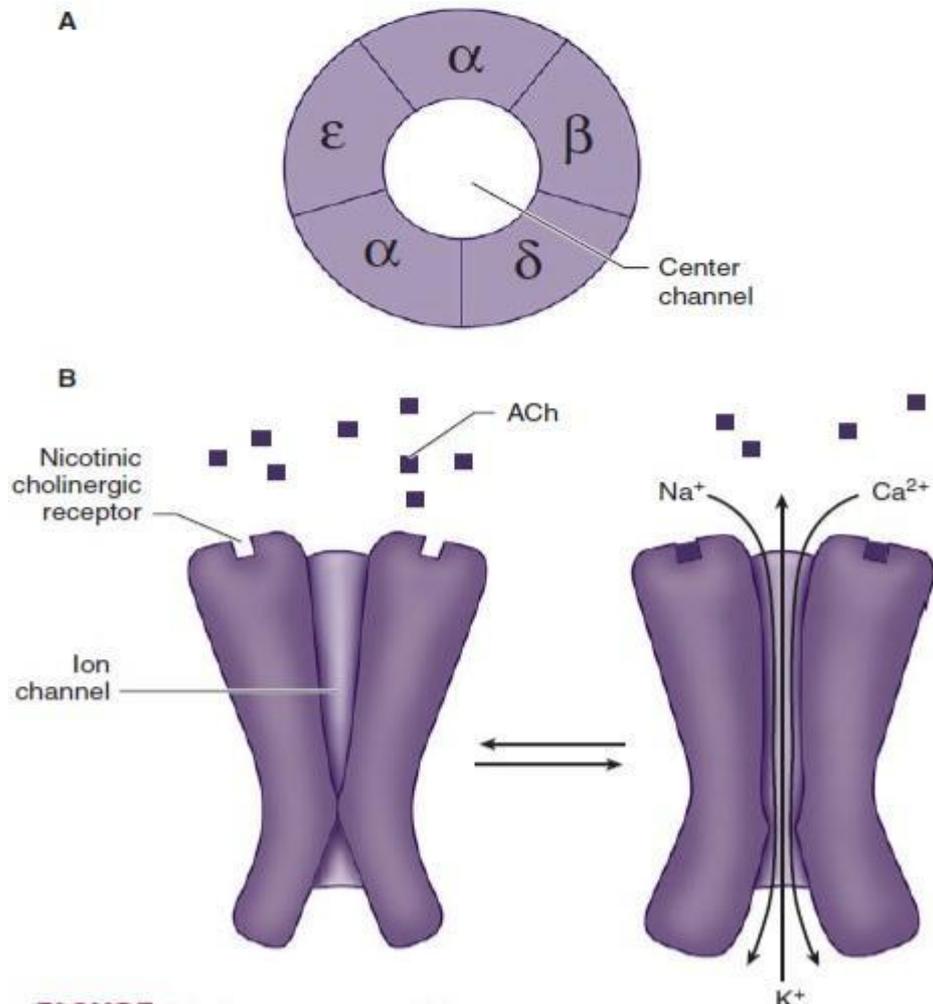


Figure 2: Neuromuscular Junction³⁷

ACH RECEPTOR



Consists of 5 subunits

Figure 3: Acetylcholine Receptor³⁷

An end plate potential is achieved because of movement of cations across the open ACh receptor channels. As soon as enough receptors are occupied by ACh, the perijunctional membrane gets depolarized. The action potential thus produced will result in the release of calcium ions from sarcoplasmic reticulum and helps the actin and myosin filaments to produce muscle contraction.¹²

MECHANISM AND PATHOGENESIS OF **FASCICULATIONS AND MYALGIA**

Fasciculations are arising from the prejunctional depolarization caused by succinylcholine, which leads to evident twitching movements due to repeated firing of motor nerve terminals. Studies with drugs and neurotoxins that act especially at the prejunctional site have been employed in studies to support this theory and showed significant attenuation of fasciculations in animal models. Fasciculations arise due to axonal depolarisations formed by agonists action of Sch at NMJ (prejunctional nicotinic receptors).¹⁹

Many theories have been elucidated about postoperative myalgia, usually attributed to repeated and vigorous muscle activity or after an unfamiliar physical activity which is involuntary. Fasciculations causes a synchronized forceful contraction of muscle bundles, that causes damage to muscle fibers and will lead to pain. These involuntary muscle contractions due to fasciculations at the initial period of muscle relaxation in anaesthesia and these shearing forces are causing muscle damage of varying degree. Studies with electromyography has shown that these fasciculations are causing micromanage development in the muscles.^{17,19}

To find out if any relation exists between these muscle injuries caused by Sch induced fasciculations and muscle stiffness, studies were done to see whether any changes happened in serum creatine phosphokinase levels after administering Sch and was found to be unrelated. Another hypothesis about release of lactic acid in huge amount was implicated but lacks supporting evidences. Other studies have shown an increase release of potassium in patients who showed fasciculations with those who didn't. ¹⁰

The studies conducted to understand the relation between these two entities and to relate it with pain severity has not succeeded till date. All studies are eventhough suggesting pretreatment can decrease incidence of fasciculations, the relation between fasciculations and frequency of postoperative myalgia are yet unclear. Sufficient studies with larger sample size are also less for the same.

PRESSOR RESPONSE TO LARYNGOSCOPY **AND INTUBATION**

Endotracheal intubation is an plays a major role in Airway Management. Both laryngoscopy and intubation are associated with an enhanced sympathetic over activity leading to a sudden rise in blood pressure and heart rate. Even though these responses stay for a short duration of time, it is sufficient enough to cause adverse effects in patient with high risk and can cause dysrhythmias, myocardial infarction, Cardiac failure raised ICP, cerebral hemorrhage, etc. ^{1,7}

Various methods have been advocated through studies to attenuate this response and this can be done by any of the following like:-

1. Blocking the afferent pathway by giving topical local anaesthetic or a local infiltration to block Superior laryngeal nerve. ⁷
2. Blockade of Central pathway using opioids, alpha-2-agonists like Dexmedetomidine and Clonidine, Gabapentin, Pregabalin, etc. ⁷
3. Blocking the efferent pathway using Beta blockers, Calcium channel blockers, intravenous lignocaine, etc. ⁷

SUCCINYLCHOLINE

INTRODUCTION

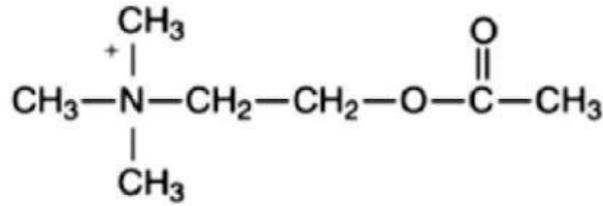
Succinylcholine(Sch) belongs to the group of depolarising muscle relaxants and is a Quarternary ammonium compound that produces sustained depolarization of prejunctional membrane of NMJ.The blockade produced is phase I block which will produce initial muscle fasciculations and later relaxation of skeletal muscles Later these fasciculations result in severe myalgia in the post operative period. ¹⁵

MOLECULAR STRUCTURE

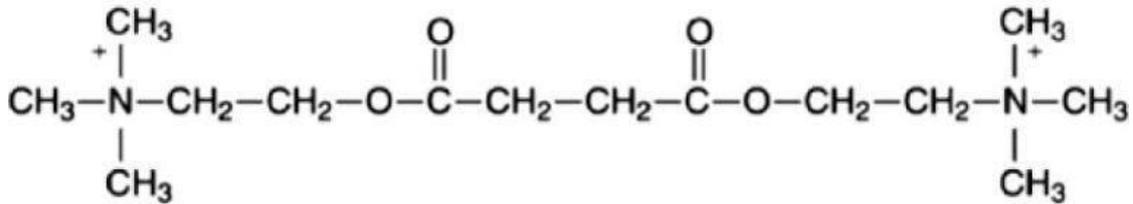
Structurally, Sch is two molecules of Ach combined together by acetate methyl groups.

Molecular formula: $C_{14}H_{30}N_2O_4$

Formed by esterification of succinic acid and choline



Acetylcholine



Succinylcholine

Figure 4: Chemical Structure of Succinylcholine¹⁶

PHYSICAL PROPERTIES: Clear and Aqueous, stored at 4°C.

PHARMACOKINETICS AND DYNAMICS

MECHANISM OF ACTION: Results in sustained depolarization of the motor end plate. It is a short acting muscle relaxant since rapidly get hydrolyzed to succinyl monocholeline and Choline by plasmacholinesterase (Butyrylcholinesterase) and ultimately to succinic acid and choline. The blockade reversal depends on the displacement of Sch away from neuromuscular junction down a concentration gradient.¹²

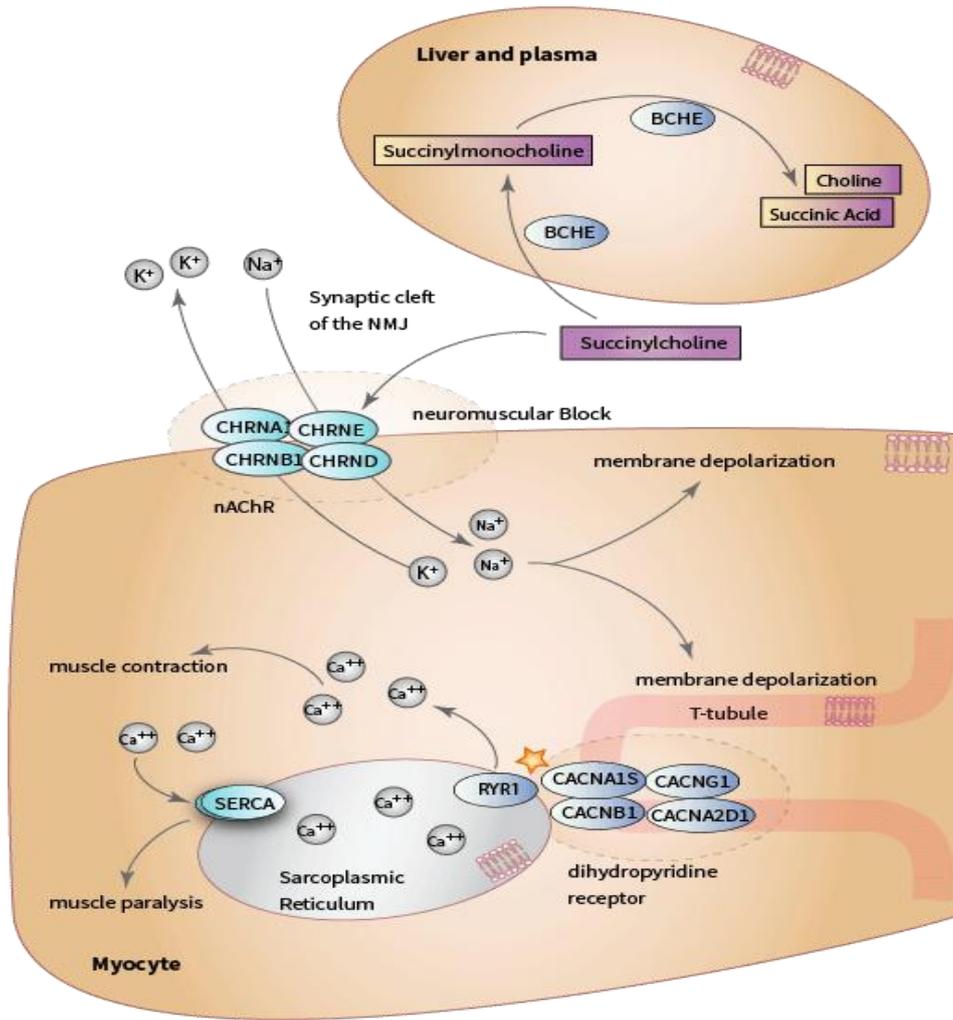


Figure 5: Mechanism of action of Succinylcholine ⁴⁰

ED95: 0.3mg/kg

Endotracheal Intubation dose: 1-1.5mg/kg

Complete neuromuscular response to stimulation gets attenuated by 60 seconds.

Treatment of laryngospasm: 0.1mg/kg

ECT: 0.5mg/kg

Duration of Action: 3-5 minutes

Protein binding: yes but extent not predictable

Elimination $t_{1/2}$: 47 seconds and follows first order kinetics

Excretion: 2-10% excreted unchanged in urine

ADVERSE EFFECTS ^{12,15}

- **HYPERKALEMIA:** should be careful in cases like Burns, Motor neuron palsies, Neuromuscular disorders as it can lead to dysrhythmias.
- **PHASE II BLOCK:** Multiple doses/prolonged exposure to high doses leads to phase II blockade which resembles the block produced by NDMR that may be due to conformation changes in the receptors producing desensitization which is characterized by fading tetanus and TOF, post tetanic potentiation, prolonged recovery time, reversibility with anticholinesterases.
- **SUCCINYLCHOLINE APNOEA:** can occur due to deficiency of pseudocholinesterase. Patient will be paralysed for longer duration and emergence from anaesthesia will be delayed.

- **FASCICULATIONS AND MYALGIA:** Fasciculation is a common adverse effect observed after administering Sch which eventually leads to post-operative myalgia. A wide range of factors have been described such as low preponderance in pregnant women due to hormones like estrogen and progesterone, less seen in children and old age, less predominant in patients who are having good muscular fitness, minor surgeries and early ambulatory increases risk, etc. ^{12,7}

Various techniques are employed to reduce postoperative myalgia but lack much evidence like:- Stretch exercise, supplementing Vitamin C, Dantrolene sodium to interfere with intracellular Ca^{2+} release, Calcium gluconate as a membrane stabilizer, Lidocaine, Phenytoin, Magnesium, NSAIDs, Benzodiazepines, Precurarization, etc. ^{15,7}

- **MALIGNANT HYPERTHERMIA :** In patients who are susceptible to this condition, Sch induced persistent depolarization can predispose to accumulation of intracellular calcium ions which increases the duration of contracture.
- **CARDIOVASCULAR EFFECTS:** Most common are sinus bradycardia, junctional rhythm and sinus arrest. Sometimes effects on autonomic

nervous system can present as tachycardia and hypertension. Ventricular dysrhythmias can happen due to laryngoscopy or intubation.

- **MYOGLOBINURIA** : seen especially in paediatric population and can be attributed to fasciculations caused by Sch.
- **MASSETER SPASM**
- **INCREASED INTRAOCULAR PRESSURE**
- **INCREASED INTRAGASTRIC PRESSURE**
- **INCREASED INTRACRANIAL PRESSURE**

CONTRAINDICATIONS

- Pregnancy
- Cardiac, Liver or Renal failure
- Hypoproteinemia
- Thyrotoxicosis
- Tetanus
- Muscular dystrophy
- Burns

PREGABALIN

INTRODUCTION

Pregabalin is structurally similar to the inhibitory Neurotransmitter GABA, yet functionally not related. It exhibits a wide range of activities like anxiolysis, analgesia, anti convulsions action, attenuation of stress response, etc. ¹⁵

MOLECULAR STRUCTURE

S-(+)-3-isobutylgaba : produced as lipophilic analogue of GABA which is substituted at 3-position to allow diffusion and to help cross BBB. It exists in isomeric forms and S-(+)-3-isobutylgaba is the enantiomer that is pharmacologically active one.

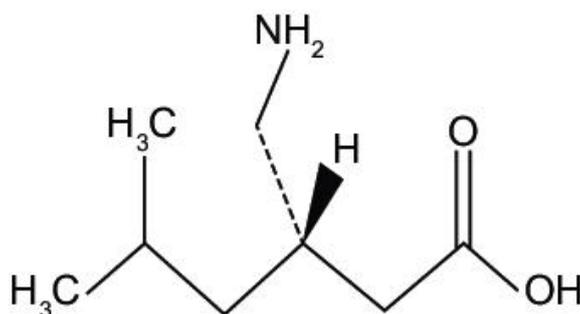


Figure 6: Chemical Structure of Pregabalin ³⁸

MECHANISM OF ACTION ^{15,21}

Pregabalin belongs to Gabapentinoid group of drugs that bind to $\alpha 2\delta$ subunit of voltage gated Ca^{2+} channel thereby restricting influx of calcium channels and thereby excitatory neurotransmitters are not released. Release of neurotransmitters like glutamine, dopamine, serotonin, norepinephrine, and substance P. ^{15,21} Analgesic effect mainly depends upon the receptors or proteins that interacts with like:-

Ca ²⁺ channel subunit	Prion protein
Thrombospondins	BK channels
A-neurexins	LRP1
NMDA receptors	GABA-A receptors

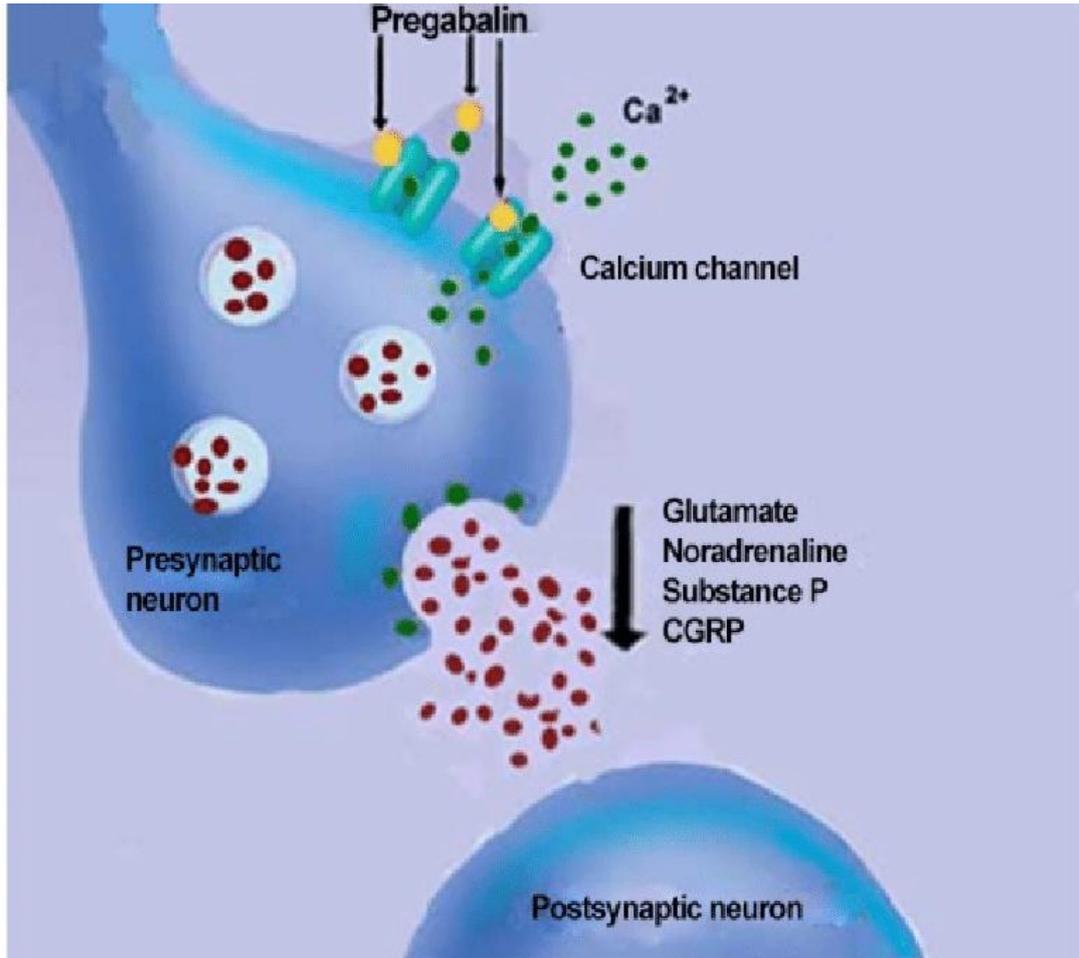


Figure 7: Mechanism of Action of Pregabalin ³⁹

PHARMACOKINETICS

Absorption: Rapidly via oral route and more effective while fasting

Plasma concentration: Reached within 1 hour following single or multiple dose and steady state achieved in 24 to 48 hours following repeated doses.

Dose: 75-150mg/ day upto 450-600mg/ day

Bioavailability: Orally $\geq 90\%$, dose independent

Protein Binding: Absent

Elimination $t_{1/2}$: 6.3 hours and dose independent

Distribution: Crosses BBB as it is a substrate known to help in transport of large amino acids across brain.

Metabolism: <2% metabolized and excreted unchanged via kidneys.

Not an enzyme inducer or inhibitor, thereby having less drug-drug interactions.

LACK OF DRUG INTERACTIONS

The pharmacokinetic properties of pregabalin shows that the drug has very less drug-drug interaction potential as pregabalin is neither metabolized nor it binds to plasma proteins. Also studies done using human liver microsomes have found that pregabalin does not have any effect on cytochrome P450 at its therapeutic Dosage, neither affects the metabolism of the drugs eliminated via this route. ¹⁵

USES ^{14,15}

- Peripheral neuropathic pain
- Anxiolysis in Generalized anxiety disorder
- Adjunct for epilepsy management
- Attenuation of stress response during intubation
- Fibromyalgia
- Post herpetic neuralgia

- Neuropathy due to spinal cord injury
- Intractable migraine headache
- As a premedication to provide post operative analgesia

ADVERSE EFFECTS ^{14,15}

- Increased somnolence
- Dizziness
- Cognitive impairment
- Fatigue
- Ataxia
- Rarely: Hepatotoxicity, Thrombocytopenia, Dermatologic and Hematologic reactions

PREGABALIN IN ANESTHESIA^{2,3,4}

Other than management of acute/chronic pain, Pregabalin plays an important role in routine anaesthesia practice. The most common among them are its role in:-

A. ANXIOLYSIS

B. ATTENUATION OF PRESSOR RESPONSE

C. DURATION OF SPINAL ANAESTHESIA

D. OPIOID FREE ANAESTHESIA

E. POST OPERATIVE PAIN MANAGEMENT

ANXIOLYSIS : In General Anaesthesia, administration of pregabalin is shown to be very effective in reducing anxiety preoperatively. Studies have shown that supplementation of even low doses like 75 mg sufficient enough to reduce anxiety level of patients. By this we can achieve a smooth induction during GA thereby facilitating a smooth perioperative period.

ATTENUATION OF PRESSOR RESPONSE : Noxious stimuli during procedures like laryngoscopy and intubation can predispose to pressor response thereby hampering the hemodynamic stability. It can cause a sudden increase in Blood pressure and Heart rate within 30 seconds and settle back by 5 to 10 minutes. Various studies have been employed to understand action of pregabalin on pressor response and it was found to have some significant effects.

Pregabalin is given preoperatively 1 to 2 hours prior to laryngoscopy and intubation for attenuating pressor response.

DURATION OF SPINAL ANAESTHESIA : The mechanism of action of pregabalin in prolonging the duration of sensory and motor blocks in spinal anaesthesia is not clear. It can be multifactorial. The potentiation of inhibitory Neurotransmitter like GABA and suppressing the release of excitatory neurotransmitters along with anxiolysis and euphoria can be the reason.

OPIOID FREE ANAESTHESIA : Pregabalin is known to reduce use of opioids during general anaesthesia but extent to which it is effective is still being studied. But by giving pregabalin intraoperative opioid requirement can be reduced and opioid sparing anaesthesia can be tried. It also reduces the post operative requirement of analgesia.

POST OPERATIVE PAIN MANAGEMENT : Post operative pain management plays a pivotal role in the surgical outcome of the patient and also can reduce distressing myalgia especially due to Sch induced fasciculations and thereby reducing the duration of hospital stay. It is usually combined with other drugs as a part of multimedia analgesia.

MATERIALS AND METHODS

SOURCE OF DATA:

This study was carried out on patients undergoing Surgery under General Anaesthesia in B.L.D.E. U's Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura.

METHOD OF COLLECTION OF DATA:

Study Design: Prospective randomized, double-blind Study.

Study Period: One and a half year from November 2022 to April 2024.

Sample Size: 201 patients of both genders are randomly divided into three groups of 67 each as:-

- Group A : Cap Pregabalin 75mg
- Group B : Cap Pregabalin 150mg
- Group C : Saccharine pill 10mg

STATISTICAL DATA

Sample size:

With Anticipated incidence and severity of postoperative myalgia between control and Pregabalin with 150mg, 25.7 % and 7.1% resp, the study required a sample size of 67 per group.¹⁰ (i.e., a total sample size of 201 of three groups assuming equal group sizes), to achieve a power of 80% for detecting a difference in proportions between groups at a two-sided p-value of 0.05, using Statulator software. (<http://statulator.com/SampleSize/ss2P.html>)

(Sample size was calculated using two proportions of control and Pregabalin with 150mg, But in the present study, three groups were included (Because of non-availability of three group study))

Total sample size=(67+67+67=201)

Formula used

- $n = \frac{(z\alpha + z\beta)^2 \cdot 2 \cdot p \cdot q}{MD^2}$

MD²

Where Z= Z statistic at a level of significance

MD= Anticipated difference between two proportions

P=Common Proportion

$$q = 100 - p$$

Statistical Analysis

- The data obtained were entered in a Microsoft Excel sheet, and statistical analysis was performed using statistical package for the social sciences (Version 20).
- Results were presented as Mean \pm SD, Median and interquartile range, frequency, percentages, and diagrams.
- For normally distributed continuous variables between three groups were compared using ANOVA test. For not normally distributed variables Kruskal walli's test was used. Categorical variables between two groups were compared using Chi square test. $p < 0.05$ was considered statistically significant. All statistical tests were performed two-tailed.

INCLUSION CRITERIA:

- Patients undergoing surgery under General Anaesthesia
- Age group 18 to 60
- ASA 1 or 2

EXCLUSION CRITERIA:

- Patients with drug allergies
- Patient Refusal
- Seizure history
- Diabetes mellitus
- Hypertension
- Cardiac diseases
- Impaired kidney or liver function
- Raised ICP or IOP
- On Antiepileptics, antidepressants, calcium channel blockers
- Pregnant and lactating females

- This study was started after CTRI Registration (Reg no: CTRI/2023/03/050162) and was carried out in the operation theatre complex of Shri B M Patil medical college hospital on patients undergoing surgery under General Anaesthesia. The adequate sample size calculated was 201 and the patients were randomly assigned into three groups having 67 each, Group A (Pregabalin 75mg), Group B (Pregabalin 150mg) and Group C (Placebo- Saccharine pill 10mg).
- Blinding:- This study was carried out as a double blinded study where the person who is administering the drugs and the person who is observing the parameters were blinded.
- Patients were advised strict NBM for 6 hours. Procedure was explained to the patient and consent to participate in the study was obtained. Patients were given Pregabalin or Saccharine pill in preoperative room , two hours prior to induction of anaesthesia and patient was monitored for any changes in vital parameters and also any adverse effects like, bradycardia, increased somnolence, drowsiness and nausea.
- Patient shifted inside operating room, intravenous access secured and started iv fluids. Baseline vitals recorded. All patients were premedicated

with inj Glycopyrrolate 0.2mg iv, inj Midazolam 1mg iv, inj Ondansetron 4mg iv. For analgesia, inj Fentanyl 2mcg/kg was given and induced using inj Propofol 2mg/kg. Inj Succinylcholine 1.5mg/kg was administered. Immediately after Sch, patient was observed by a doctor who was blinded for both incidence and severity and given a score of 0 to 3 as follows:-

GRADE	SEVERITY
0	NIL (No fasciculation)
1	MILD (Fine fasciculations at the eyes, neck, face or fingers without limb movement)
2	MODERATE (Fasciculations on both sides and obvious limb movement)
3	SEVERE (Widespread, sustained fasciculation)

Table 1: Severity of Fasciculations Grading ⁶

- After one minute post Sch administration, endotracheal intubation was carried out using proper sized ET tube, bilateral air entry confirmed by auscultation and tube was secured using plasters. Maintenance of anaesthesia done using Nitrous oxide 50%, Oxygen 50%, Isoflurane 0.6% and intermittent doses of Atracurium. Post surgery, reversal of neuromuscular blockade done using Neostigmine and Glycopyrrolate.

- The Incidence and severity of myalgia was noted by a blinded observer after 24 hours of surgery and severity was given a score of 0 to 3 as follows:-

GRADE	SEVERITY
0	NIL (no muscle pain)
1	MILD (Muscle stiffness or pain on one area only but no treatment required)
2	MODERATE (Muscle stiffness or pain indicated by the patient himself and treatment required)
3	SEVERE (Generalized, severe pain requiring more treatment)

Table 2: severity of Myalgia Grading ⁶

- The efficacy on attenuation of pressor response during laryngoscopy and intubation were assessed using SBP, DBP, MAP and HR recorded before induction, during induction, intubation, after 1minute, 3 minutes, 5 minutes, 10 minutes and 15 minutes respectively.
- The patient's requirement for postoperative analgesia and the time of the first dose of postoperative analgesic (inj Diclofenac 75mg) were recorded.

- The sedation level of the patient was assessed at 2 hours and 6 hours after supplementing pregabalin or placebo using Ramsay Sedation Score.

Ramsay Sedation Score

<u>Sedation Level</u>	<u>Score</u>
Patient anxious & agitated or restless or both	1
Patient cooperative, oriented & tranquil	2
Patient responds to commands only	3
Patient exhibits a brisk response to light glabellar tap or loud auditory stimulus	4
Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus	5
Patient exhibits no response	6

Table 3: Ramsay Sedation Score⁶

OBSERVATION AND RESULTS

- The study was conducted for a period of one and half years on patients between 18 to 60 years undergoing surgery under GA.
- The data collected from the study was listed in the Master Chart and evaluated.
- Total Sample size : 201 (67 in each group)..
- Group A is Cap Pregabalin 75mg
- Group B is Cap Pregabalin 150mg
- Group C is Saccharine pill 10mg
- Tests used are Chi Square Test and Kruskal-Wallis Test according to data.
- P value less than 0.05 considered as statistically significant.
- All categorical data like age distribution, Sex, Incidence of fasciculation and myalgia, Association of fasciculation and myalgia, Incidence of Adverse effects have been assessed using Chi Square Test.
- All not normally distributed data like mean Age, BMI, Duration of Surgery, Severity of Fasciculations and myalgia, SBP, DBP, MAP, HR, sedation score, time of first analgesic dose have been assessed using Kruskal-Wallis Test.

AGE DISTRIBUTION AMONG STUDY GROUPS

Table 4 : Age Distribution in groups

AGE	GROUP A	GROUP B	GROUP C	Total	Chi Square test	P value
<20	5 (7.50%)	7 (10.40%)	7 (10.40%)	19 (9.50%)	13.416	0.098
20-29	26 (38.80%)	10 (14.90%)	18 (26.90%)	54 (26.90%)		
30-39	13 (19.40%)	16 (23.90%)	16 (23.90%)	45 (22.40%)		
40-49	8 (11.90%)	20 (29.90%)	14 (20.90%)	42 (20.90%)		
50+	15 (22.40%)	14 (20.90%)	12 (17.90%)	40 (20.40%)		
Total	67 (100%)	67 (100%)	67 (100%)	201 (100%)		

Statistically not significant

Age (years) of patients in Group A, Group B and Group C were assessed using Chi Square test. The groups were comparable with a p value of 0.098.

Graph 1 : Age Distribution in groups

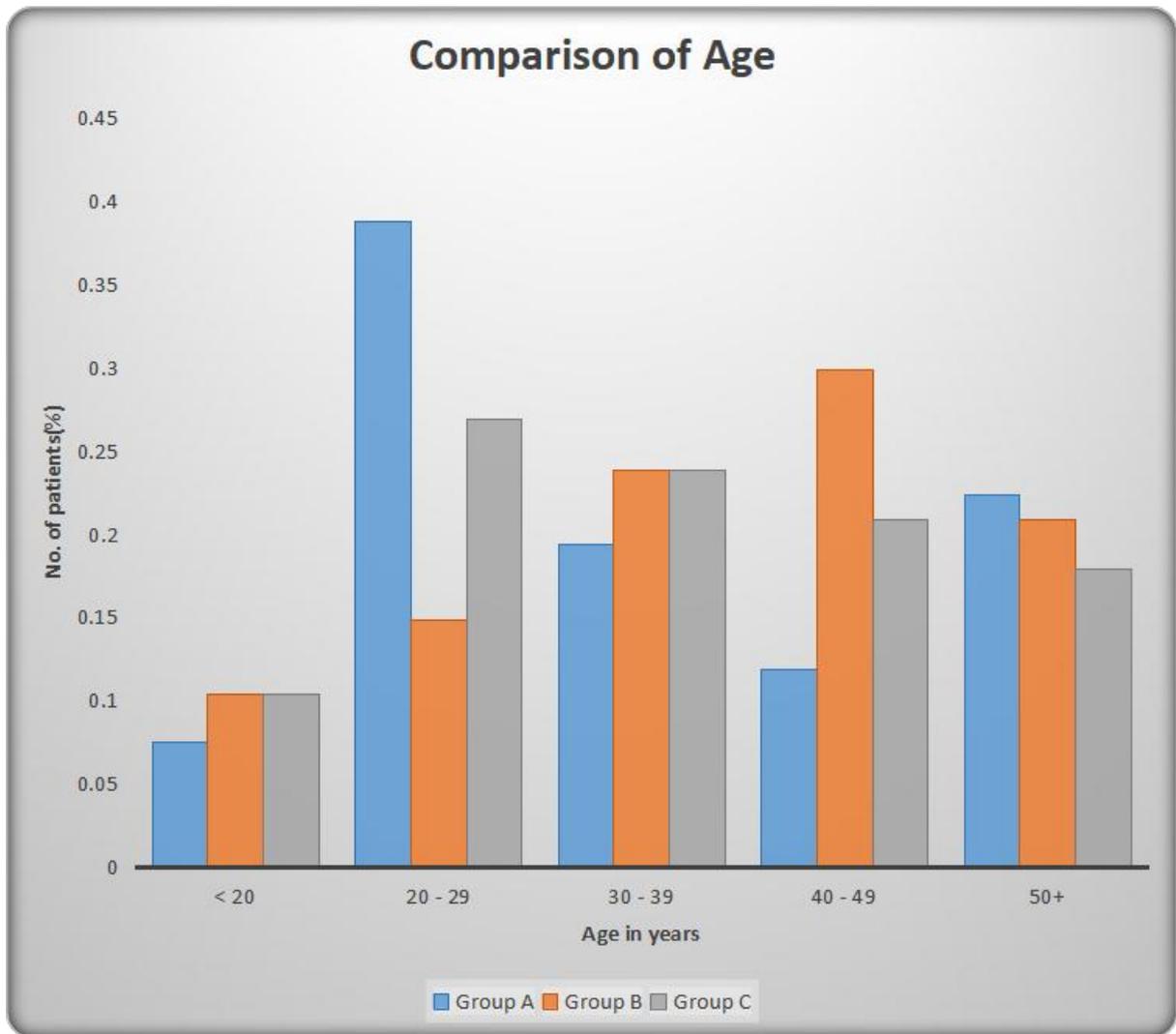
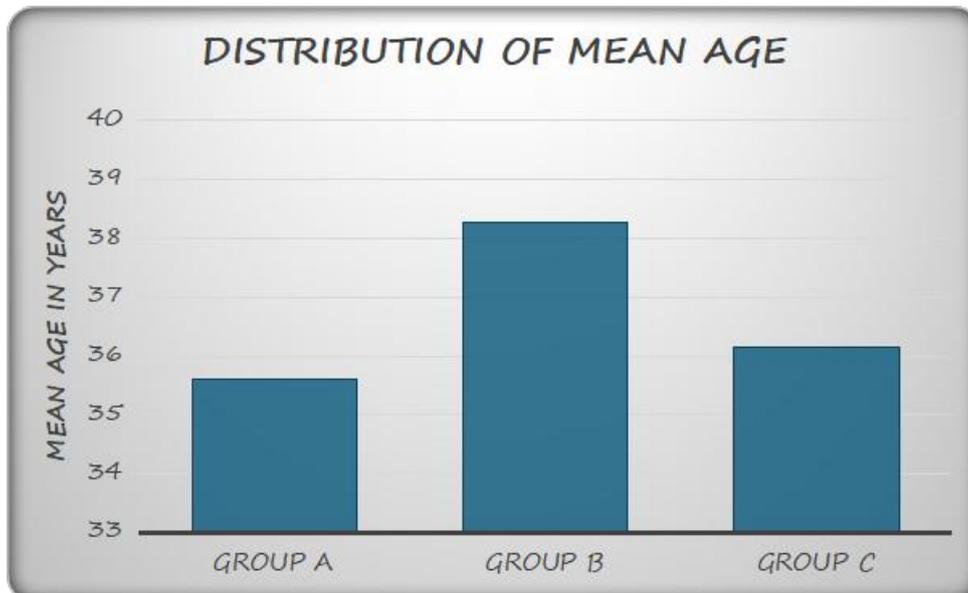


Table 5: Distribution of Mean Age among Groups

	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
AGE	35.6	13.528	38.28	12.196	36.15	13.285	2.193	0.334

Statistically not significant

Mean Age in years among Group A, Group B and Group C were assessed using Kruskal-Wallis test. These groups were comparable with a p value of 0.334.

Graph 2: Distribution of Mean Age among groups

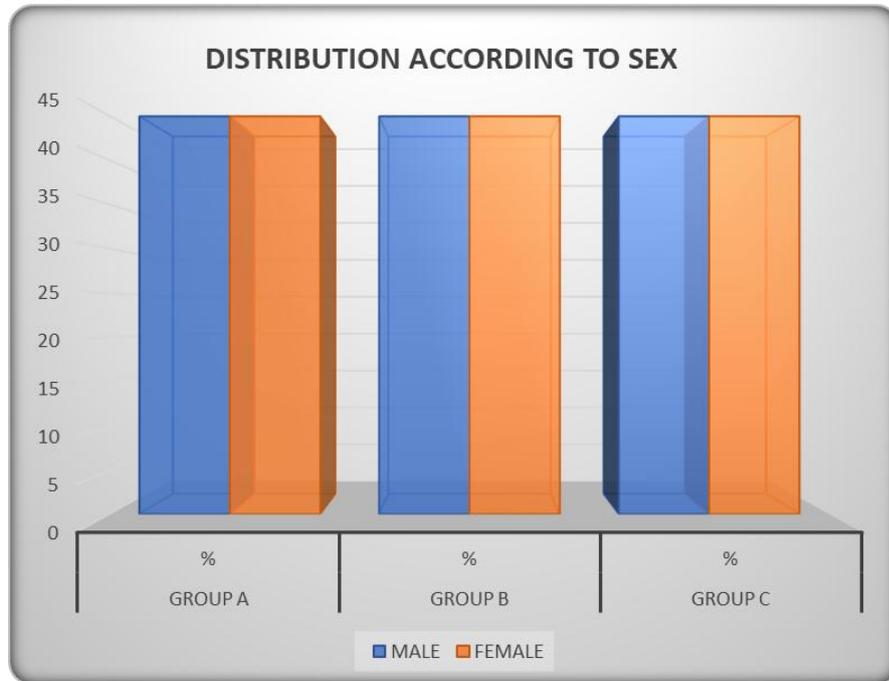
DISTRIBUTION ACCORDING TO SEX**Table 6: Distribution of Sex among groups**

SEX	GROUP A		GROUP B		GROUP C		Chi Square test	p value
	N	%	N	%	N	%		
MALE	34	51	32	48	34	51	0.159	0.923
FEMALE	33	49	35	52	33	49		

Statistically not significant

Number of Male and female patients have been compared among groups and evaluated using Chi Square Test. The groups were comparable with a p value of 0.923.

Graph 3: Distribution of Sex among groups



On analyzing data, patients belonging to both gender (Male and Female) were almost equally distributed

DISTRIBUTION OF BMI

Table 7: Distribution of BMI among groups

BMI	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
		23.452	2.6365	22.89	1.7556	23.445	1.8114	2.145

Statistically not significant

BMI (Kg/m²) among three groups have been evaluated using Kruskal Wallis Test. The groups were comparable with a p value of 0.342.

Graph 4: Distribution of BMI among groups

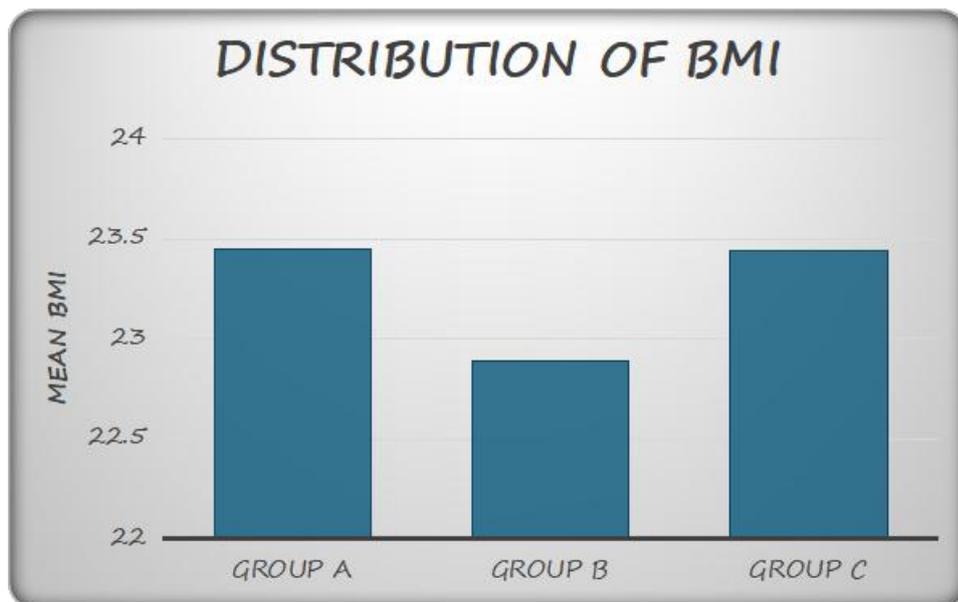
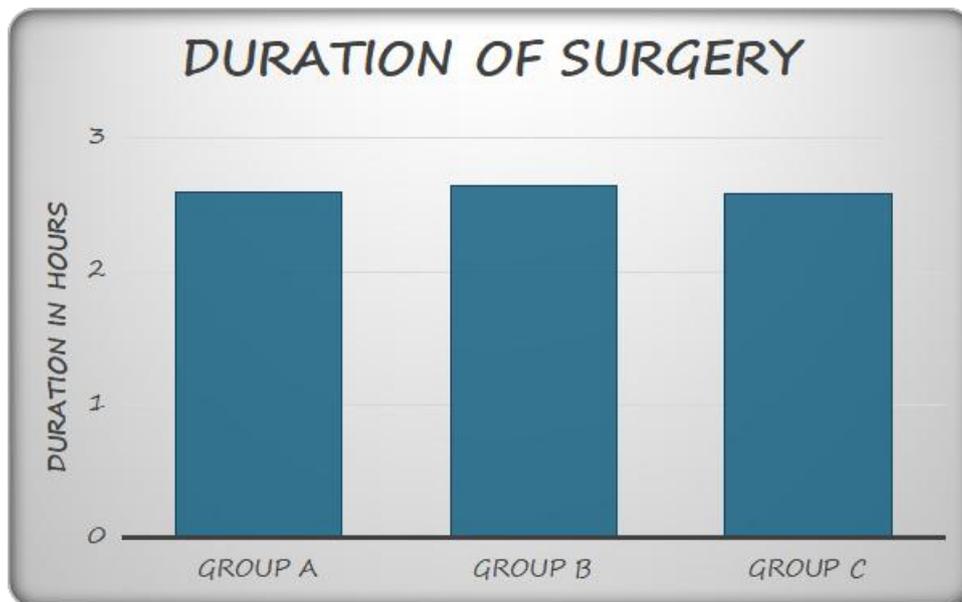


Table 8: Distribution of Duration of Surgery

DURATION OF SURGERY	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
		2.6	0.605	2.64	0.62	2.58	0.607	0.335

Statistically not significant

Duration of Surgery among Group A, Group B and Group C were assessed using Kruskal Wallis Test. The groups were comparable with a p value of 0.846.

Graph 5: Distribution of Duration of Surgery

INCIDENCE OF FASCICULATION

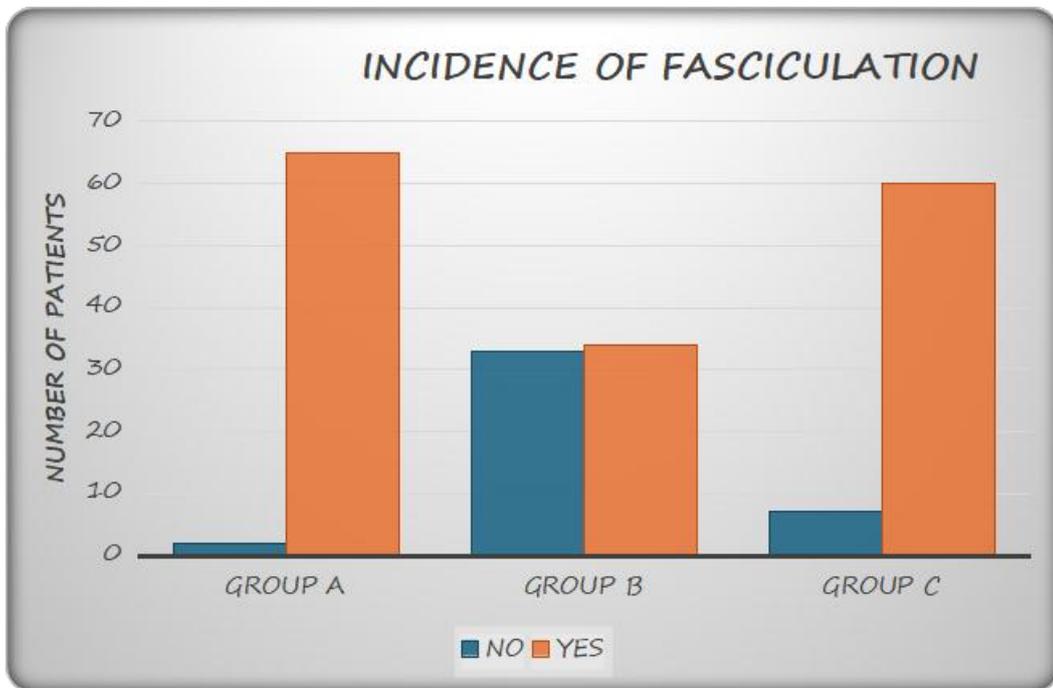
Table 9: Incidence of Fasciculation among groups

INCIDENCE OF FASCICULATION	GROUP A		GROUP B		GROUP C		Chi Square	p value
	N	%	N	%	N	%		
NO	2	3	33	49.3	7	10.4	50.024	<0.001*
YES	65	97	34	50.7	60	89.6		

*Statistically Significant at 5% level of significance (p<0.05)

Incidence of fasciculation among Group A, Group B and Group C were assessed using Chi Square Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 6: Incidence of Fasciculation among groups



The incidence of Fasciculation was significantly less in Group B, compared to Group A and Group C.

SEVERITY OF FASCICULATION

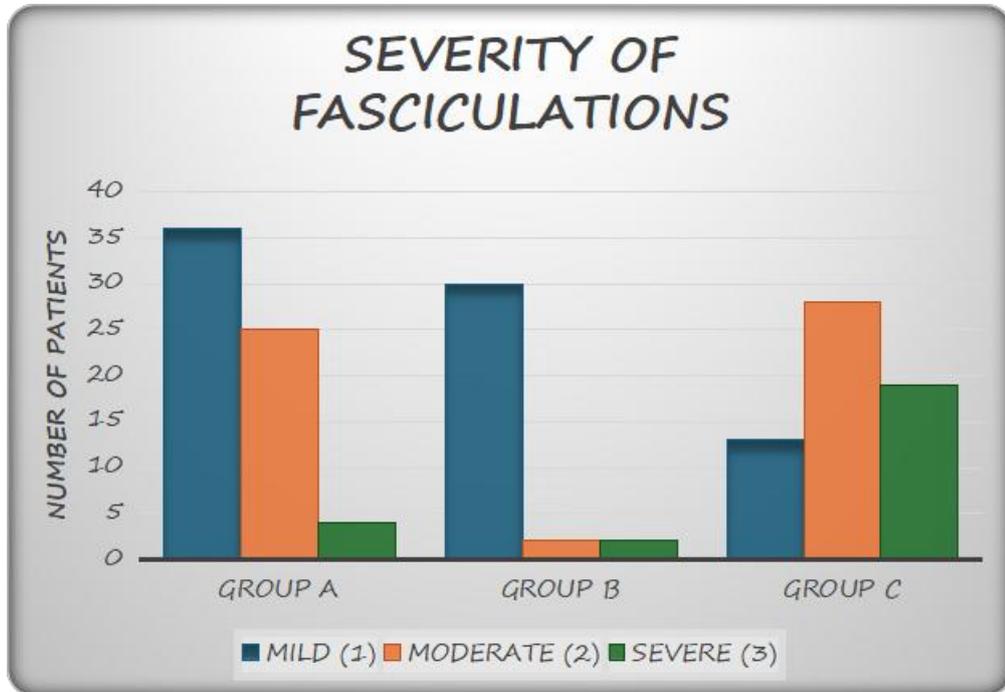
Table 10: Severity of Fasciculations among Groups

FASCICULATION GRADE	GROUP A		GROUP B		GROUP C		Kruskal-Wallis test	p value
	N	%	N	%	N	%		
MILD (1)	36	53.7	30	44.8	13	19.4	67.706	<0.001*
MODERATE (2)	25	37.3	2	3	28	41.6		
SEVERE (3)	4	6	2	3	19	28.4		

*Statistically Significant at 5% level of significance (p<0.05)

Severity of fasciculation among Group A, Group B and Group C were assessed using Chi Square Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 7: Severity of Fasciculation among groups



The Severity of Fasciculation was significantly less in Group B, compared to Group A and Group C.

Majority in Group A had mild to moderate fasciculation.

Majority in Group B had only mild fasciculation.

Majority in Group C had moderate to severe fasciculations.

Table 11: Comparison of Fasciculation between groups

	P value
GROUP A vs B	<0.001*
GROUP B vs C	<0.001*
Group A vs C	=0.057

*Statistically Significant at 5% level of significance ($p < 0.05$)

Assessment of Fasciculation between each groups were done using Kruskal Wallis Test. A significant p value of <0.001 was obtained between both Group A vs B and B vs C, whereas it was statistically insignificant between Group A vs C.

By analyzing data from Table 5, 6 and 7, it can be concluded that Incidence and severity of fasciculations were significantly less in Group B compared to other two groups.

INCIDENCE OF MYALGIA

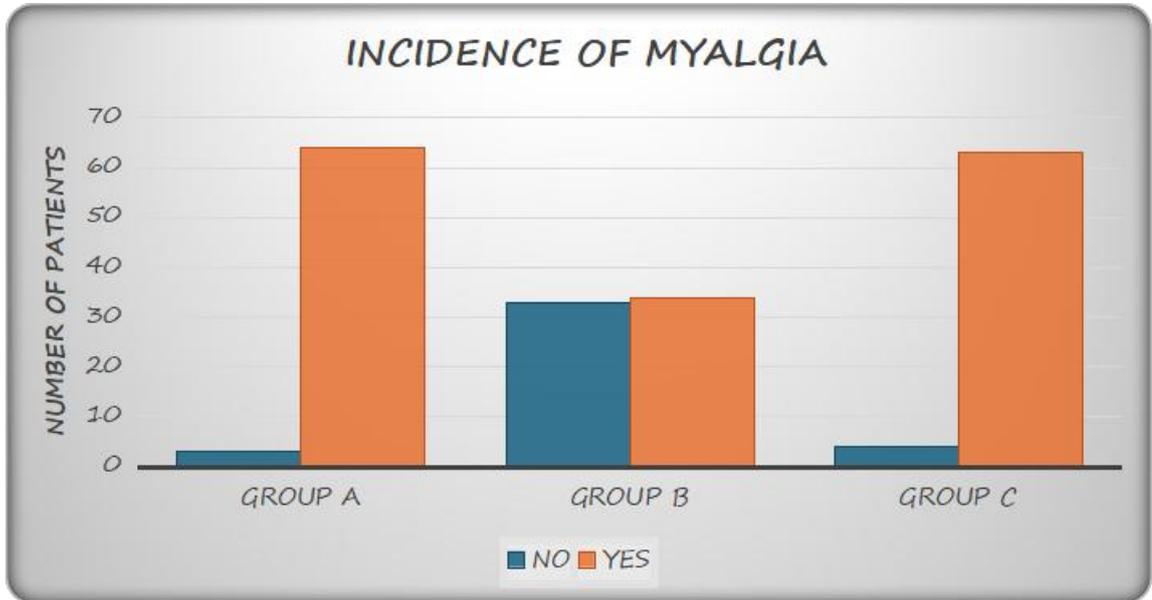
Table 12: Incidence of Myalgia among groups

INCIDENCE OF MYALGIA	GROUP A		GROUP B		GROUP C		Chi Square Test	p value
	N	%	N	%	N	%		
NO	3	4.5	33	49.3	4	6	54.37	<0.001*
YES	64	95.5	34	51.7	63	94		

*Statistically Significant at 5% level of significance (p<0.05)

Incidence of Myalgia among Group A, Group B and Group C were assessed using Chi Square Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 8: Incidence of Myalgia among groups



The incidence of Myalgia was significantly less in Group B, compared to Group A and Group C.

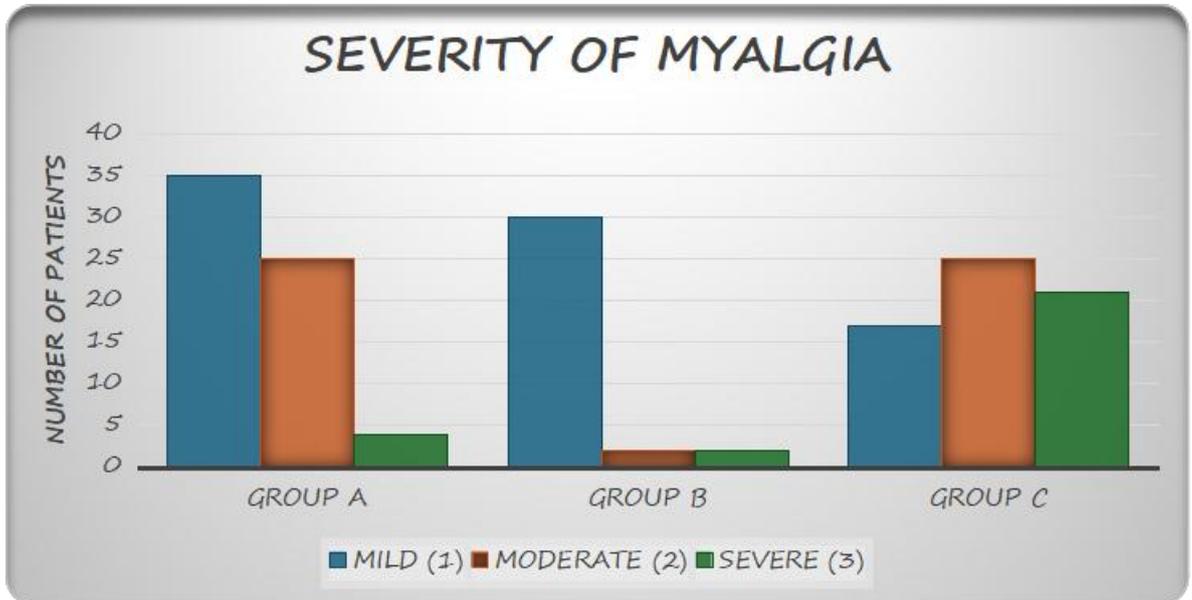
SEVERITY OF MYALGIA

Table 13: Severity of Myalgia among Groups

MYALGIA GRADE	GROUP A		GROUP B		GROUP C		Kruskal-Wallis test	p value
	N	%	N	%	N	%		
MILD (1)	35	52.2	30	44.8	17	25.4	72.101	<0.001*
MODERATE (2)	25	37.3	2	3	25	37.3		
SEVERE (3)	4	6	2	3	21	31.3		

*Statistically Significant at 5% level of significance (p<0.05)

Severity of Myalgia among Group A, Group B and Group C were assessed using Chi Square Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 9: Severity of Myalgia among groups

The Severity of Fasciculation was significantly less in Group B, compared to Group A and Group C.

Majority in Group A had mild to moderate fasciculation.

Majority in Group B had only mild fasciculation.

Majority in Group C had moderate to severe fasciculations.

Table 14: Comparison of Myalgia between groups

	P value
GROUP A vs B	<0.001*
GROUP B vs C	<0.001*
Group A vs C	=0.019

*Statistically Significant at 5% level of significance (p<0.05)

Assessment of Myalgia between each groups were done using Kruskal Wallis Test. A significant p value of <0.001 was obtained between all the groups.

By analyzing data from Table 8, 9 and 10, it can be concluded that Incidence and severity of myalgia were significantly less in Group B, followed by Group A compared to Group C.

ASSOCIATION BETWEEN FASCICULATION AND MYALGIA

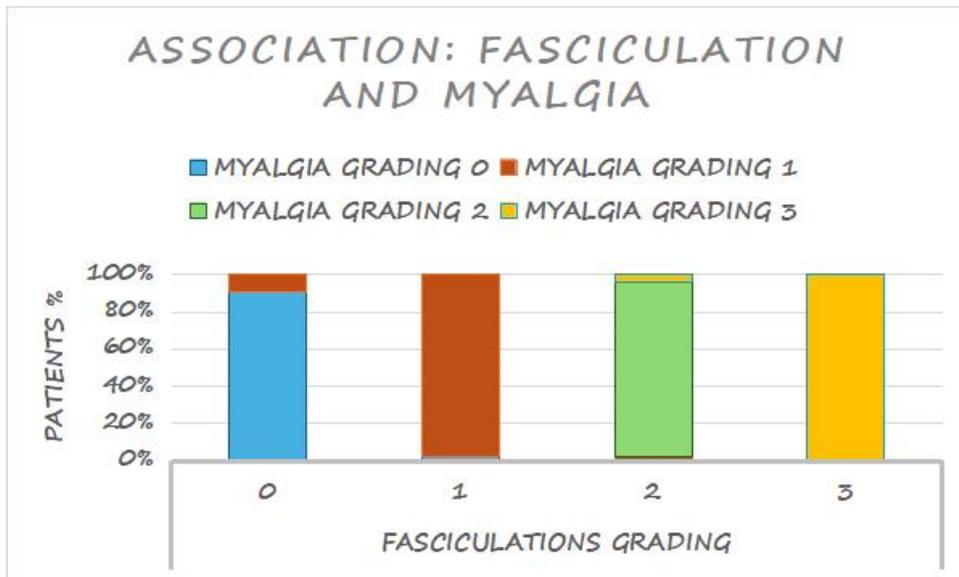
Table 15: Association of Fasciculation and Myalgia among Groups

		MYALGIA GRADING				Total	Chi Square TEST	p value
		0	1	2	3			
FASCICULATIONS GRADING	0	38	4	0	0	42	533.652	<0.001*
		95.00%	4.90%	0.00%	0.00%	20.90%		
	1	2	77	0	0	79		
		5.00%	93.90%	0.00%	0.00%	39.30%		
	2	0	1	52	2	55		
		0.00%	1.20%	100.00%	7.40%	27.40%		
	3	0	0	0	25	25		
		0.00%	0.00%	0.00%	92.60%	12.40%		
Total		40	82	52	27	201		
		100.00%	100.00%	100.00%	100.00%	100.00%		

*Statistically Significant at 5% level of significance (p<0.05)

Association between Fasciculation and Myalgia assessed using Chi Square Test.

A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 10: Association of Fasciculation and Myalgia among Groups

Comparing the data from Table 11 and Figure 9, it can be concluded that both Fasciculation and Myalgia shows a Positive Association (As grade of fasciculation increases, myalgia also increases).

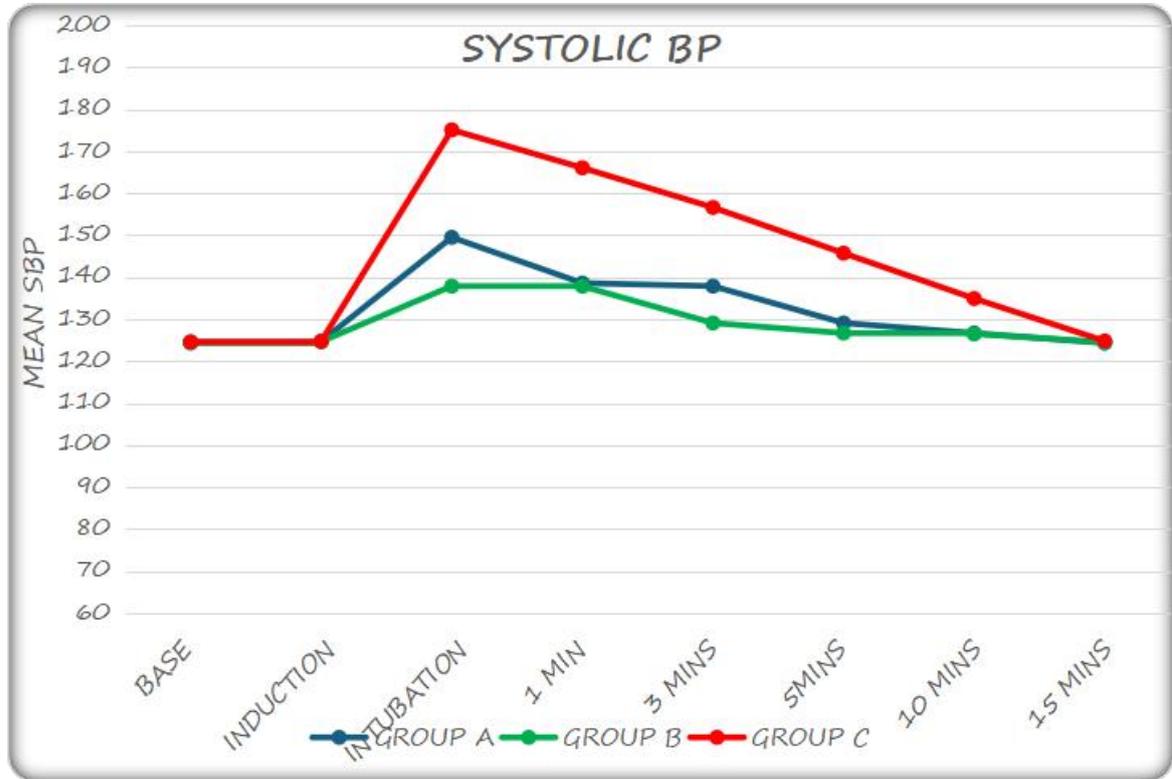
ASSESSMENT OF VITAL PARAMETERS

**Table 16: DISTRIBUTION OF MEAN SYSTOLIC BLOOD
PRESSURE**

SBP	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
BASE	124.6	9.244	124.33	9.083	124.54	9.727	0.182	0.913
INDUCTION	124.72	7.883	124.69	7.867	124.72	10.016	0.068	0.967
INTUBATION	149.49	7.857	137.88	7.442	175.1	7.112	155.58	<0.001*
1 MIN	138.6	7.985	137.85	7.421	166.06	7.699	133.974	<0.001*
3 MINS	137.88	7.442	129.1	8.81	156.63	9.04	131.693	<0.001*
5MINS	129.1	8.81	126.69	8.866	145.73	7.45	101.847	<0.001*
10 MINS	126.69	8.866	126.51	8.879	134.93	6.526	40.885	<0.001*
15 MINS	124.33	9.083	124.51	9.148	124.81	9.245	1.604	0.448

*Statistically Significant at 5% level of significance ($p < 0.05$)

The mean SBP among Group A, B and C were assessed using Kruskal-Wallis Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance ($p < 0.05$)] for mean SBP at Intubation, 1min, 3 mins, 5 mins and 10 mins.

Graph 11: DISTRIBUTION OF MEAN SYSTOLIC BP

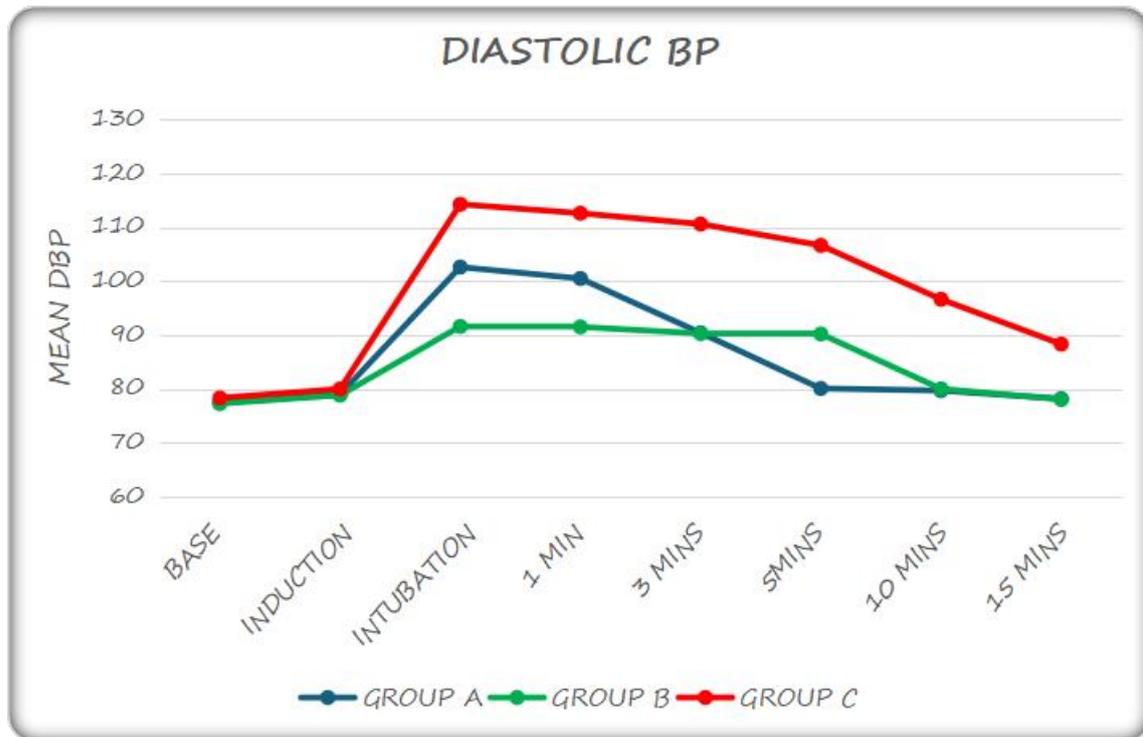
The mean SBP at different time intervals were plotted for each group. A sudden surge in SBP was observed at intubation in all 3 groups as mean SBP in Group C > Group A > Group B. The rise in SBP was significantly high in Group C > Group A > Group B. The attenuation of SBP surge and maintenance of SBP back to baseline was significantly better and faster in Group B followed by Group A and then by Group C.

Table 17: DISTRIBUTION OF MEAN DIASTOLIC BP

DBP	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
BASE	77.46	6.166	77.31	6.036	78.36	6.875	0.968	0.616
INDUCTION	79.04	5.168	78.87	5.178	80.03	6.434	0.334	0.846
INTUBATION	102.66	5.618	91.64	5.404	114.33	4.084	158.762	<0.001*
1 MIN	100.54	5.378	91.55	5.346	112.66	3.722	153.579	<0.001*
3 MINS	90.45	5.536	90.33	5.511	110.66	3.772	134.715	<0.001*
5MINS	80.12	6.009	90.24	5.543	106.69	3.775	157.93	<0.001*
10 MINS	79.73	5.688	80.06	5.969	96.69	1.5	132.478	<0.001*
15 MINS	78.21	5.235	78.09	4.941	88.36	2.144	126.207	<0.001*

*Statistically Significant at 5% level of significance ($p < 0.05$)

The mean DBP among Group A, B and C were assessed using Kruskal-Wallis Test. A significant p value of < 0.001 was obtained [Statistically significant data at 5% level of significance ($p < 0.05$)] for mean DBP at Intubation, 1 min, 3 mins, 5 mins, 10 mins and 15 mins.

Graph 12: DISTRIBUTION OF MEAN DIASTOLIC BP

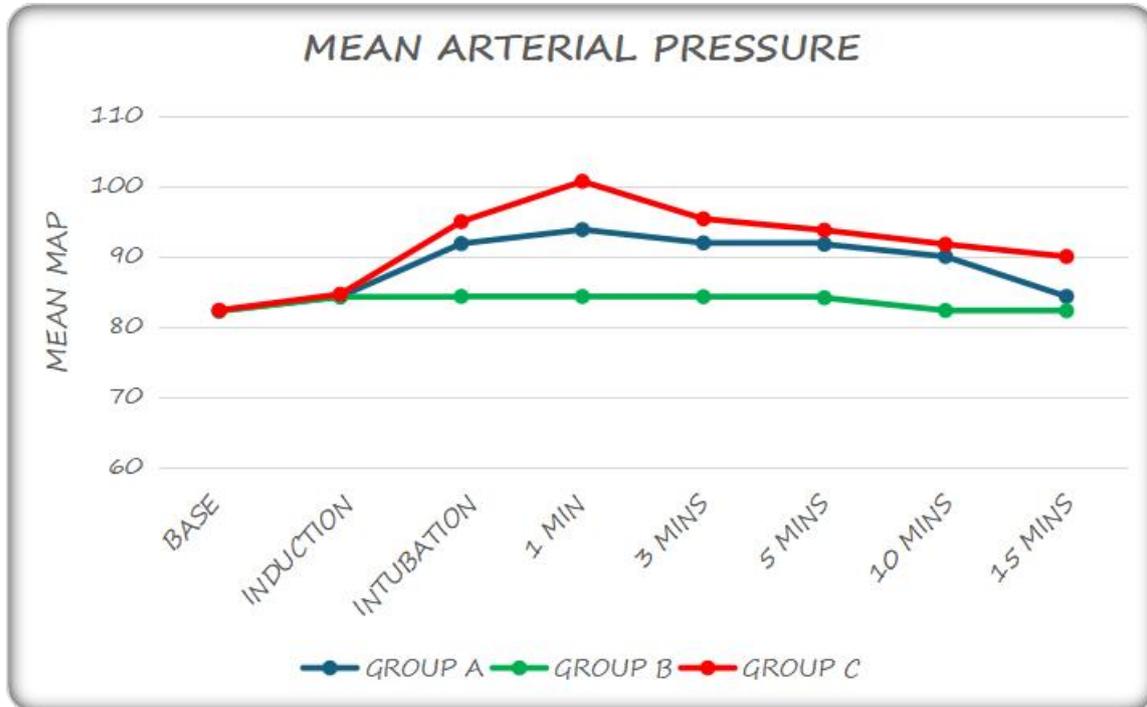
The mean DBP at different time intervals were plotted for each group. A sudden surge in DBP was observed at intubation in all 3 groups as mean DBP in Group C > Group A > Group B. The rise in DBP was significantly high in Group C > Group A > Group B. The attenuation of DBP surge and maintenance of DBP back to baseline was significantly better and faster in Group B followed by Group A and then by Group C.

Table 18: DISTRIBUTION OF MEAN ARTERIAL PRESSURE

MAP	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
BASE	82.37	1.486	82.3	1.457	82.43	1.448	0.155	0.925
INDUCTION	84.37	1.486	84.34	2.447	84.72	1.631	1.232	0.54
INTUBATION	91.93	1.531	84.4	1.538	95.07	2.04	159.537	<0.001*
1 MIN	93.93	1.531	84.39	1.507	100.81	2.432	178.804	<0.001*
3 MINS	92.03	1.586	84.36	1.474	95.46	1.579	166.192	<0.001*
5 MINS	91.84	1.366	84.21	1.431	93.85	1.158	160.369	<0.001*
10 MINS	90.09	1.454	82.4	1.467	91.84	1.366	153.104	<0.001*
15 MINS	84.4	1.538	82.36	1.484	90.09	1.454	153.389	<0.001*

*Statistically Significant at 5% level of significance ($p < 0.05$)

The mean of MAP among Group A, B and C were assessed using Kruskal-Wallis Test. A significant p value of < 0.001 was obtained [Statistically significant data at 5% level of significance ($p < 0.05$)] for mean of MAP at Intubation, 1min, 3 mins, 5 mins, 10 mins and 15 mins.

Graph 13: DISTRIBUTION OF MEAN ARTERIAL PRESSURE

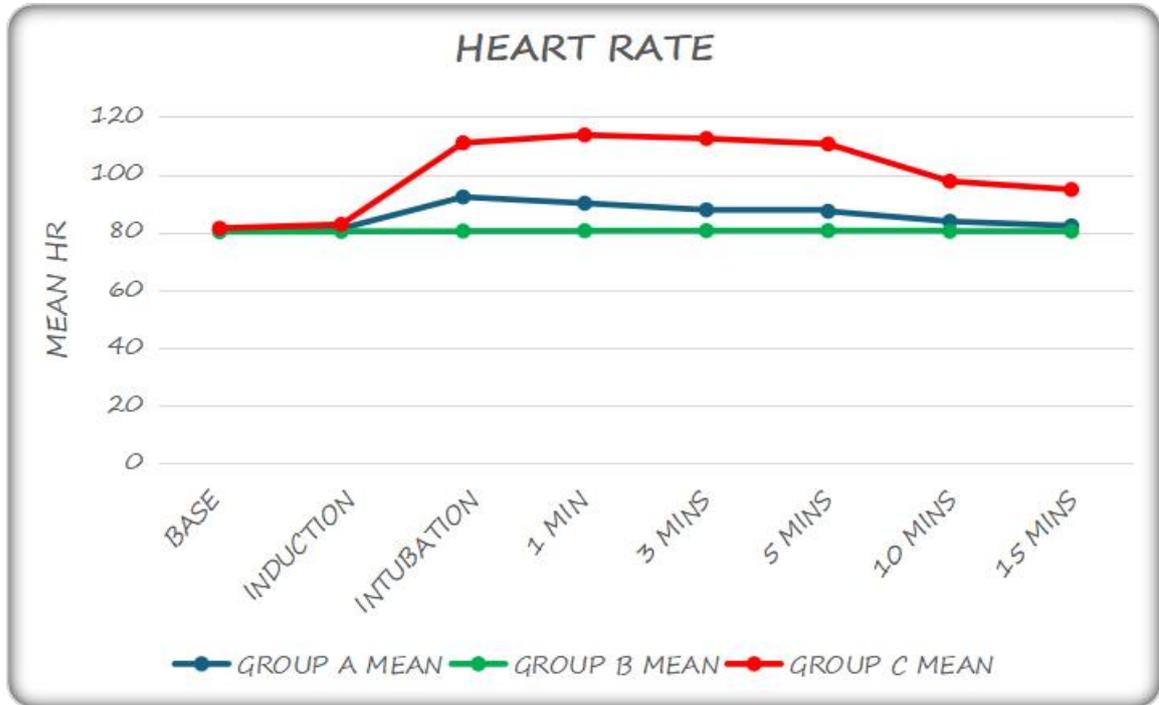
The mean MAP at different time intervals were plotted for each group. A sudden surge in MAP was observed at intubation in all 3 groups as mean MAP in Group C > Group A > Group B. The rise in MAP was significantly high in Group C > Group A > Group B. The attenuation of MAP surge and maintenance of MAP back to baseline was significantly better and faster in Group B followed by Group A and then by Group C.

Table 19: DISTRIBUTION OF HEART RATE

HR	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
BASE	81.03	2.504	80.24	8.711	81.45	2.814	0.902	0.637
INDUCTION	81.33	2.531	80.37	8.723	82.78	2.461	8.203	0.017*
INTUBATION	92.27	2.711	80.46	8.643	111.01	4.866	162.126	<0.001*
1 MIN	90.1	2.583	80.58	8.779	113.73	4.959	154.414	<0.001*
3 MINS	87.81	2.069	80.61	8.787	112.51	4.283	146.597	<0.001*
5 MINS	87.31	4.233	80.6	8.858	110.63	4.42	144.174	<0.001*
10 MINS	83.82	2.276	80.4	8.825	97.7	3.233	132.058	<0.001*
15 MINS	82.27	2.502	80.42	8.878	94.84	1.711	120.848	<0.001*

*Statistically Significant at 5% level of significance ($p < 0.05$)

The mean HR among Group A, B and C were assessed using Kruskal-Wallis Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance ($p < 0.05$)] for mean of HR at Induction, Intubation, 1min, 3 mins, 5 mins, 10 mins and 15 mins.

Graph 14: DISTRIBUTION OF MEAN HEART RATE

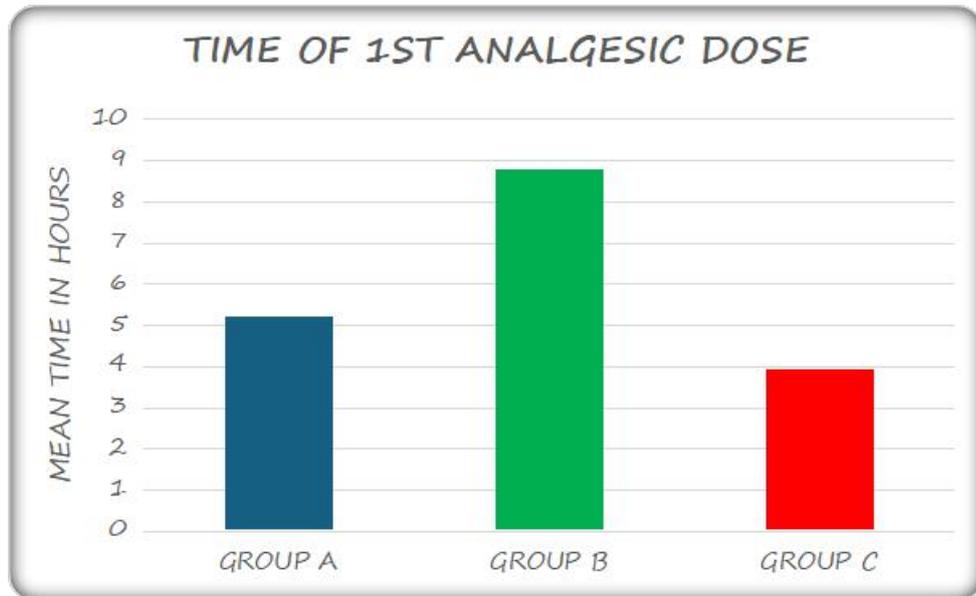
The mean HR at different time intervals were plotted for each group. A sudden surge in HR was observed at intubation in all 3 groups as mean HR in Group C > Group A > Group B. The rise in HR was significantly high in Group C > Group A > Group B. The attenuation of HR surge and maintenance of HR back to baseline was significantly better and faster in Group B followed by Group A and then by Group C.

Table 20: TIME OF FIRST ANALGESIC DOSE

TIME OF 1ST ANALGESIC DOSE (IN HOURS)	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
	5.22	0.982	8.81	1.672	3.94	1.466	132.739	<0.001*

*Statistically Significant at 5% level of significance (p<0.05)

The mean time of first analgesic requirement among groups (in hours) were assessed using Kruskal-Wallis Test. A significant p value of <0.001 was obtained [Statistically significant data at 5% level of significance (p<0.05)].

Graph 15: TIME OF FIRST ANALGESIC DOSE

The mean time of first analgesic requirement among groups (in hours) were graphically represented. The time of first analgesia was observed to be significantly immediate for Group C followed by Group A and then by Group B.

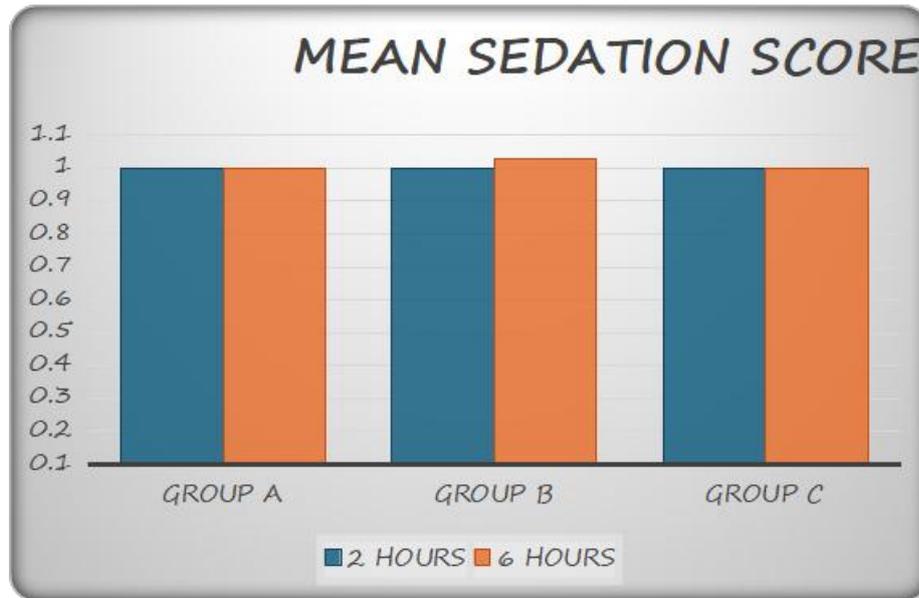
ASSESSMENT OF SEDATION SCORE

Table 21: DISTRIBUTION OF MEAN SEDATION SCORE

SEDATION SCORE	GROUP A		GROUP B		GROUP C		KRUSKAL WALLIS TEST	p value
	MEAN	SD	MEAN	SD	MEAN	SD		
2 HOURS	1	0	1	0	1	0	0	1
6 HOURS	1	0	1.03	0.171	1	0	4.02	0.134

The mean sedation score at 2 hours and 6 hours among groups were assessed using Kruskal-Wallis Test. A p value of 0.132 was calculated and observed to be insignificant.

Graph 16: DISTRIBUTION OF MEAN SEDATION SCORE



The mean sedation score at 2 hours and 6 hours among groups were represented graphically and it was observed to be insignificant.

No respiratory depression was observed in any patients, airway reflexes were intact and patients were responding to verbal commands.

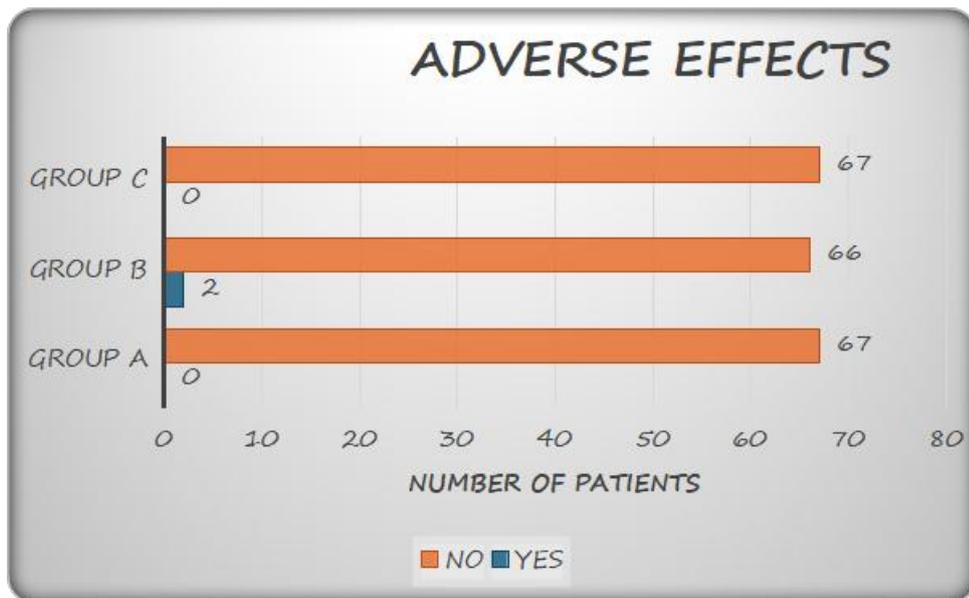
INCIDENCE OF ADVERSE EFFECTS

Table 22: DISTRIBUTION OF INCIDENCE OF ADVERSE EFFECTS

ADVERSE EFFECTS	GROUP A	GROUP B	GROUP C	Chi Square Teat	p value
YES	0	2	0	4.04	0.133*
NO	67	66	67		

The incidence of Adverse Effects among groups were assessed using Kruskal-Wallis Test. A p value of 0.133 was calculated and observed to be insignificant.

Graph 17: DISTRIBUTION OF INCIDENCE OF ADVERSE EFFECTS



The incidence of Adverse Effects among groups were represented graphically and it was observed to be insignificant.

Only 2 patients in Group B had Adverse effects like Drowsiness and nausea.

None of the patients in Group A and C show any adverse effects.

DISCUSSION

Sch is a short acting depolarising muscle relaxant commonly used for laryngoscopy and intubation for patients undergoing surgery under GA. Eventhough developed countries especially western regions are using other muscle relaxants, developing countries like India still consider Sch for laryngoscopy and intubation. Since Sch provides a much better relaxation and intubation condition, Sch remains one of the best drug that can be continued for the same. ⁹

Sch is known to cause its commonest side effect, fasciculations which leads to severe post operative myalgia in these patients. These side effects are very distressing for the patients especially who are posted for day care surgeries as it can lead to prolonged hospital stay. ⁸

Eventhough self limiting, inorder to reduce the incidence and severity of these side effects, various methods and medications have been studied. ⁶

Various studies have been done about the role of drugs like Lidocaine, MgSO₄, Clonidine, NSAIDs, NMDRs like Rocuronium, Cisatracurium, etc on the

efficacy of prevention of Sch induced fasciculations and myalgia. Most of these drugs helped in reducing severity of fasciculations but not the incidence. Later on gabapentinoid group (Gabapentin and Pregabalin) was also been studied with higher doses for the same and found to be effective. But studies using low doses and larger sample size were less especially for pregabalin. Here in this study we compared both low dose and higher dose of pregabalin with a control group for prevention of Sch induced fasciculations and myalgia. ^{17,18,26}

Procedures like laryngoscopy and intubation can also cause an exaggerated pressor response characterized by a sudden surge in Blood pressure, Heart Rate, etc. Drugs like Gabapentinoid group are also been used to attenuate this response to maintain hemodynamic stability of which Pregabalin is known to be the one with lesser side effects like sedation compared to gabapentin. In our study two different doses of pregabalin (75mg and 150mg) were compared with a control group to assess the efficacy of attenuation of pressor response in addition to effect on sch induced fasciculations and myalgia.

Gabapentinoid group of drugs are known for its sedative effect, but pregabalin has lesser sedative effect compared to gabapentin. Much more serious side effects like bradycardia also seen less with pregabalin compared to gabapentin. ¹

Since Gabapentinoid group is known to reduce fasciculations, myalgia, pressor response, post operative analgesic requirement, etc, it makes these agents a better choice compared to other drugs. ¹

As per the observed results from our study, Pregabalin 75 mg and 150 mg, both were effective in reducing both incidence and severity of fasciculation and myalgia, where 150mg was more effective. Our study demonstrates that pressor response was also attenuated by both doses of pregabalin where 150mg was comparatively better. On assessing time of first analgesic dose also both prolonged time of requirement for post operative analgesics, where 150mg was more effective. On assessing sedation level, none of the group showed any significance. Adverse effects were also very negligible on comparing incidence among the groups.

Velez et al, demonstrated in their study that incidence of myalgia significantly reduced in patients who was given gabapentinoid (Gabapentin or Pregabalin) compared to placebo group. In our study also incidence of myalgia was significantly low in both higher dose 150mg and low dose 75mg pregabalin group compared to placebo group.

Rashmi et al, demonstrated in their study that low dose oral pregabalin 75mg reduced severity of fasciculations and myalgia whereas there was not much effect on incidence of both. Our study showed that both incidence and severity of fasciculations and myalgia was reduced with pregabalin 75mg and 150 mg but more effective with 150mg.

Iqbal et al, conducted a study on the preventing fasciculations, myalgia and hyperkalemia due to succinylcholine in patients posted for spine surgery. One group received oral pregabalin 150mg and other group received placebo one hour prior to surgery. It was observed that severity of fasciculations, incidence and severity of myalgia, serum potassium levels were reduced by pregabalin. Total opioid consumption was also found to be reduced in pregabalin group. Our study showed that both incidence and severity of fasciculations and myalgia was reduced with pregabalin 150 mg and time of first analgesic requirement was prolonged.

Khan et al, demonstrated in their study that severity of fasciculations were reduced in patients who took pregabalin 150mg compared to placebo group whereas both both incidence and severity of myalgia was reduced to pregabalin 150mg group. In our study, it was observed that both incidence and severity of

fasciculations were reduced with pregabalin, even with a low dose of 75mg but comparatively better was 150mg.

Shrivastava et al, conducted a study in two groups, one group received pregabalin 150mg and other group received placebo one hour prior to induction of anaesthesia. It was observed that incidence of fasciculations was not significant in both groups whereas severity was moderate to severe in placebo group. Both incidence and severity of myalgia was low in pregabalin group. In our study, it was observed that both incidence and severity of fasciculations were reduced with pregabalin, even with a low dose of 75mg but comparatively better was 150mg.

Parveen et al, conducted a study with Oral Clonidine 0.3mg and Pregabalin 150mg administered 60 minutes prior surgery for attenuation of pressor response in 80 patients posted for laparoscopic cholecystectomy. It was observed that both clonidine and pregabalin reduced pressor response to laryngoscopy and intubation where clonidine was better but showed more bradycardia. In our study, none of the patients both low dose and high dose pregabalin show any bradycardia, making it more hemodynamically stable.

Jain et al, demonstrated in their study that the group who received pregabalin 75mg had less post operative pain and lesser requirement of other analgesics compared to placebo group. In our study also the time of first analgesic requirement was prolonged in patients who received even low dose 75mg pregabalin.

Rastogi et al, demonstrated that MAP was significantly attenuated with pregabalin 150mg and there was no significant change in any group. In our study, there was significant attenuation of SBP, DBP, MAP and HR even in patients who received low dose 75mg pregabalin but comparatively more attenuation happened with pregabalin 150mg.

CONCLUSION

We conclude that preoperative prophylactic administration of oral pregabalin at 75 mg and 150 mg reduced incidence and severity of succinylcholine induced fasciculations and myalgia. A dose of 150 mg was found to be more effective than 75 mg. Side effects were not significant at a dose of 150 mg. Pressor response attenuation was found to be more effective at a dose of 150 mg compared to 75 mg. Hemodynamic stability was maintained at both pregabalin doses .

Hence it is concluded that preoperative oral Pregabalin is an effective and safe method for prevention of Succinylcholine induced fasciculations and myalgia.

SUMMARY

“COMPARISON OF TWO DOSES OF PREGABALIN FOR PREVENTING SUCCINYLMCHOLINE INDUCED FASCICULATIONS AND MYALGIA IN PATIENTS UNDERGOING SURGERY UNDER GENERAL ANAESTHESIA : A RANDOMISED CONTROLLED STUDY”.

This study was carried out on 201 patients undergoing Surgery under General Anaesthesia in B.L.D.E. U's Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura.

Group A received Cap Pregabalin 75mg, Group B received Cap Pregabalin 150mg and Group C received Saccharine pill 10mg.

Both incidence and severity of fasciculations and myalgia was reduced in patients who received pregabalin compared to placebo group (Group B>A>C).

It was observed that as severity of fasciculations increased, severity of myalgia also increased.

Time of 1st analgesic dose was prolonged in pregabalin group (Group B>A>C).

Attenuation of pressor response and hemodynamic stability was more in pregabalin group (Group B>A>C).

Sedation levels were insignificant among groups.

Incidence of adverse effects were also insignificant among groups.

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INFORMED CONSENT FORM

B.L.D.E(Deemed to be University) SHRI B.M PATIL MEDICAL
COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYPURA-
586103, KARNATAKA

TITLE OF THE PROJECT: “COMPARISON OF TWO DOSES OF
PREGABALIN FOR PREVENTING SUCCINYLCOLINE INDUCED
FASCICULATIONS AND MYALGIA IN PATIENTS UNDERGOING
SURGERY UNDER GENERAL ANAESTHESIA : A RANDOMISED
CONTROLLED STUDY”

PRINCIPAL INVESTIGATOR: DR ,MALAVIKA SASIDHARAN

Department of Anesthesiology

BLDE (Deemed to be University)

Shri B.M Patil Medical College and Research Centre, Vijaypura-586103

PG GUIDE: DR. RENUKA HOLYACHI

Professor and HOD

Department of Anesthesiology

BLDE(Deemed to be University)

Shri B.M Patil Medical College and Research Centre, Vijaypura-586103

I have been informed that this study is on “COMPARISON OF TWO DOSES OF PREGABALIN FOR PREVENTING SUCCINYLCHOLINE INDUCED FASCICULATIONS AND MYALGIA IN PATIENTS UNDERGOING SURGERY UNDER GENERAL ANAESTHESIA : A RANDOMISED CONTROLLED STUDY”.

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 knowledge.

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 the name to numbers will be kept in a separate secure location. If the data are used for publication in the medical literature or teaching purposes, no names will be used, and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the 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 Dr MALAVIKA SASIDHARAN available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation. If during this study, or later, I wish to discuss my participation or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for my careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION: I understand that my participation is voluntary, and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. MALAVIKA SASIDHARAN 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 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's Signature:

Name :

Date :

DR. RENUKA HOLYACHI

(Guide)

DR MALAVIKA SASIDHARAN

(Investigator)

SCHEME OF CASE TAKING

PATIENT DETAILS

Name: Age: Gender:

Diagnosis: Surgical procedure:

Past history:

General physical examination:

Pallor icterus cyanosis clubbing lymphadenopathy edema

Height: Weight: BMI:

Group allotted by randomization: Group (pregabalin 75mg) Group B (pregabalin 150mg) Group C (placebo)

Mallampati grade: ASA grade:

Vitals

BP: PR: RR:

TEMPERATURE: SPO2:

Systemic Examination

CVS: CNS:

CNS: GIT:

INVESTIGATIONS

CBC:

RBS:

Others (if indicated):

	Group A (Pregabalin 75mg)	Group B (Pregabalin 150mg)	Group C (Placebo)
Fasciculations 0 1 2 3			
Myalgia 0 1 2 3			
Postoperative Analgesic Requirement			
Time to first Systemic Analgesic dose			

	SBP	DBP	MAP	HR
Base				
Induction				
Intubation				
1 minute				
3 minutes				
5 minutes				
10 minutes				
15 minutes				

RAMSAY SEDATION SCORE

TIME	SCORE					
	1	2	3	4	5	6
2 hours						
6 hours						

Anaesthesia Starting Time:

Surgery Starting Time:

Surgery Ending Time:

Sign of PI:-

Sign of Staff:-

BIODATA OF THE GUIDE

GUIDE NAME: DR RENUKA HOLYACHI

DATE OF BIRTH: 03/08/1980

EDUCATION: **MBBS**

KARNATAKA INSTITUTE OF MEDICAL SCIENCES

HUBLI, KARNATAKA

MD ANAESTHESIOLOGY

KARNATAKA INSTITUTE OF MEDICAL SCIENCES

HUBLI, KARNATAKA

DESIGNATION: **PROFESSOR AND HOD,**

DEPARTMENT OF ANAESTHESIOLOGY

TEACHING EXPERIENCE: 14 YEARS

ADDRESS: PROFESSOR AND HOD,

DEPARTMENT OF ANAESTHESIOLOGY

BL.D.E (Deemed to be University)

Shri B M Patil medical college Hospital and Research Centre

Vijayapura- 586103

MOBILE NO: **9886492178**

EMAIL: **renuka312@gmail.com**

BIODATA OF THE INVESTIGATOR

GUIDE NAME: DR MALAVIKA SASIDHARAN

DATE OF BIRTH: 12/07/1993

EDUCATION: **MBBS**

KARUNA MEDICAL COLLEGE,PALAKKAD, KERALA

KMC REG NO: 147650

ADDRESS: DEPARTMENT OF
ANAESTHESIOLOGY

BL.D.E (Deemed to be University)

Shri B M Patil medical college Hospital and Research Centre

Vijayapura- 586103

Karnataka

MOBILE NO: **7034085160**

EMAIL: **malavikas040@gmail.com**



BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 781/2022-23

30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "Comparison of two doses of Pregabalin for Preventing Succinylcholine-induced fasciculations and myalgia in patients undergoing surgery under General Anaesthesia: A Randomized controlled study".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: Dr.Malavika Sasidharan.

NAME OF THE GUIDE: Dr.Renuka Holyachi, Associate Professor, Dept. of Anaesthesiology

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,

Institutional Ethical Committee,
BLDE (Deemed to be University),
Vijayapura

Dr. Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103, Karnataka

Following documents were placed before Ethical Committee for Scrutiny

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.

BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldehu.ac.in, E-mail: office@bldehu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bangpncprincipal@bldehu.ac.in

MASTER CHART - GROUP A (CAP PREGABALIN 75mg)

IN	PATIENT NAME	AGE	SEX	HT	WT	BIA	DATE	TIME	GRAD I	SYSTOLIC BP(mmHg)					DIASTOLIC BP(mmHg)					MEAN ARTERIAL PRESSURE					HEART RATE					SpO2	Aery	Suff														
										base	1mi	3mi	5mi	5mi	base	1mi	3mi	5mi	5mi	base	1mi	3mi	5mi	5mi	base	1mi	3mi	5mi	5mi																	
1	SHARAV	39	F	150	50	22.2	1	1	1	130	132	154	146	144	134	132	130	80	82	106	104	94	86	84	80	84	86	94	96	91	90	88	78	78	88	86	84	82	80	78	100	6	3	nil		
2	CHETAN	20	M	158	51	20.2	1	1	1	124	120	146	138	140	130	124	120	80	80	104	102	92	84	84	82	82	84	92	94	92	92	90	84	80	81	94	90	88	86	82	80	100	6	3	nil	
3	SHRISAI	27	M	158	51	20.2	1	1	2	2	130	130	156	144	144	136	132	130	80	80	104	104	92	82	82	80	80	82	90	92	90	90	88	82	86	86	96	94	90	88	87	86	100	4	3	nil
4	ASHWIN	22	F	162	62	23.6	1	1	1	110	112	158	128	128	116	114	110	70	74	90	90	88	78	76	74	83	85	93	93	91	92	91	85	82	82	90	88	86	84	84	100	6	2	nil		
5	CHINNAM	20	M	165	60	22	1	1	2	2	120	122	144	132	130	122	122	120	70	72	94	92	86	74	74	70	82	84	92	94	92	91	89	84	80	80	95	93	90	87	85	83	100	6	2	nil
6	BALAPP	60	M	170	78	27	1	1	2	2	142	140	160	152	152	148	146	140	80	84	102	100	94	84	84	80	83	85	93	93	92	92	91	85	82	82	91	90	89	86	83	83	100	6	2	nil
7	GANGAI	40	F	165	56	20.6	1	1	1	110	112	138	126	126	118	116	110	80	80	104	102	96	84	84	82	84	86	94	96	94	95	93	86	79	80	92	90	88	97	86	82	100	6	3	nil	
8	GEETA	47	F	160	50	19.5	1	1	0	0	122	118	142	130	132	126	124	120	80	84	106	104	94	86	84	82	80	82	90	92	90	89	82	78	78	88	86	84	82	80	78	100	6	3	nil	
9	SURSKH	35	F	162	54	20.6	1	1	1	1	130	130	150	142	140	134	132	130	80	82	102	102	96	86	82	80	84	86	94	96	94	91	90	86	80	80	94	90	88	86	82	80	100	6	3	nil
10	L B SIRU	60	M	168	70	24.8	1	1	2	2	130	132	152	144	142	136	132	130	80	80	104	102	92	82	82	80	84	86	94	96	94	92	90	86	86	86	96	94	90	88	87	86	100	4	2	nil
11	RASULA	60	F	163	48	18.1	1	1	0	0	110	112	134	126	126	118	114	110	70	72	96	94	86	74	74	72	82	84	92	94	92	90	88	84	82	82	90	88	86	84	84	99	6	2	nil	
12	RAHUL	18	M	172	68	23	1	1	2	2	130	130	152	140	140	130	130	130	70	74	92	92	84	72	72	70	80	82	90	92	92	91	82	80	82	95	93	90	87	85	83	100	4	2	nil	
13	SANGAI	58	F	165	60	22	1	1	1	1	120	120	148	134	136	124	122	120	80	80	106	104	96	86	84	82	83	85	93	93	91	91	89	85	82	82	91	90	89	86	83	83	100	4	3	nil
14	BASANG	27	M	168	75	26.6	1	1	3	3	130	130	156	142	142	136	134	130	80	82	104	102	94	86	84	80	82	84	92	94	94	92	91	84	79	79	92	90	89	87	86	82	99	6	3	nil
15	RAJESH	33	F	162	58	22.1	1	1	1	1	120	122	144	136	136	124	122	120	70	72	98	96	82	74	74	70	83	85	93	93	91	95	93	85	78	78	88	86	84	82	80	78	100	6	3	nil
16	SANDEE	18	M	170	70	24.2	1	1	2	2	120	120	148	134	134	128	124	120	80	80	108	106	92	80	80	80	84	86	94	96	94	92	89	86	80	80	94	90	88	86	82	80	100	6	3	nil
17	SUDHIR	29	M	172	75	25.4	1	1	2	2	120	122	146	134	132	124	122	120	70	70	94	92	84	72	72	70	80	82	90	92	90	91	90	82	86	86	96	94	90	88	87	86	100	6	2	nil
18	HEERA	55	F	163	58	21.8	1	1	1	1	120	120	146	132	132	124	120	120	80	80	108	106	94	82	82	82	84	86	94	96	94	92	90	86	82	82	90	88	86	84	84	100	6	2	nil	
19	LAXMI	28	F	166	60	21.8	1	1	1	1	120	118	142	130	130	120	120	120	80	80	106	104	92	82	82	80	82	84	92	94	92	90	88	84	80	80	95	93	90	87	85	83	100	6	2	nil
20	NEELAM	60	F	163	62	23.3	1	1	1	1	134	130	156	142	140	132	132	130	90	88	110	108	96	84	82	80	83	85	93	93	91	92	91	85	82	82	91	90	89	86	83	83	99	6	2	nil
21	DHYANE	19	M	170	68	23.5	1	1	1	1	110	112	138	128	128	116	114	110	80	80	102	100	90	80	80	80	80	82	90	92	90	91	89	82	79	81	92	90	88	97	86	82	100	6	3	nil
22	KASHMI	45	F	158	55	22	1	1	1	1	130	130	156	144	144	136	134	130	80	82	104	102	92	80	80	82	82	84	92	94	92	92	91	84	78	78	88	86	84	82	80	78	100	6	3	nil
23	SHIVAB	43	M	170	78	27	1	1	1	1	140	140	162	150	148	142	140	140	90	88	114	112	102	94	90	90	84	86	94	96	94	95	93	86	80	80	94	90	88	86	82	80	99	6	2	nil
24	ANJANA	25	F	165	63	23.1	1	1	1	1	120	122	148	136	136	128	124	120	70	74	96	94	86	82	82	80	80	82	90	92	90	92	90	86	86	86	96	94	90	88	87	86	100	6	3	nil
25	GOURAJ	48	F	162	65	24.8	1	1	1	1	130	128	152	144	144	134	132	130	80	84	108	106	96	84	84	82	82	84	92	94	92	91	90	84	82	82	90	88	86	84	84	100	4	3	nil	
26	PARASH	28	M	172	78	26.4	1	1	1	1	130	130	154	142	140	130	130	130	80	82	104	104	94	82	82	80	80	82	90	92	90	92	90	82	80	80	95	93	90	87	85	83	100	6	2	nil
27	HANAM	40	F	165	68	25	1	1	1	1	120	122	146	136	136	126	124	120	70	74	96	94	86	82	82	80	80	82	90	92	90	90	88	85	82	82	91	90	89	86	83	83	100	6	3	nil
28	ARJUN	55	M	178	74	23.4	1	1	2	2	130	128	156	142	140	132	130	130	70	72	96	96	82	80	80	82	82	84	92	94	92	92	91	84	79	79	92	90	88	97	86	82	100	4	4	nil
29	GURUBA	28	F	160	55	21.5	1	1	1	1	140	138	162	152	152	146	144	140	80	80	104	102	94	82	82	80	83	85	93	93	91	91	89	85	78	78	88	86	84	82	80	78	100	6	3	nil
30	SANDEE	30	M	168	70	24.8	1	1	2	2	130	130	156	146	146	138	136	130	80	80	108	104	96	84	84	80	84	86	94	96	94	92	91	86	80	80	94	90	88	86	82	80	100	4	3	nil
31	LATA YA	29	F	166	70	25.4	1	1	2	2	110	112	138	126	128	114	112	110	80	84	106	102	92	80	80	80	80	82	90	92	90	95	93	82	86											

MASTER CHART - GROUP B (CAP PREGABALIN 150mg)

No	PATIENT	AGE	SEX	HT	WT	BMI	SEDATE	FAS	MVA	SFS/STU	DIASTOLIC BP(mmHg)				MEAN ARTERIAL PRESSURE				HEART RATE				SpO ₂	TMR	side effects																							
											base	1st	2nd	3rd	base	1st	2nd	3rd	base	1st	2nd	3rd				base	1st	2nd	3rd																			
											2hr				6hr																																	
											base	1st	2nd	3rd	base	1st	2nd	3rd	base	1st	2nd	3rd	base	1st	2nd	3rd	base	1st	2nd	3rd																		
1	ARAVIND	21	M	166	70	25.4	1	1	2	2	130	132	144	142	134	132	130	130	80	82	92	92	94	94	82	80	84	82	88	87	86	85	84	84	78	80	81	80	81	80	81	80	78	78	100	4	4	nil
2	BASAVAR	18	M	168	70	24.8	1	1	1	1	120	120	140	140	130	124	124	122	80	80	94	92	92	92	84	80	82	81	84	84	84	84	82	82	80	80	80	80	83	82	80	80	100	8	2	nil		
3	PREMA S	32	F	158	50	20.1	2	0	0	0	130	130	144	144	136	132	132	130	80	80	94	92	92	92	82	80	80	80	82	82	82	80	80	86	86	86	86	86	86	86	86	100	12	3	iness,nausea			
4	RAMIJA	47	F	165	60	22	1	1	0	0	110	112	128	128	116	114	112	110	70	74	80	80	88	88	78	74	83	84	85	85	85	85	83	83	82	82	82	82	82	82	82	82	100	12	3	nil		
5	BHAVANI	42	F	158	65	26	1	1	3	3	120	122	130	130	122	122	122	120	70	72	82	82	86	86	74	70	82	86	84	84	84	84	82	82	80	80	80	80	80	80	80	80	100	4	3	nil		
6	RUKMAN	45	F	160	55	21.5	1	1	0	0	140	140	152	152	148	146	146	140	80	84	90	90	94	94	84	80	83	87	85	85	85	85	83	82	82	82	82	82	82	82	82	82	82	100	10	4	nil	
7	SUNDRA	34	F	162	52	20.3	1	1	0	0	110	112	126	126	118	116	116	110	80	80	90	90	92	90	84	80	84	88	86	86	85	85	84	84	79	79	79	80	81	80	79	79	100	10	2	nil		
8	SAVITRI S	55	F	158	55	22	1	1	0	0	120	120	132	132	126	124	124	120	80	80	92	92	94	94	86	82	80	84	82	82	82	82	80	80	81	84	81	81	81	81	81	81	100	10	2	nil		
9	AVINASH	22	M	170	68	23.5	1	1	1	1	130	130	140	140	134	132	132	130	80	82	94	94	96	96	86	80	84	83	86	86	86	86	84	84	78	78	80	78	78	78	80	78	100	8	3	nil		
10	DHANSIN	48	M	168	70	24.8	1	1	1	1	130	132	142	142	136	132	130	130	80	80	90	92	92	92	82	80	84	85	86	86	86	84	84	83	83	83	83	83	83	83	83	100	8	2	nil			
11	MAHADRI	45	F	158	50	20	1	1	0	0	110	112	126	126	118	114	114	110	70	72	84	84	84	82	74	72	82	82	84	84	84	82	82	87	87	87	88	89	88	87	87	99	10	2	nil			
12	MADIWA	50	M	170	65	22.5	1	1	1	1	130	130	140	140	130	130	130	130	70	74	82	82	84	84	72	70	80	84	82	82	82	80	80	86	86	86	86	86	86	86	86	100	8	3	nil			
13	NANDESH	19	M	168	65	23	1	1	1	1	120	120	136	136	124	122	122	120	80	80	96	96	96	96	86	80	82	84	85	85	85	83	83	83	83	82	82	82	82	82	82	82	100	8	3	nil		
14	KAMALA	40	F	156	60	24.7	1	1	0	0	130	128	142	142	136	134	134	132	80	82	94	94	94	94	86	80	82	82	84	84	84	82	82	90	90	90	90	90	90	90	90	99	10	4	nil			
15	PRIYANK	18	F	158	55	22	1	1	0	0	120	122	136	136	124	122	122	120	70	70	86	86	82	82	74	70	83	85	85	85	85	83	83	76	78	80	76	76	76	76	76	100	10	2	nil			
16	SHANTAR	60	F	162	60	22.9	1	1	0	0	120	118	134	134	128	124	122	120	80	80	96	96	92	92	80	80	84	82	86	86	86	84	84	85	85	86	86	86	85	85	100	10	2	nil				
17	SUNAND	40	F	160	62	24.2	1	1	0	0	120	122	132	132	124	122	122	120	70	70	84	84	84	84	72	70	80	84	82	82	82	80	80	86	86	86	86	86	86	86	87	100	10	2	nil			
18	RAGHVEN	40	M	172	78	26.4	1	1	3	3	120	120	132	132	124	120	120	120	78	80	96	96	90	90	82	80	82	83	86	86	86	85	84	90	90	90	90	90	90	90	100	4	3	nil				
19	BALASAR	45	M	168	65	23	1	1	1	1	120	118	130	130	120	120	120	120	80	80	94	94	92	92	82	80	82	86	84	84	84	82	82	87	87	87	87	87	87	87	87	100	8	2	nil			
20	VISHALAJ	43	F	162	63	24	1	1	0	0	130	130	140	140	132	132	132	130	90	88	100	98	96	96	84	80	83	83	85	85	85	83	83	82	82	84	82	82	82	82	82	99	10	3	nil			
21	ANNAMTI	60	F	158	56	22.4	1	1	0	0	110	112	128	128	116	114	114	110	78	76	90	90	90	90	80	82	80	84	82	82	82	80	80	84	86	84	86	85	84	84	85	100	10	2	nil			
22	VINOD	22	M	168	70	24.8	1	1	1	1	130	130	144	144	136	134	134	130	80	80	94	94	92	92	80	80	82	86	84	84	84	82	82	95	95	95	95	95	95	95	95	100	8	2	nil			
23	CHIDANA	38	M	170	72	24.9	1	1	1	1	140	140	148	148	142	140	140	140	90	88	102	102	98	94	86	84	88	86	86	86	84	84	76	78	76	76	76	76	76	76	99	8	3	nil				
24	ANKITH	19	M	167	65	23.3	1	1	1	1	120	122	136	136	128	124	122	120	70	72	86	86	82	82	70	70	84	88	86	86	86	84	84	68	68	68	67	68	67	68	68	100	8	3	nil			
25	KALAPPA	45	M	169	68	23.8	1	1	1	1	130	128	144	144	134	132	132	130	80	84	96	96	96	96	84	82	82	86	84	84	84	82	82	76	76	76	76	76	76	76	100	8	2	nil				
26	SHANTA	55	F	160	58	22.7	1	1	0	0	130	130	140	140	130	130	130	130	80	82	94	94	94	94	82	80	80	80	82	82	82	80	80	72	72	72	72	72	72	72	72	100	10	3	nil			
27	SADDAM	18	M	170	68	23.5	1	1	1	1	120	122	136	136	126	124	124	120	70	74	86	86	86	86	82	80	83	80	85	85	85	83	83	94	94	94	94	94	94	94	100	8	3	nil				
28	VINOD	49	M	168	51	20.2	1	1	1	1	130	128	140	140	132	130	130	130	70	72	84	84	82	82	82	82	82	84	84	84	82	82	87	87	87	87	87	87	87	87	100	8	2	nil				
29	MOHAM	29	M	162	62	23.6	1	1	1	1	140	138	152	152	146	144	144	140	80	80	94	94	94	94	84	82	83	81	85	85	85	83	83	68	68	68	68	68	68	68	68	100	8	3	nil			
30	SANJEEV	38	M	168	70	24.8	1	1	1	1	130	130	146	146	138	136	134	130	80	80	96	96	96	96	84	80	84	88	86	86	86	84	84	70	70	70	70	70	70	70	100	8	4	nil				
31	VARUN	30	M	164	64	23.8	1	1	1	1	110	112	128	128	114	112	112	110	80	84	94	94	92	92	80	80	80	84	82	82	82	80	80	93	93	93	93	93	93	93	93	100	8	3	nil			
32	AYAPPA	50	M	161	68	22.4	1	1	1	1	130	128	140	140	132	130	130	130	80	82	98	98	96	96	82	80	82	88	86	86	86	84	84	85	85	85	85	85	85	85	85	100	10	3	nil			
33	VIKAS	28	M	176	65	21	1	1	1	1	140	140	148	148	144	142	142	140	80	86	96	94	94	94	82	84	84	88	86	86	86	85	84	84	76	76	76	76	76	76	76	99	8	4	nil			
34	SHRUTHI	25	F	168	55	19.5	1	1	0	0	120	122	134	134	124	120	120	120	80	82	94	94	94	94	84	80	82	86	84	84	84	82	82	90	90	90	90	90	90	90	100	10	3	nil				
35	KASHIBA	28	F	156	58	23.8	1	1	0	0	110	112	126	126	122	116	116	110	70	74	84	84	82	82	72	70	80	84	82	82	82	80	80	74	74	74	74	74	74	74	100	10	3	nil				
36	RAVIKUM	30	M	168	64	22.7	1	1	1	1																																						

MASTER CHART - GROUP C (SACCHARINE PILL 10mg)

PATIENT N°	AGE	SEX	HT	WT	BMI	SEQ	PAS	MYA	SYSTOLIC BP(mmHg)												DIASTOLIC BP(mmHg)												MEAN ARTERIAL PRESSURE												HEART RATE												SpO2	ANA	TMR	SID
									2hr/6hr												base ind intul 1 m 3m 5m 10 m 15m base/duccintul 1m 3m 5m 10m 15m												base/duccintul 1m 3m 5m 10m 15m												base/duccintul 1m 3m 5m 10m 15m															
1	SAWITA	35	F	160	65	25.4	1	1	2	2	134	132	180	172	164	152	140	130	80	82	116	112	110	108	98	90	84	88	96	100	94	94	91	90	78	80	112	114	112	110	96	92	100	6	2	nil														
2	PRABHA	33	F	158	48	19.2	1	1	3	3	122	124	170	164	156	144	136	122	80	80	114	114	112	106	96	88	82	84	92	97	94	93	92	90	80	82	114	116	114	112	98	96	100	2	3	nil														
3	VIJAYKUM	60	M	167	68	24.4	1	1	2	1	130	130	182	174	166	154	142	132	80	80	112	110	108	104	98	90	80	82	94	101	96	93	90	88	86	88	100	102	104	102	96	94	100	4	3	nil														
4	MAHADE	22	F	160	60	23.4	1	1	3	3	120	122	166	158	144	134	126	112	70	74	110	108	106	102	94	84	83	85	97	103	96	94	92	91	82	84	116	118	120	118	106	98	100	3	2	nil														
5	KASTURI	45	F	165	68	25	1	1	2	2	124	120	174	164	152	144	132	124	70	72	114	112	110	106	96	88	86	90	93	98	93	92	91	89	80	82	114	116	114	112	98	96	100	4	3	nil														
6	PARVATI	60	F	158	55	22	1	1	3	3	140	142	186	176	168	154	142	140	90	92	122	120	118	114	98	90	83	85	98	105	97	95	92	91	90	84	108	112	110	108	96	94	100	3	3	nil														
7	MEENAK	46	F	160	68	26.6	1	1	0	1	110	112	168	154	146	138	126	114	80	82	114	112	110	108	98	90	84	86	97	101	98	96	95	93	92	81	113	117	114	114	97	95	100	6	2	nil														
8	SANGAW	50	F	158	56	22.4	1	1	3	3	130	132	180	172	164	152	140	130	80	80	116	114	112	106	96	88	80	82	94	102	96	94	92	89	81	81	112	116	113	110	95	94	100	3	3	nil														
9	NEELAPP	31	M	170	78	27	1	1	0	0	120	124	170	164	156	144	136	122	80	80	112	110	108	104	98	90	82	86	96	100	94	94	91	90	78	80	112	114	112	110	96	92	100	8	4	nil														
10	SATISH B	17	M	168	65	23	1	1	2	2	130	130	182	174	166	154	142	132	70	74	110	108	106	102	94	84	82	84	92	97	94	93	92	90	80	82	114	116	114	112	98	96	100	3	3	nil														
11	HARSHA	23	F	158	56	22.4	1	1	2	2	112	112	166	158	144	134	126	112	70	72	114	112	110	106	96	88	83	85	94	101	96	93	90	88	86	88	100	102	104	102	96	94	99	3	3	nil														
12	RUMALLA	41	F	165	70	25.7	1	1	1	1	122	120	174	164	152	144	132	124	90	92	122	120	118	114	98	90	83	85	97	103	96	94	92	91	82	84	116	118	120	118	106	98	100	8	4	nil														
13	JAYSHREE	40	F	165	66	24.2	1	1	3	3	140	142	186	176	168	154	142	140	80	82	114	112	110	108	98	90	82	84	93	98	93	92	91	89	80	82	114	116	114	112	98	96	100	4	3	nil														
14	VEENA C	22	F	162	60	22.9	1	1	2	2	120	112	168	154	146	138	126	114	80	80	116	114	112	106	96	88	83	85	98	105	97	95	92	91	82	84	108	112	110	108	96	94	99	3	3	nil														
15	SUNIL K	20	M	168	70	24.8	1	1	2	2	130	132	180	172	164	152	140	130	80	80	112	110	108	104	98	90	84	86	97	101	98	96	95	93	79	81	113	117	114	114	97	95	100	4	3	nil														
16	RAJU TIP	28	M	168	70	24.8	1	1	2	2	120	124	170	164	156	144	136	122	70	74	112	108	106	102	94	84	82	84	94	102	96	94	92	89	81	81	112	116	113	110	95	94	100	3	2	nil														
17	DILSHAD	40	F	158	52	20.8	1	1	3	3	130	130	182	174	166	154	142	132	70	72	114	112	110	106	96	88	83	86	96	100	94	94	91	90	80	82	114	116	112	110	96	92	100	2	2	nil														
18	ANIL CH	32	M	172	78	26.4	1	1	0	1	110	112	166	158	144	134	126	112	90	92	122	120	118	114	98	90	82	84	92	97	94	93	92	90	80	82	114	116	114	112	98	96	100	6	2	nil														
19	MARSHIN	56	M	170	78	27	1	1	0	1	120	120	174	164	152	144	132	124	80	82	114	112	110	108	98	90	84	86	94	101	96	93	90	88	86	88	100	102	104	102	96	94	100	6	3	nil														
20	AKSHATA	18	F	160	66	25.8	1	1	1	1	142	142	186	176	168	154	142	140	80	80	116	114	112	106	96	88	83	85	97	103	96	94	92	91	82	84	116	118	120	118	106	98	99	8	3	nil														
21	SHANKR	60	M	168	72	25.5	1	1	1	1	112	112	168	154	146	138	126	114	80	80	112	110	108	104	98	90	82	84	93	98	93	92	91	89	80	82	114	116	114	112	98	96	100	4	3	nil														
22	VILAS	29	M	168	66	23.4	1	1	2	2	134	132	180	172	164	152	140	130	70	74	110	108	106	102	94	84	83	85	98	105	97	95	92	91	82	84	108	112	110	108	96	94	100	3	2	nil														
23	RAMESH	18	M	168	70	24.8	1	1	1	1	124	124	170	164	156	144	136	122	70	72	114	112	110	106	96	88	84	86	97	101	98	96	95	93	79	81	113	117	114	114	97	95	99	4	2	nil														
24	KASHMA	18	M	168	66	23.4	1	1	2	2	130	130	182	174	166	154	142	132	70	72	114	112	110	108	98	90	80	82	94	102	96	94	92	89	81	81	112	116	113	110	95	94	100	3	2	nil														
25	HASEENA	47	F	160	55	21.5	1	1	2	3	110	112	166	158	144	134	126	112	80	82	124	112	110	108	98	90	81	86	96	100	94	94	91	90	78	80	112	114	112	110	96	92	100	3	3	nil														
26	VINAY	21	M	168	68	24.1	1	1	1	1	122	120	174	164	152	144	132	124	80	80	116	114	112	106	96	88	82	84	92	97	94	93	92	90	80	82	114	116	114	112	98	96	100	4	3	nil														
27	SUATHA	35	F	168	58	22.7	1	1	2	2	140	142	186	176	168	154	142	140	80	80	112	110	108	104	98	90	80	82	94	101	96	93	90	88	86	88	100	102	104	102	96	94	100	3	3	nil														
28	ANITA	42	F	165	69	25.3	1	1	1	1	110	112	168	154	146	138	126	114	70	74	110	108	106	102	94	84	83	85	97	103	96	94	92	91	82	84	116	118	120	118	106	98	100	4	2	nil														
29	MULGAPP	40	M	170	75	26	1	1	0	0	136	132	180	172	164	152	140	130	70	72	116	112	110	106	96	88	82	84	93	98	93	92	91	89	80	82	114	116	114	112	98	96	100	6	2	nil														
30	SHREEKA	20	M	166	65	23.6	1	1	2	2	124	124	170	164	156	144	136	122	90	92	120	120	118	114	98	90	83	85	98	105	97	95	92	91	82	84	108	112	110	108	96	94	100	4	2	nil														
31	PRASHU	25	M	168	72	25.5	1	1	1	1	130	130	182	174	166	154	142	132	70	72	114	112	110	108	98	90	84	86	97	101	98	96	95	93	79	81	113	117	114	114	97	95	100	4	2	nil														
32	CHIDANA	59	M	169	68	23.8	1	1	2	2	110	112	166	158	144	134	126	112	80	80	114	114	112	106	96	88	84	86	94	102	96	94	92	89	81	81	112	116	113	110	95	94	100	4	3	nil														
33	JAYSHREE	26	F	160	58	22.7	1	1	3	3	124	120	174	164	152	144	132	124	80	80	112	110	108	104	98	90	82	86	96	100	94	94	91	90	80	82	114	116	112	110	96	92	99	3	4	nil														
34	SUBASH	22	M	170	68	23.5	1	1	2	2	140	142	186	176	168	154	142	140	80	80	112	110	108	104	98	90	80	82	94	101	96	93	90	88	86	88	100	102	104	102	96	94	100	3	3	nil														
35	RAVIKUM	30	M	158	51	20.2	1	1	3	3	118	112																																																



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