

COMPARATIVE STUDY ON THE EFFECTS OF PRETREATMENT WITH MAGNESIUM SULPHATE AND PROPOFOL INDUCTION ON SERUM CREATINE PHOSPHOKINASE AND URINARY MYOGLOBIN LEVELS ASSOCIATED WITH THE USE OF SUCCINYLCHOLINESadhana Roy¹, Mrunalini K², G. Venkateshwarlu³, A. Sowmya Sri⁴**HOW TO CITE THIS ARTICLE:**

Sadhana Roy, Mrunalini K, G. Venkateshwarlu, A. Sowmya Sri. "Comparative Study on the Effects of Pretreatment with Magnesium Sulphate and Propofol Induction on Serum Creatine Phosphokinase and Urinary Myoglobin Levels Associated with the use of Succinylcholine". *Journal of Evolution of Medical and Dental Sciences* 2015; Vol. 4, Issue 55, July 09; Page: 9568-9580, DOI: 10.14260/jemds/2015/1383

ABSTRACT: Succinyl Choline possess unique properties of rapid onset and short duration of action to facilitate endo tracheal intubation but myalgias, hyperkalemia, increase in serum myoglobin, creatine phosphokinase and masseter spasm are adverse effects associated with its use in apparently healthy population. The aim of present study is to compare the effects of with and without pretreatment with magnesium sulphate and propofol induction on serum creatine phosphokinase and urinary myoglobin levels associated with use of succinyl choline. 60 patients aged between 18-60 years of both sexes of ASA Grade-I and II undergoing elective Surgery with minimal or no muscle damage were divided into two groups randomly. After taking informed consent, patient was shifting to operation table, monitors were connected, vital parameters recorded, intravenous line secured and 2ml of blood was collected in plain bottle and 10-15ml of urine sample was collected and set to lab for serum creatine phosphokinase and urinary myoglobin estimation. Patients of both groups were preoxygenated for 5 minutes, premedicated with Inj. Glycopyrolate (0.2mg) iv, Inj. Fentanyl 2 Micro Grams per Kg iv and induced with Inj. Propofol 2mg/kg and succinyl choline 2mg./kg was given to facilitate endotracheal intubation. One group was pretreated with 10cc of 0.9% Normal saline and other group with magnesium sulphate 40mg/kg in 10ml slowly over 10 minutes before induction with propofol. The occurrence of fasciculations was noted. 10-15ml of urine was collected in both groups for myoglobin estimation 20 minutes after intubation. At the end of surgery patients was reversed with neostigmine (0.07mg/kg) and Inj. Glycopyrdate (0.01mg/kg). After complete recovery extubation was done and patient shifted to postoperative ward 2ml of blood was collected 20-24 hours post-surgery for serum creatine phosphokinase estimations and results tabulated. The study found that there was raise in serum phosphokinase levels in both groups. The raise was significantly lower in magnesium sulphate group compared to other group, urinary myoglobin was detected in both groups but significantly lower in magnesium sulphate group. Fasciculations and postoperative myalgias were significantly lower in magnesium sulphate group. In conclusion magnesium sulphate is effective in lowering serum creatine phosphokinase levels, urinary myoglobin levels, postoperative myalgias and fasciculations associated with use of succinyl choline.

KEYWORDS: Succinyl Choline: Magnesium Sulphate, Serum Creatine Phosphokinase: Urinary Myoglobin.

INTRODUCTION: In 1942 Cullen described the use of d-tubocurarine as a safe drug to use during surgery to provide skeletal muscle relaxation in 131 patients.¹

Succinylcholine was introduced by the sleff and Foldes in 1952. Its rapid onset of effect and ultrashort duration of action permitted rapid sequence intubation.² With Succinylcholine and

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Vecuronium bromide introduction, knowledge of physiology of neuromuscular junction and reversal of its blockade, the technique of general anesthesia has become popular.

Succinylcholine possesses the unique properties of rapid onset and short duration of action but its use is often accompanied by adverse effects like Myalgias, Masseter spasm, Hyperkalemia, increase in Serum Myoglobin levels and Creatine phosphokinase levels in apparently healthy population. Cardiac dysrhythmias manifested as sinus bradycardia and cardiac arrest is caused by Succinylcholine in patients with hyperkalemia.

It also increases intraocular pressure, intracranial pressure, intragastric pressure and also causes rhabdomyolysis and acidosis.

Magnesium sulphate which is commonly used in the treatment of Eclampsia and Torsades de pointes has got an action of decreasing release of prejunctional Ach at neuromuscular junction.³ It is thus thought to decrease muscle fasciculations when given along with SCh.

In view of the above advantages with Magnesium sulphate, a comparative study of Succinyl choline and pretreatment with Magnesium sulphate is undertaken to quantitatively assess the effect Magnesium sulphate on Succinylcholine induced CPK levels and urine Myoglobin.

MATERIALS AND METHODS: A clinical study was undertaken to compare the raise of Serum Creatine phosphokinase and urinary Myoglobin with and without pretreatment with Magnesium sulphate followed by Succinylcholine intubation in ASA Grade I-II adult patients of age between 18 to 60 years, who were undergoing elective surgeries with minimal or no muscle damage at Gandhi Hospital, Musheerabad, Secunderabad, Telangana.

60 patients aged between 18 to 60 years of both sexes belonging to ASA I-II, undergoing elective surgery were selected from Gandhi hospital for the study. They were divided into two groups randomly Group-NS and Group-MS. Each group consisted of 30 patients. After obtaining permission from institutional approval committee, informed consent was taken from all the patients. Preanesthetic check was conducted and detailed history was obtained. Complete clinical examination and surgical profile were done. These patients were instructed to fast for 6hours prior to surgery.

Type of study was prospective randomized double blind study.

Exclusion Criteria: Family history of muscular dystrophy, Myopathies, Muscle cutting surgeries, Trauma, Burns, Previous history of CAD, History of unexplained high fever.

Surgical Procedures Included in the Study: Laparoscopic cholecystectomy, Laparoscopic ovarian cystectomy, Laparoscopic appendicectomy, Laparoscopic meshplasty, Diagnostic laparoscopy.

After the confirmation of fasting status and informed consent, patient was shifted to the theatre, transferred to operation table. They were connected with monitors. After recording the vital parameters, an intravenous line secured and 2ml of blood was collected in a plain bottle. 10 to 15ml of urine sample was collected. These samples were sent to lab for serum creatine phosphokinase levels and urine myoglobin. Patients were then pre-oxygenated for 5minutes with 100% oxygen. Inj. Glycopyrrolate 0.2mg, Inj. Fentanyl 2mcg/kg was given as premedication. Group-NS were induced with Inj. Propofol 2mg/kg and Succinyl choline 2mg/kg was given to facilitate endotracheal intubation. They were pretreated with 10cc of 0.9% normal saline. Group-MS were pretreated with Magnesium sulphate 40mg/kg in 10ml slowly over 10minutes and induced with Inj. Propofol 2mg/kg and Inj. Succinylcholine 2mg/kg for intubation. The occurrence of fasciculations was noted.

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Storage Instructions and Reagent Stability: All the components of the kit are stable until the expiry date on the label, when stored at 2-8°C, protected from light and contamination is prevented.

Materials Required: Spectrophotometer or colorimeter measuring at 340nm, Thermostatic bath at 25°C, 30°C and 37°C, Matched cuvettes 1.0 cm light path, General lab equipment.

Specimen: Serum free of haemolysis or heparin plasma. Stability for 7days at 2-8°C, protected from light.

Assay Procedure: Assay conditions wavelength of 340nm, cuvettes-1cm light path, constant temperature of 37°C Adjust the instrument to zero with distilled water or air Pipette into a cuvette-working reagent (1.0 ml) and sample (40 microlit) Mix and incubate for 10min Feed the sample to instrument and read the value given

Reference Range: In males: 24 to 195u/L in females: 24 to 170 u/L.

Chemical Examination: Albumin - 1+ to 3+, Sugar - nil, Ketone bodies - nil, Bile salts and pigments - nil, Blood - nil, Urobilinogen - nil.

Combination of dipstick test for protein and test for occult blood in urine is considered as myoglobinuria positive.

Other Characteristics:

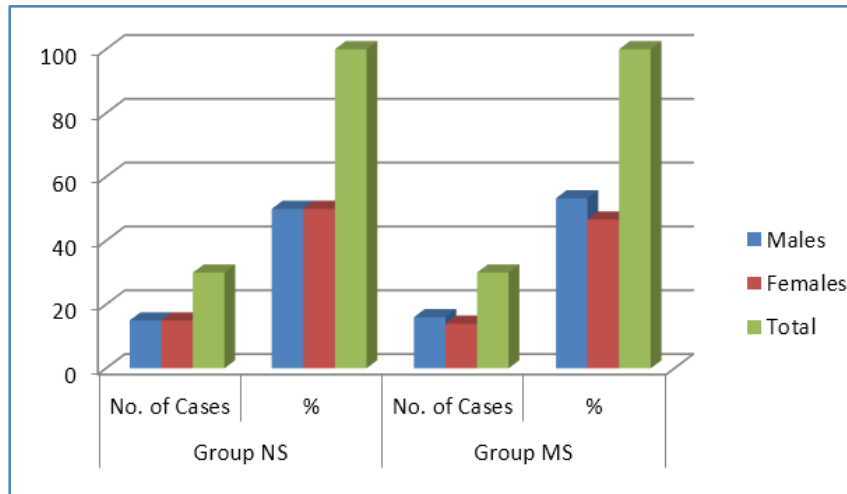
Blood: Pinkish red in colour, normal in consistency and haeme crystals seen under microscope. Myoglobin: Smoky grey in colour, turbid in consistency, haeme crystals are not seen under microscope.

Fasiculations: Fasiculations were observed for on table and presence or absence was noted.

Post-operative myalgia were enquired 20 to 24 hours in the post-operative period and recorded as present or absent.

OBSERVATION AND RESULTS: Statistical analysis in present study is expressed as mean and standard deviation wherever appropriate. Statistical analysis was done for age, weight, sex, preoperative and postoperative serum creatine phosphokinase levels and difference between preop and postop values Qualitative analysis of urine myoglobin was done as we are not having quantitative analysis in our hospital setting. Statistical analysis was done using unpaired 't' test for parametric data and chi square test for non-parametric data.

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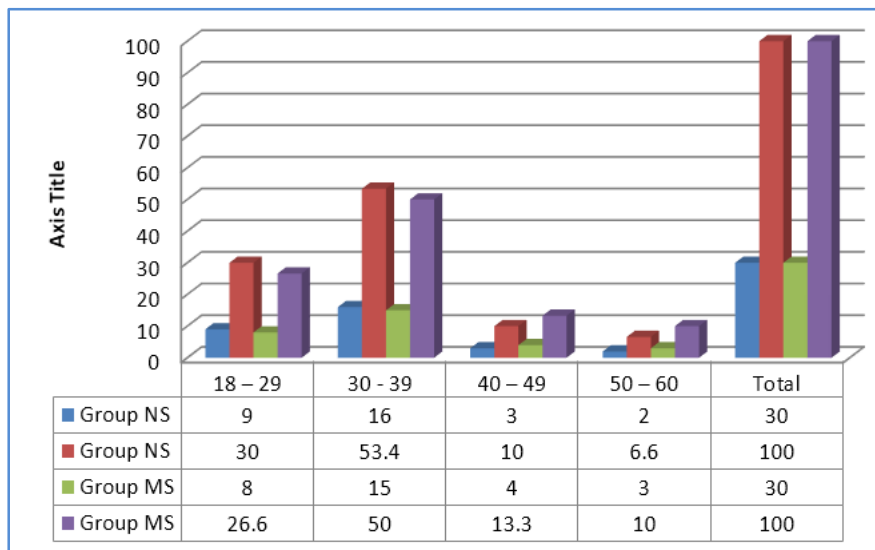


Graph 1: Gender wise distribution of study

Sex	Group NS		Group MS	
	No. of Cases	%	No. of Cases	%
Males	15	50	16	53.3
Females	15	50	14	46.6
Total	30	100	30	100.0

Table 1

From the above table, sex distribution in both the groups was comparable and statistically insignificant.



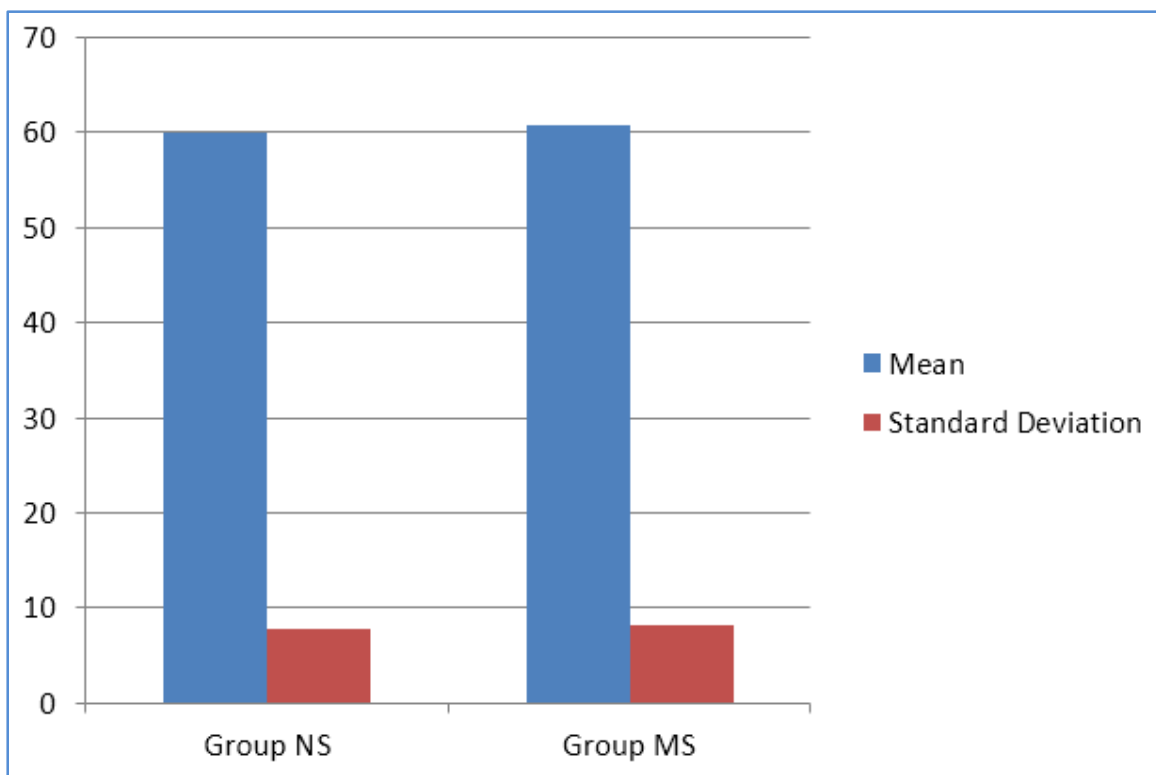
Graph 2: Distribution of study subjects according to age

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Age (Years)	Group NS	Group NS	Group MS	Group MS
18 - 29	9	30	8	26.6
30 - 39	16	53.4	15	50
40 - 49	3	10	4	13.3
50 - 60	2	6.6	3	10
Total	30	100	30	100

Table 2

From the above table, mean age of Group - NS is 37.43 Years and in Group - MS is 35.53. The age groups are comparable and statistically insignificant.



Graph 3: Group wise distribution of body weight, mean weight

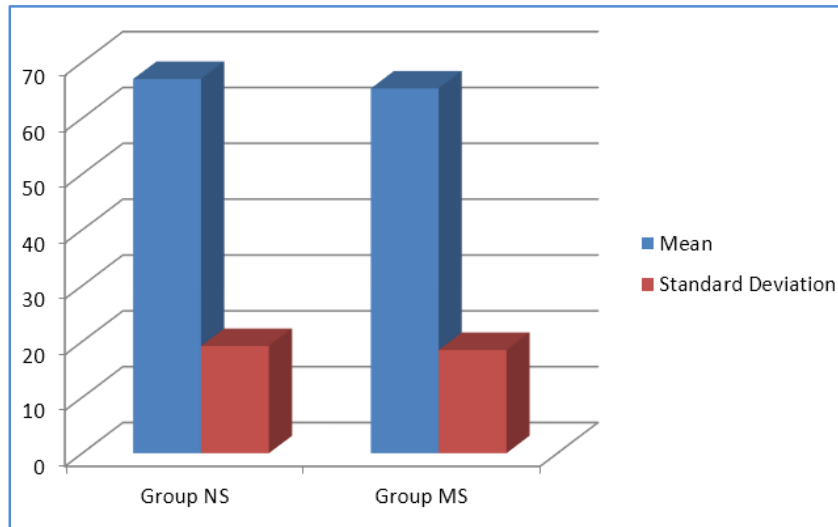
Body Weight	Group NS	Group MS
Mean	59.94	60.8
Standard Deviation	7.80	8.13

Table 3

P. Value more than 0.05.

The above table shows mean weight of the two groups are comparable and difference in weight is statistically insignificant.

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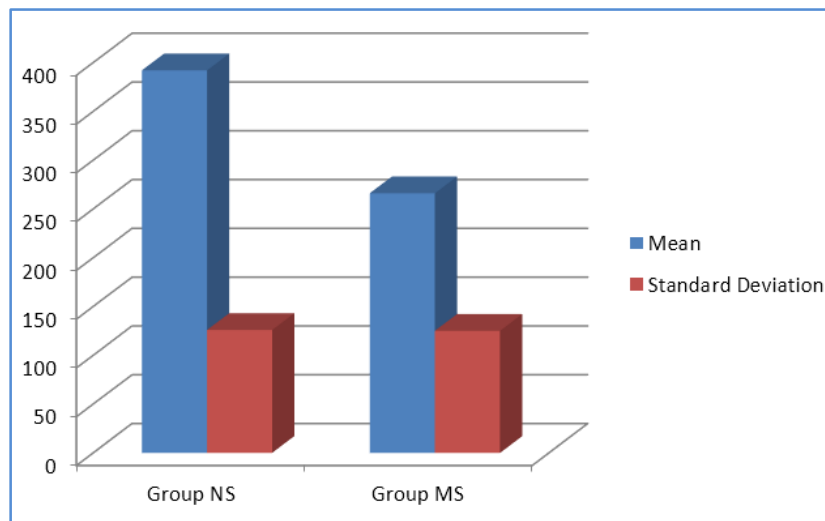
Graph 4: Preoperative values of serum creatine phosphokinase levels, mean pre-op CPK

Pre op CPK Levels	Group NS	Group MS
Mean	67.0	65.3
Standard Deviation	19.2	18.47

Table 4

P. Value greater than 0.001.

The above table shows preop cpk levels in two groups which are comparable and statistically insignificant.



Graph 5: Post-operative values of serum creatine phosphokinase levels, mean post op CPK

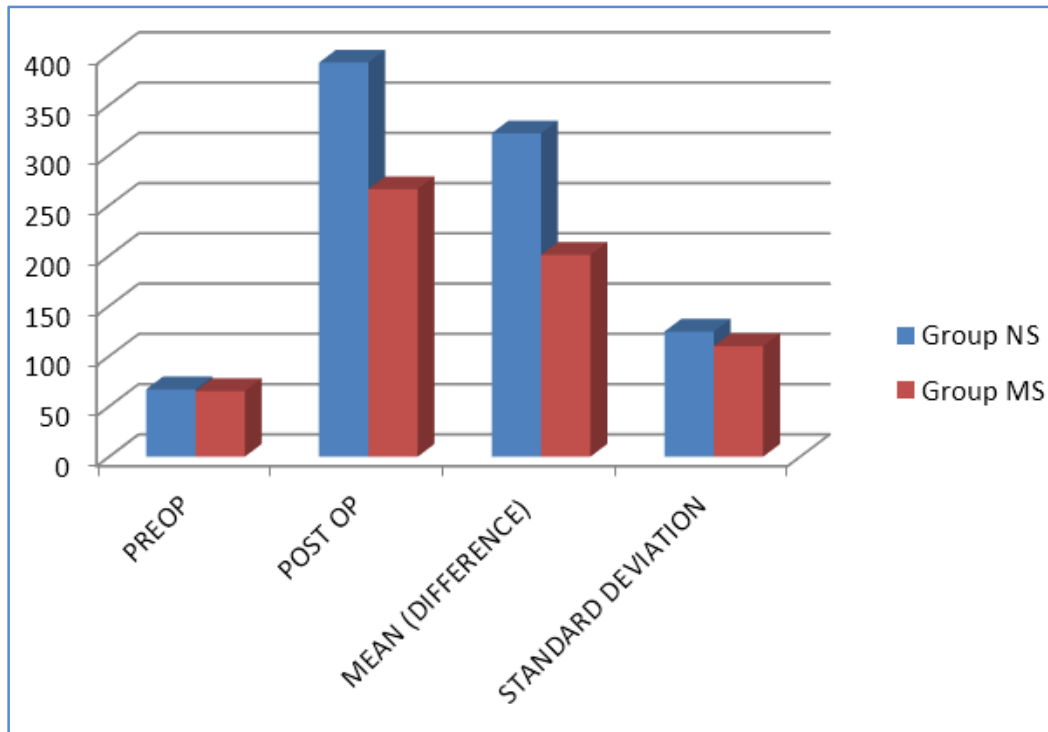
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Post OP CPK Levels	Group NS	Group MS
Mean	392.1	266.13
Standard Deviation	126.0	125.1

Table 5

P. Value is 0.003 when both the groups are compared.

The above table shows the mean post op cpk levels raise in the two groups and is statistically significant.



Graph 6: Difference in the raise of serum creatine phosphokinase levels, difference in CPK levels

	Group NS	Group MS
PREOP	67	65.3
POST OP	392.1	266.13
MEAN (DIFFERENCE)	321.7	200.833
STANDARD DEVIATION	124.41	110.00

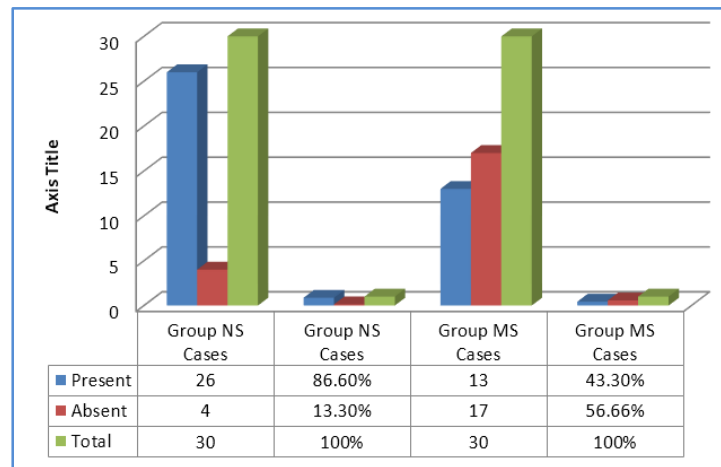
Table 6

P. Value is 0.0002 when compared to two groups.

The above table shows difference in cpk levels between the two groups.

The raised in cpk levels are statistically highly significant.

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Graph 7: Difference in urinary myoglobin level changes

Urine Myoglobin	Group NS Cases		Group MS Cases	
Present	26	86.6%	13	43.3%
Absent	4	13.3%	17	56.66%
Total	30	100%	30	100%

Table 7

CHI SQUARE Test was used.

$X^2 = 12.675$.

P VALUE IS < 0.001 .

The above table shows that postoperative urinary myoglobin was present in 87% of the control group and only 43% is study group i.e. group MS. The difference is statistically highly significant.



Graph 8: Comparison of occurrence of fasciculations

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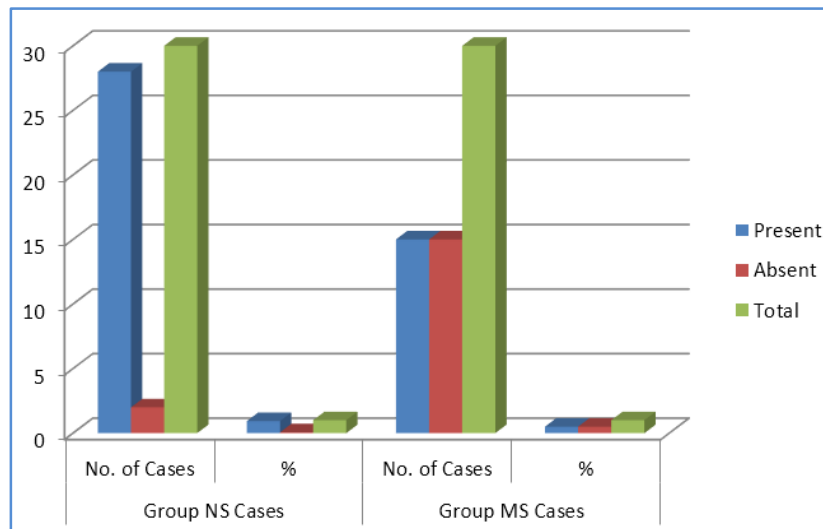
Fasciculation's	Group NS Cases		Group MS Cases	
	No. of Cases	%	No. of Cases	%
Present	28	93.3%	15	50%
Absent	2	6.66%	15	50%
Total	30	100%	30	100%

Table 8

$X^2 = 11.8$, P VALUE IS $<.001$.

The above table compares the occurrence of fasciculations in both groups.

Fasciculations were present in 93% of cases in group NS and only 50% in group MS and is statistically highly significant.



Graph 9: Comparison of occurrence of postoperative

	Group NS Cases		Group MS Cases	
	No. of Cases	%	No. of Cases	%
Myalgias				
Present	24	80%	3	10%
Absent	6	20%	27	90%
Total	30	100%	30	100%

Table 9

$X^2 = 26.93$, P VALUE is < 0.001 .

The above table shows that 90% of pts in Group MS did not experience fasciculations while compared to 20% in Group NS, which is statistically highly significant.

DISCUSSION: Recent advancement in medical system and introduction of newer muscle relaxants have changed scenario of general anesthesia.

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However, Succinylcholine, a depolarizing muscle relaxant has a unique role in clinical practice because it causes quick and excellent skeletal muscle relaxation for few minutes followed by spontaneous recovery. Unfortunately its use is often accompanied by muscle fasciculations, postoperative myalgia and biochemical evidence of skeletal muscle damage with raised Creatine phosphokinase concentration, Myoglobinemia and Myoglobinuria. With all these adverse effects, Succinylcholine has lowered its popularity among the surgical procedures.

Fasciculations have been attributed to a prejunctional depolarizing action of Succinylcholine, resulting in repetitive firing of the motor nerve terminals and antidromic discharges that manifest as uncoordinated vigorous contraction of the muscle bundles with no possibility of shortening and without synchronous activity in adjacent bundles. This might produce fibre rupture and damage thus causing increase in serum Creatine phosphokinase levels and Myoglobinuria.

Post-operative myalgias are either attributed to shearing forces associated with the fasciculations at the onset of phase I block or due to accumulation of lactic acid in muscle.

Many strategies have been used to reduce the side effects of succinylcholine like precurarisation with non-depolarizing muscle relaxant, stretching exercises, Dantrolene Sodium, Calcium gluconate, Vitamin C, Lidocaine, Magnesium, Diazepam and Midazolam, self-taming with Succinylcholine and more.⁴

M.A. Yousef et al have studied the changes in serum Creatine phosphokinase levels and anesthesia induced rhabdomyolysis after major and minor surgical procedures in children and showed that Creatine phosphokinase levels increased in both groups.⁵ The raise was significantly higher in major surgical group. In this study we have included procedures with minimal or no muscle damage.

Creatine phosphokinase is found in the heart and skeletal muscles. Any damage to this tissues can lead to raise in its levels. In the present study, all precautions were taken to prevent excessive muscle injury. Patients with family history of muscular dystrophy, myopathies or previous history of myocardial infarction are excluded from the study.

Waters et al in their study have shown that there is a rise in Creatine phosphokinase levels due to shearing of soft tissues due to unsynchronized contractions of adjacent muscle fibres just before the onset of paralysis.⁶ This damage to muscle has been substantiated as increase in Creatine phosphokinase levels.

A study was conducted by Mohammed Naguib et al (2006) to know the dose of Succinylcholine required for excellent endotracheal intubating conditions. They started with different doses of Succinyl choline. The intubation was performed 60 seconds later. Blind investigator has performed all laryngoscopy and graded intubating conditions. The intubating conditions was excellent in patients who received 2mg/kg Succinylcholine. So in the present study we have taken 2mg/kg of the drug to facilitate endotracheal intubation.

According to Maddineni VR, Mirakhur RK, Cooper AR, study on Myalgia and biochemical changes following Suxamethonium after induction of anaesthesia with Thiopentone or Propofol it is concluded that neither the induction agent nor the time between the induction agent and Suxamethonium administration has any significant influence on the incidence of muscle pains or Creatine kinase elevation following Suxamethonium.⁷ In the present study we have used 2mg/kg body weight of Inj. Propofol as induction agent.

Manataki et al studied the effect of continuous Propofol administration and Isoflurane administration on Creatine kinase and Suxamethonium-induced postoperative myalgia in 50 patients.

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Creative kinase was measured before and after operation. Myalgia was evaluated postoperatively by a blinded observer. The median level of myalgia was reduced significantly in the continuous propofol group than in isoflurane group.⁸

James MF, Cork RC, Dennett JE studied the effect of pretreatment with 60mg/kg Magnesium sulfate on the neuromuscular blockade and consequent potassium release produced by 1.5mg/kg Succinylcholine. They mentioned that Magnesium sulphate decreases Succinyl choline induced fasciculations.⁹

Ryu et al. injected Magnesium sulfate 50 mg/kg IV as bolus and then 15 mg/kg/hr IV infusion till the end of surgery. Serum magnesium levels were found to be significantly higher in patients who received Magnesium sulfate than those who received saline only (1.5 ± 0.2 vs. 0.9 ± 0.1 mmol/l).

Magnesium toxicity begins at the concentration of 2.5-5 mmol/l, which is much higher than highest level observed in their study. When serum magnesium level reaches 3.1mmol/l, depression of deep tendon reflexes occurs as a sign of toxicity. In the present study, a bolus of Magnesium 40 mg/kg without infusion was used which is a safe dose considering the result of above study and no patient had any signs of Magnesium toxicity.

Laurence AS at studied about Myalgia and biochemical changes following intermittent Suxamethonium and administration and effects of alcuronium, lignocaine, midazolam and Suxamethonium pretreatments on serum Myoglobin, Creatinine kinase and myalgia in 100 patients and confirmed that the fasciculations followed by Succinylcholine lead to increase in Creatine phosphokinase levels.¹⁰ In the present study, we have correlated occurrence of fasciculations with Creatine phosphokinase levels.

However, occurrence of fasciculations do not correlate to occurrence of myalgias. Mc Loughlin et al, conducted a study on muscle pains and biomedical changes following Suxamethonium administration after six pretreatments regimens and showed no correlation between fasciculations and postoperative myalgia.¹¹

Shreiber and colleagues conducted a metaanalysis of 52 randomised controlled trials attempted at prevention of succinylcholine induced fasciculations and myalgia and concluded that there is no clear relation between Succinylcholine related fasciculation and myalgia.¹²

Mahender et al conducted a study regarding the effects of Magnesium sulphate with Propofol induction of anesthesia on Succinylcholine induced fasciculations and myalgia. It was concluded that Magnesium sulphate 40mg/kg intravenously maybe used with Propofol for induction of anesthesia to control Succinylcholine induced fasciculations and myalgia.¹³ In the present study, the results are similar to the above mentioned.

Stacey and colleagues studied the effects of Magnesium sulphate on Succinylcholine induced complications during rapid sequence induction of anaesthesia with Thiopentone. They observed that the incidence of fasciculations was significantly lower in the patients pretreated with magnesium in comparison to control group whereas there was no difference between the groups in the incidence of myalgia after surgery.¹⁴

CONCLUSION: The following conclusions were made from the study;

- There was a raise in serum Creatine phosphokinase levels in the two groups.
- The raise of serum Creatine phosphokinase levels was significantly lower in Magnesium sulphate group (Group MS) compared to the other group.

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- Urinary Myoglobin was detected in both the groups, but significantly lower in Magnesium sulphate group (Group MS).
- Fasciculations were significantly lower in Group MS.
- Postoperative myalgias were significantly lower in Group MS.

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