

# COMPARATIVE STUDY OF RAISE OF SERUM CREATINE PHOSPHOKINASE CONCENTRATION WITH DEPOLARIZING MUSCLE RELAXANT SUCCINYL CHOLINE AND NON-DEPOLARIZING MUSCLE RELAXANT VECURONIUM IN ASA GRADE-I PATIENT IN PAEDIATRIC AGE GROUP

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## ABSTRACT

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### BACKGROUND

Neuromuscular blocking agents are classified as depolarising and non-depolarising agents. Each category of drug has its own advantages and along with them comes the side-effects. Selection of neuromuscular blocking agent therefore depends on their actions.

### AIM OF STUDY

Present study is undertaken to compare the raise of serum creatine phosphokinase concentration with depolarising muscle relaxant (succinyl choline) and non-depolarizing muscle relaxant (vecuronium) in ASA grade 1 patients in paediatric age group undergoing minor surgeries (minimal or no muscle cutting)

### MATERIALS AND METHODS

In the present study, 80 paediatric patients (aged between 1-12 years) were randomly selected into Group A and Group B with 40 patients in each. Group A received inj. succinylcholine 2mg/kg and Group B received inj. vecuronium 0.1mg/kg to facilitate intubation. Pre-operative and post-operative blood samples were collected and Serum creatine phosphokinase levels were recorded.

### RESULTS

The rise in serum creatine phosphokinase was observed in both group A and group B. But, the rise in group A was statistically significant.

### CONCLUSION

Group A recorded a significant rise in serum creatine phosphokinase and Group B although recorded a rise in the enzyme levels it was statistically insignificant. So, whenever possible an alternative drug for succinylcholine to facilitate endotracheal intubation has to be sought in paediatric age group.

### KEYWORDS

Succinylcholine, Vecuronium, Non-depolarising muscle relaxants, Serum creatine phosphokinase.

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**HOW TO CITE THIS ARTICLE:** Reddy PV, Raghavender M. Comparative study of raise of serum creatine phosphokinase concentration with depolarizing muscle relaxant succinyl choline and non-depolarizing muscle relaxant vecuronium in ASA grade-I patient in paediatric age group. *J. Evid. Based Med. Healthc.* 2016; 3(14), 472-476. DOI: 10.18410/jebmh/2016/109

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**INTRODUCTION:** In 1942 Griffth and Johnson suggested that d-tubocurarine is a safe drug to use during surgery to provide skeletal muscle relaxation.<sup>1</sup> But in 1954 Becchar and Todd reported a six-fold increase in mortality in patients receiving d-tubocurarine versus those who had not received a relaxant. The increased mortality was due to general lack of understanding of pharmacology of neuromuscular blocked and their antagonist.

Theslen introduced succinylcholine, Folder and his colleagues in 1952 used succinylcholine for rapid sequence intubation.<sup>2</sup>

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, hyperkalaemia, increase in myoglobin level, Increase in Creatine phosphokinase level in apparently healthy children. Intractable cardiac arrest is caused by succinylcholine in patients with hyperkalaemia. Rhabdomyolysis and acidosis are encountered particularly in patients with unsuspected muscular dystrophy of Duchenne type. Neonates and infants are more sensitive than adults to neuromuscular blocking effect.

Non depolarising muscle relaxant like vecuronium are commonly administered to children. The popularity of this drug in children most likely stems from the benefits like faster onset of action in children than in adults with minimal

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*Submission 18-01-2016, Peer Review 03-02-2016, Acceptance 11-02-2016, Published 18-02-2016.*

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*DOI: 10.18410/jebmh/2016/109*

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residual paralysis seen in post-operative periods without other complications that are encountered with succinylcholine.

In view of the above merits and demerits, and to know a relative safe muscle relaxant a comparative study with succinylcholine and vecuronium is undertaken to compare the raise of serum creatinine phosphokinase concentration in paediatric age group in ASA grade I patients undergoing minor surgery.

**Creatine Phosphokinase:** It is an enzyme found primarily in the heart and skeletal muscles, and to a lesser extent in the brain. Significant injury to any of these structures will lead to a measurable increase in CK levels. Elevated levels of CPK are noted in life threatening conditions like malignant hyperthermia.

**The creatine phosphokinase levels are elevated in:**

- Myocardial infarction.
- Crushing muscular trauma.
- Any cardiac or muscle disease, but not myasthenia gravis or multiple sclerosis.
- Brain injury.
- Hypothyroidism.
- Hypokalaemia.

**MATERIALS AND METHODS:** A clinical study was undertaken to compare the raise of Serum Creatine Phospho-Kinase concentration in depolarizing muscle relaxant (succinyl choline) with a non-depolarizing muscle relaxant (vecuronium) in ASA grade 1 patients in paediatric age group who were undergoing minor surgical procedures with minimal or no muscle cutting at Prathima institute of medical sciences, Nagunoor, Karimnagar, Telangana. The study was a prospective randomized clinical trial.

80 patients aged between 1-12yrs of both sexes belonging to ASA grade 1 were chosen from Prathima hospital and they were divided into 2 groups randomly, Group-A and Group-B, each consisting of 40 patients. Permission was taken from Institutional approval committee. An informed consent was taken from all the patients attendants. Pre-anaesthetic check-up was conducted and a detailed history was obtained. Complete clinical examination was done. Routine investigations like Complete blood picture, Blood grouping, Rh typing, Clotting time, Bleeding time were done. These patients were instructed to fast for a period of 6 hours prior to surgery.

**Exclusion Criteria Included:**

1. Family history of muscular dystrophy.
2. Myopathies.
3. History of unexplained high fever.
4. Muscle cramps.
5. Muscle cutting and Muscle injury due to open surgery.
6. Trauma.

On the day of surgery, all the equipment required for general anaesthesia were kept ready including the CRASH

trolley. Review PAC was done. After confirmation of the NBM status and informed consent patient was shifted to operation theatre and transferred on to operation table, monitors (BP cuff, temperature probe, pulse oximeter) were connected, after recording the vital parameters an intravenous line was secured and blood sample, 2ml was collected in a plain bottle and connected to Isolyte-P drip. Blood sample was sent to bio-chemistry lab for Serum Creatine Phosphokinase level estimation. Patients were pre-oxygenated with 100% Oxygen for about 5 minutes. Inj. Atropine 20 µ/kg and Inj. Midazolam 0.05 ml/kg were given as premedication. Group-A Patients were induced with Inj. Thiopentone Sodium 5mg/Kg and Inj. Succinyl Choline was used as an adjuvant to facilitate endotracheal intubation. Group-B were induced with Inj. Thiopentone Sodium 5mg/Kg and Inj. Vecuronium 0.1mg/Kg was used as an adjuvant to facilitate endotracheal intubation. Both the groups were maintained with Oxygen+Nitrogen-50:50 and Inj. Vecuronium for muscle relaxation. Care was taken during surgery for minimal use of cautery. Intra Operative monitoring of pulse rate, blood pressure was done every 3 minutes for first 10 minutes and then every 5 minutes there after till the end of the surgery. At the end of the surgery residual block was reversed with Inj. Neostigmine 0.07 mg/Kg. and Inj. Atropine 0.04 mg/Kg. After complete recovery from the neuromuscular block, extubation was done after through suction and patient was shifted to post-operative ward. 20 to 24 hours after the surgery 2ml of blood is collected in a plain bottle and sent for Bio-chemistry Lab for Serum Creatine Phosphokinase estimation and the results are tabulated.

**OBSERVATION AND RESULTS:** Our Clinical study consists of 80 patients who are aged between 1-12 years both males and females who are randomly chosen and divided into two groups. Group A-40 Patients and Group B-40 Patients.

Statistical analysis in our study data is expressed as mean and standard deviation where it is appropriate. Statistical analysis was done for age, weight, sex, Creatine phosphokinase-preoperative and postoperative and difference in pre and postoperative values. The statistical analysis was done by using paired "T" test. Probability value <0.001 was considered as statistically significant.

Sex	Group-A (Succinylcholine)		Group-B (Vecuronium)	
	No. of cases	%	No. of cases	%
Males	31	77.5	32	80
Females	9	22.5	8	20
<b>Total</b>	<b>40</b>	<b>100</b>	<b>40</b>	<b>100</b>

**Table I: Sex Distribution**

P value is >0.001. Table I shows sex distribution of both groups which is comparable and statistically insignificant.

Age in years	Group A (Succinylcholine)		Group B (Vecuronium)	
	No. of Cases	%	No. of Cases	%
1-3	12	30	13	32.5
4-6	10	25	11	27.5
7-9	9	22.5	9	22.5
10-12	9	22.5	7	27.5
Total	40	100	40	100
Mean	6.7		5.32	
Standard deviation	3.18		2.86	

**Table II: Age distribution**

P-value>0.001.

Table II shows age distribution of both groups which is comparable and statistically insignificant.

Sl. No.	Surgical procedures	No. of patients	
		Group A (succinyl choline)	Group B (vecuronium)
1	Hypospadiasis	5	8
2	Phimosis	3	2
3	Hydrocele	7	10
4	Hernia	17	13
5	Undescended testis	4	5
6	Perineal surgery	1	0
7	Angular dermoid	1	1
8	Post-operative urethroplasty fistula repair	2	0
9	Megalourethral correction	0	1
	<b>Total</b>	<b>40</b>	<b>40</b>

**Table III: Shows type of surgery**

	Group A	Group B
Mean	14.125	11.66
Standard deviation	5.9	5.0

**Table IV: Difference in weight among Group A and group B patients**

P value is >0001,

Table IV shows weight of both groups which is comparable and statistically insignificant.

	Group A	Group B
Mean	48.2	45.8
Standard deviations	18.16	20.20

**Table V: Pre-operative values of serum creatine phosphokinase levels**

P value is >0.001

Table V shows preoperative values of serum creatine levels in both groups which is comparable and statistically insignificant.

	Group A	Group B
Mean	99.6	58.7
Standard Deviation	22.4	21.6

**Table VI: Post-operative values of serum creatine phosphokinase levels**

P value is <0.001

Table VI shows postoperative values of serum creatine levels in both groups which is comparable and statistically significant.

	Group A	Group B
Mean	51.1	12.9
Standard Deviation	13.9	6.99

**Table VII: Difference in the raise of serum Creatine phosphokinase levels in both groups**

P value <0.001

Table VII shows difference in rise of serum creatinine phosphokinase levels in both groups which is comparable and statistically significant.

**DISCUSSION:** Recent advancement in medical system and introduction of newer muscle relaxants have changed scenario of general anaesthesia. Both the depolarizing muscle relaxants and non-depolarizing muscle relaxants have their own uniqueness in administration with fewer side effects.

Succinyl choline possesses the unique properties of rapid onset and short duration of action, but its use is often accompanied by post-operative myalgia and bio-chemical evidence of muscle damage with raised serum creatine phosphokinase concentration in many subjects.

M.A. Yousuf et al (2006) have studied the change in creatine phosphokinase concentration after major and minor surgical procedures in children and showed that creatine phosphokinase levels are increased in both minor and major surgical procedures. The raise was significantly high with major surgical procedures than minor surgical procedures. In our study we have taken only minor surgical procedures involving no muscle cutting.<sup>3</sup>

The creatine phosphokinase is found in the heart and skeletal muscle and any damage to these structures, creatine phosphokinase is released. In our study all precautions were taken to prevent excessive muscle injury. Electrical cautery was used minimally. Patients with family history of muscular dystrophy and myopathies are excluded from the study.

Waters et al (9171) 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. This damage to muscle has been substantiated by an increase in creatine phosphokinase.<sup>4</sup>

Many studies have been subsequently conducted by giving priming dose of various types of Non-depolarizing muscle relaxants before giving depolarizing muscle relaxants. Several groups have investigated and have

recommended that a small sub-paralysing dose of Non-depolarizing muscle relaxants about 20% of ED 90 or about 10% of the intubating dose be given 2 to 4 minutes before administering a second large dose for tracheal intubation. However the efficacy of this approach of priming in preventing muscle pains is questionable. In our study we have not given any priming dose of muscle relaxant.

A study was conducted by Mohamed Naguib et al (2006) to know the dose of Succinyl choline required for excellent endotracheal intubating conditions. They started with 0.3, 0.5, 1.5 or 2.0mg/kg succinylcholine. The intubation was performed 60 sec later. Blind investigator has performed all laryngoscopy and graded intubating conditions. The intubating condition was very good in patients receiving 2.0mg/kg succinylcholine. So in our study we have taken 2.0 mg/kg succinylcholine to facilitate endotracheal intubation.

A study was done by Munshi et al in 1995 evaluating vecuronium bromide as neuromuscular blocking agent in infants and children and compared with pancuronium and came to conclusion that vecuronium has rapid onset of action, better agent in facilitating rapid intubation in paediatric patients. Duration was longer in patients below 3 months of age compared with that in infants of more than 3 months to 1 year and older children.<sup>5</sup> It's cardiovascular stability, lack of histamine release, ease of supplementation and ease of reversal make vecuronium a more suitable agent for use in paediatric anaesthesia as compared to pancuronium. In our study we have not studied the above parameters of vecuronium still because of the above said positive criteria we have chosen vecuronium among the non-depolarising muscle relaxant in comparison with succinylcholine.

A study was undertaken by Park D.H et al in 1982, the effect of diazepam on succinylcholine induced side effects and found that diazepam pre-treatment has no significant changes in prevention of muscle fasciculations in succinylcholine group and control group and they have also assessed serum potassium and creatine phosphokinase levels and found that there is no change in serum potassium and creatine phosphokinase levels even after diazepam pre-treatment.<sup>6</sup> In our study we have not studied the muscle fasciculations and serum potassium levels. We have not given diazepam before giving succinylcholine, instead in premedication we have given midazolam 0.05mg/kg and only raise in serum creatine phosphokinase levels were studied and found that there is a marked rise in serum creatine phosphokinase.

Ozilio et al (2002) has studied the administration of rocuronium before succinylcholine (pre-treatment) and studied the effects on muscle derived enzymes and myoglobins and found that myoglobulin and creatine phosphokinase levels are much less in rocuronium group when given as pre-treatment. In our study we have not estimated the levels of myoglobin and not given rocuronium as pre-treatment, we have only estimated serum creatine phosphokinase levels and found to be raised significantly.<sup>7</sup>

Indu M et al (2003) has studied different doses of succinylcholine on post-operative myalgia and compared the

intubation conditions and creatine phosphokinase levels, he has given doses of 1, 1.5, 2.5mg/kg and found that myalgia was less with 2.5mg/kg of succinylcholine, intubating condition were significantly better with 1.5 and 2.5mg/kg, creatine phosphokinase levels were higher after 24hrs with 2.5mg/kg. In our study we have not compared the myalgia and intubating conditions, only serum creatine phosphokinase levels after 24 hours of giving succinylcholine were measured and found there is significant raise.<sup>8</sup>

Noguchi et al (199) has studied the effects of succinylcholine on serum levels of myoglobin and creatine phosphokinase levels in children under halothane or enflurane anaesthesia and the results indicated that there was an increase in myoglobin and creatine phosphokinase levels with succinylcholine and this might play some role in development of malignant hyperthermia.<sup>9</sup>

In other study conducted by A. Kudoh et al (1997), they have compared the increase in serum creatine phosphokinase concentrations with succinylcholine during sevoflurane and isoflurane anaesthesia in children. In our study we have not included the effects of inhalation anaesthetics.<sup>10</sup>

**CONCLUSION:** In the present study the following conclusions were made:

- There was raise in Serum concentration of Creatine Phosphokinase levels in both Succinyl Choline and Vecuronium Groups.
- The raise of serum creatine phosphokinase levels was significantly high with Succinylcholine Group
- The raise of creatine phosphokinase levels was insignificant with Vecuronium Group.
- So, whenever it is possible an alternative drug for succinylcholine has to be used to facilitate endotracheal intubation in paediatric age group.

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