

Precurarization with Rocuronium Prevents Succinylcholine induced Hyperkalemia

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Abstract

Background: To assess the effects of Rocuronium pretreatment on Succinylcholine induced rise in serum potassium.

Methods: In this randomized controlled experimental study, sixty adults ASA I or II patients who presented for elective general surgical procedures were included. The patients were divided in two groups of thirty each by a simple randomization. Group "A" received succinylcholine and group "B" received precurarization dose of rocuronium followed by succinylcholine for intubation. Venous blood samples were obtained for estimation of serum potassium (K⁺) at 0 minutes and after five minutes of intubation.

Results: There was a significant rise in serum K⁺ level from the start of the study to five minutes in group A ($p < 0.001$). In group B, increase in serum K⁺ level from start of the study to five minutes was significant ($p = 0.001$) but it remained within the normal range. The increase in serum K⁺ level was significantly more in group A as compared to group B ($p < 0.001$).

Conclusion: Pretreatment with rocuronium prevents the rise in serum potassium induced by succinylcholine.

Key words: Succinylcholine, Rocuronium, Potassium, Precurarization

Introduction

Succinylcholine is commonly used for muscle relaxation at the time of endotracheal intubation. It is a depolarizing muscle relaxant, producing profound neuromuscular block with rapid onset but short duration. Its short half life becomes life saving in the event of difficult intubation or failed intubation. Succinylcholine produces many undesired side effects such as muscle fasciculations, post operative myalgias, increased serum levels of creatinine kinase (CK) and K⁺, succinyl apnea, malignant hyperthermia, raised intraocular pressure and intracranial pressure. The administration of succinylcholine in humans results in a mild and transient hyperkalemia. In normal individuals, the increase in serum K⁺ is approximately 0.5–1.0 mEq/L, occurs within 3–5 minutes after the IV administration of succinylcholine, and lasts less than 10–15 minutes. However, in certain conditions, such as

trauma, burns, infection, and certain neuromuscular disorders, there is an exaggerated increase in the serum K⁺ level that may manifest clinically in cardiac dysrhythmias and even cardiac arrest. It is related to proliferation of extrajunctional cholinergic receptors providing more sites for K⁺ to leak outward from cells during depolarization. Severe hyperkalemia after succinylcholine resulting in cardiac arrest has also been observed in acidotic hypovolemic patients.¹⁻³

To minimize the hyperkalemia associated with succinylcholine administration, investigators have tried pretreatment with various drugs, including nondepolarizing neuromuscular relaxants, flunitrazepam, diazepam, and magnesium sulfate with mixed results. Administration of non depolarizing neuromuscular blocker before administration of succinylcholine is effective in reducing the increase in serum K⁺ concentration. Pretreatment with a nondepolarizing neuromuscular relaxant or diazepam to minimize succinylcholine-induced hyperkalemia may also be considered in the clinical setting.⁵

Rocuronium bromide, a new non-depolarizing aminosteroidal muscle relaxant is a derivative of Vecuronium. It has a more rapid onset of action compared with established non-depolarizing agents and has an intermediate duration of action (20 – 35 min) similar to that of vecuronium and atracurium. There is rapid recovery with cardiovascular stability and no significant histamine release. Hepato-biliary mechanisms primarily account for its elimination. Precurarization with this steroidal compound with stable cardiovascular profile can thus significantly decrease the side effects of succinylcholine and can maximize patients satisfaction after succinylcholine is used. It is both safe and effective provided the dose does not exceed 10% of the ED₉₅.⁶⁻⁹

Patients and Methods

This single blind, randomized, case control study was conducted in department of Anaesthesia, Combined Military Hospital, Rawalpindi. Sixty patients were allocated randomly in two groups. Patients in group "A" received succinylcholine and patients in group "B" received rocuronium for precurarization followed by succinylcholine. Both groups were comparable in respect to age, sex and

weight and undergoing general surgical procedures. Patients with no proper medical history, intraocular hypertension, history of malignant hyperthermia, ASA status III and above, Diabetes mellitus, morbidly obese, pregnant patients and suspected difficult intubation patients were excluded

Standard anaesthesia technique was employed in all patients. Direct laryngoscopy was performed and the patients were intubated via oral route, 60 seconds after succinylcholine. Anaesthesia was maintained by 67% nitrous oxide and 1% halothane in oxygen. The blood samples were collected at 0 minutes before induction of anesthesia and 05 minutes after giving the drug for intubation. The estimation of serum K⁺ was done by ion selective electrode method. Descriptive statistics were used to describe the data. Mean and standard error of mean (S.E.M) were used to describe quantitative variables like age, weight and K⁺. Paired sample t-test was used to compare initial and final values of K⁺ within the groups. Chi-square test was used to compare qualitative variables between the groups. *p* value < 0.05 was considered as significant.

Results

The mean age of Group A patients was 39.97 ± 1.833 years (range 18-65 years) and of Group B was 36.63 ± 1.791 (range 18- 65 years). At the start of the study (at 0 hours), in group A average serum K⁺ level (± S.E.M) was 4.09 (± 0.071) millimole per litre (mmol/L) and in group B it was 4.08 ± 0.072 mmol/L. There was insignificant difference between the groups (*p* = 0.744) (Table 1).

Table 1: Initial and final levels of serum potassium (K⁺) in the groups

	Group A(n= 30)	Group B(n= 30)
At 0 hrs	4.09 ± 0.071mmol/l	4.08 ± 0.072mmol/l
After 5 min	4.90 ± 0.141*mmol/l	4.32 ± 0.074*mmol/L

NS : Not Significant; * *p* value < 0.05

After five minutes of administration of the drug for intubation, average serum K⁺ level in group A was 4.90 ± 0.0141 mmol/L. In group A, increase in serum K⁺ level from the start of the study to five minutes was significant (*p* < 0.001) (Table 1). In group B average serum K⁺ level at five minutes was 4.32 ± 0.074 mmol/L. Increase in serum K⁺ level from start of the study to five minutes was significant (*p* = 0.001) but the values remained within the normal range (Table 1). Average increase in serum K⁺ level or the difference of the mean in group A was 0.810 ± 0.106 mmol/L and in group B it was 0.243 ± 0.062 mmol/L (Table 2). The increase in serum K⁺ level was significantly more in

group A as compared to group B (*p* < 0.001) (*p* < 0.001) (Table 3).

Table 2: Comparison of change in serum potassium (K⁺) level between the groups

Groups	Difference of Mean	S.E.M
Group A (n = 30)	0.810	0.106
Group B (n = 30)	0.243	0.062
<i>p</i> value	< 0.001	

Table 3: Comparison of serum potassium (K⁺) between group A and group B

	Group A(n= 30)	Group B(n= 30)
At 0 hours	4.09 ± .071mmol/L(NS)	4.08 0.072mmol/l (NS)
After five minutes	4.90 ± 0.141*mmol/l	4.32 ± 0.074*mmol/l
Difference Mean ± S.E.M	+0.810 ± 0.106	+0.243 ± 0.062

NS: Not Significant; * *p* < 0.05; S.E.M Standard Error of Mean;
+ An increase in the average after five minutes

Discussion

Succinylcholine is associated with muscular injury as it depolarizes the muscles prior to paralysis. This muscular injury is manifested in the form of fasciculations, myalgia and increased muscle enzymes like CK in the serum. Moreover, the subsequent rise in serum K⁺ as a result of its depolarizing mechanism of action can clinically manifest as cardiac arrest in the susceptible individuals. These muscular unwanted effects of succinylcholine have limited its usefulness and present distressing consequences for the patients after minor surgeries. On the other hand the nondepolarizing muscle relaxant rocuronium circumvents most of these adverse effects but the high cost and the universal non availability makes it less of a choice for intubation.¹⁰⁻¹³

There is a rise in serum K⁺ after injection of succinylcholine especially in patients with certain conditions like burns, neuromuscular disease, closed head injury, intra-abdominal infection and renal failure. The repeated doses of succinylcholine in patients with renal failure are probably best avoided. If administration of repeated doses is contemplated, pretreatment with glycopyrrolate or atropine to protect against succinylcholine-induced bradycardia should be considered. A high preoperative concentration of serum K⁺ seems to be associated with a much higher probability of cardiac arrest following administration of succinylcholine. This rise, in K⁺ is presumed to be due to ionic flux from muscles in

association with period of depolarization. With the administration of succinylcholine and the depolarization of the muscle membrane, the resultant fasciculations cause the release of K^+ into the circulation. It has been observed that this rise in plasma K^+ is greater in those patients who experience postoperative myalgia than in those who do not suffer from this untoward effect.¹⁴⁻¹⁵

The efficacy of precurarization to prevent rise in serum K^+ is recognized in a very few studies. *d*-tubocurarine 0.1 mg/kg has been shown to limit the extent of succinylcholine-induced hyperkalemia in digitalized and traumatized patients but not in normal patients. It was found that pretreatment with *d*-tubocurarine did not prevent a moderate increase in serum K^+ after succinylcholine administration in normal patients and those with renal failure. Pretreatment with a nondepolarizing agent, like rocuronium, may be considered in a clinical setting to minimize succinylcholine-induced hyperkalemia.^{16,17}

High cost of rocuronium is a limitation. The cost of this drug in the market presently is eleven times more than that of succinylcholine. As an intubating drug, it is not used routinely and it would therefore be unfair to use the drug without documented evidence of the benefit of this technique.^{18,19}

Conclusions

1. Precurarization will decrease the succinylcholine-induced hyperkalemia on one hand and on the other will minimize cost of intubation.

2. Precurarization will decrease the cardiac adverse effects improving the side effect profile of the most commonly used and cost effective neuromuscular blocking agents

References

1. Sushma, T and Sorin, J. B. Succinylcholine-Induced hyperkalemia in patients with renal failure. *Anesth Analg*, 2000; 91: 237 – 41
2. Gronert, G. A. Cardiac arrest after succinylcholine: Mortality greater with rhabdomyolysis than receptor upregulation. *Anesthesiology*, 2001; 94: 523-26.
3. Nathan, A., Ganesh, A., Godinez, R. I. Hyperkalemic cardiac arrest after cardiopulmonary bypass in a child with unsuspected Duchenne muscular dystrophy. *Anesth. Analg*, 2005; 100 (3): 672-74.
4. Radnay, P. A., El-Gawet, E. S. and Novakovic, M. Prevention of succinylcholine- induced hyperkalemia by neurolept anaesthesia and hexafluorenum in anephric patients. *Anaesthesist*, 1988; 30: 334-37.
5. True, C.A and Carter, P.J. A comp of tubocurarine, rocuronium & cisatracurium in the prevention & reduction of suxamethonium induced fasciculations. *AANA J*, 2003; 71(1): 23 – 28
6. Mirakhur, R.K, Cooper, A.R Clarke, R.S.J. Onset and intubating conditions of rocuronium bromide compared to those of suxamethonium. *Eur J Anaesth*, 1994; 11 (9): 41 – 43.
7. Wierda, J. M., de-Wit, A. P., Kuizenga, K. Clinical observations on the neuromuscular blocking action of Org 9426, a new steroidal nondepolarizing agent. *Br. J. Anaesth*, 1990; 64: 521-23.
8. Spence, D., Herbert, R. D., Boulette, E. A comparison of rocuronium and lidocaine for the prevention of postoperative myalgia after succinylcholine administration. *A. A. N. A*, 2002 ;70 (5): 367-71.
9. Donati, F. Dose inflation when using precurarization. *Anesthesiology*, 2006; 105: 222- 25.
10. Abbas N, Tariq S, Waheed A, Murtaza G. To assess the effects of rocuronium pretreatment on succinylcholine-induced fasciculations. *J. Pak. Med. Assoc*, 2009; 59: 847-49 .
11. Wong, S. F. and Chung, F. Succinylcholine associated postoperative myalgia. *Anaesthesia*, 2000; 55: 144-52.
12. Yun M J, Kim Y. H, Go Y K, Shin J E. Remifentanyl attenuates muscle fasciculations by succinylcholine. *Yonsei. Med J*, 2010; 51 (4): 585-89.
13. Donati, F. and Bevan, D. R. Neuromuscular blocking agents. In: *Clinical anaesthesiology*. Barash, P. G., Cullen, B. F., Stoelting, R. K., Cahalan, M. K. and Stock. M. C. (Ed). 6th edition, 2009 USA, Lippincot Williams and Wilkins. pp. 520-21.
14. Green DW, Bristow A.S, Fisher M. Comparison of i.v. glycopyrrolate and atropine in the prevention of bradycardia and arrhythmias following repeated doses of suxamethonium in children. *Br J Anaesth*, 1984; 56:981-85.
15. Grenert G A and Theye R A. Pathophysiology of hyperkalemia induced by succinylcholine. *Anesthesiology*, 1975 43: 89-99.
16. Theroux M C, Rose J B, Iyenger S. Succinylcholine pretreatment using gallamine or mivacurium during rapid sequence induction. *J. Clin. Anaesth*, 2001; 13(4): 287-92.
17. Hernandez-Palazon J, Noguera-Velasco J, Falcon-Arana L F. Precurarization with rocuronium prevents fasciculations and biochemical changes after succinylcholine administration. *Anaesthesiol*, 2004 51: 184-89.
18. Abraham V, Kumar A R, Afzal L. Clinical investigation and evaluation of post-succinylcholine myalgia and intubation conditions with rocuronium pretreatment. A comparison with vecuronium. *Indian. J. Anaesth*, 2009; 52 (5): 551 -55.
19. Mallon W K, Keim S M, Shoenberger J M. Rocuronium vs succinylcholine in the emergency department: *J. Emerg. Med*, 2009; 37 (2): 182-88.