

Effect of Pre-Treatment with Rocuronium on Serum Potassium, Post-Succinylcholine Fasciculations, and Myalgia PostoperativelyAshwini Kumar Patel¹, Bharti Badlani², Ajay Singh³, Kapil Raghuvanshi^{4*}¹Associate Professor, Department of Anaesthesiology, Chhindwara Institute of Medical Sciences, Chhindwara, MP, India²Assistant Professor, Department of Ophthalmology, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India³Assistant Professor, Department of Anaesthesiology, Bundelkhand Medical College, Sagar, Madhya Pradesh, India^{4*}Demonstrator, Department of Biochemistry, Chhindwara Institute of Medical Sciences, Chhindwara, MP, India

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Abstract:

Background: The best drug for endotracheal intubation is succinylcholine, which has a rapid onset, an extremely brief duration of action, and complete predictable paralysis. However, muscle fasciculations, postoperative myalgia, an increase in serum potassium level, and myoglobinuria can occur and limit the drug's use in conditions like full stomachs, burns, significant trauma, metabolic acidosis, and a few myopathies. Numerous medications have been researched with the purpose of attenuating these effects; however pre-treatment with a non-depolarizing muscle relaxant has proven to be effective.

Aims and Objective: The purpose of this study was to evaluate the impact of pre-treatment with rocuronium on post-succinylcholine fasciculations, an increase in serum potassium levels, and postoperative myalgia.

Material and Methods: 100 patients (20–50 years old, either sex; ASA grades I and II) having general anaesthesia for different surgical operations were divided into two groups at random, one for pre-treatment using rocuronium (Group R), and the other for pre-treatment with saline (Group P), before succinylcholine injection. On postoperative days 1, 2, and 3 following succinylcholine injection, the intensity of fasciculations, an increase in potassium levels in the blood after 5 minutes, and myalgia were noted.

Results: In Group R, 74% of patients had no fasciculation, compared to 36% in Group P. Both groups experienced an increase in blood potassium levels that was statistically insignificant ($p > 0.05$). On postoperative days 2 and 3, a greater proportion of patients in the placebo group experienced mild to severe myalgia.

Conclusion: With a statistically non-significant elevation in serum potassium levels, pre-treatment with rocuronium before succinylcholine resulted in greater attenuation of post-succinylcholine muscular fasciculations and postoperative myalgia.

Keywords: Rocuronium; Fasciculations; Myalgia; Potassium; Pre-treatment.

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Introduction

General anaesthetic practice underwent a conceptual shift with the introduction of neuromuscular blockers. Succinylcholine, a depolarizing muscle relaxant that provides ideal intubation conditions within 30-60 seconds and has a 3- to 5-minute effect, is frequently used to aid laryngoscopy and endotracheal intubation.[1]

The best medicine for creating perfect circumstances for endotracheal intubation is still succinylcholine, which has a low cost, a rapid onset of action, a brief duration of action, and total predicted paralysis.[2] However, several well-

documented instances of adverse effects, such as an increase in intracranial tension, intraocular pressure, intragastric pressure, muscular fasciculations, and postoperative myalgia, myoglobinuria with an increase in blood potassium levels, limit the efficacy of succinylcholine.

In 1.5 to 89% of instances, succinylcholine-induced fasciculations result in postoperative myalgia in the neck, shoulder, back, and upper abdominal muscles. This condition typically develops within 24 to 48 hours and can continue for 2 to 7 days at the most. [3,4]

In some circumstances, such as those involving severe burns, severe trauma, metabolic acidosis, or myo-neuropathies, an increase in blood potassium levels post-fasciculation might be harmful.

Different medications, which include pre-treatment with Gallamine, [5], d-tubocurarine, [5] Pancuronium, [8] Phenytoin, [7] Dantrolene, [6] Atracurium, [9] Lidocaine, [9] Ascorbic acid, [10] chlorpromazine, [11] aspirin, [11] calcium gluconate, [13] Diazepam, [14] midazolam, [15] and magnesium sulphate [15] have been researched to lessen these adverse effects linked to succinylcholine. Non depolarizing neuromuscular relaxant (NDMR) medications have been proven to be the most successful in reducing these adverse effects. [16-23]

Aims and Objectives:

The goal of the current research investigation was to evaluate and compare how pre-treatment with rocuronium affected post succinylcholine fasciculations, an increase in blood potassium, and postoperative myalgia.

Materials and methods:

This prospective, comparative, single-center clinical investigation has been approved in advance by the Institutional Ethics Committee (IEC) for final clearance (letter no. 125-140/Bio/Ethical/MC/03/13). After obtaining IEC approval, the investigation was carried out in a medical college institution of central India. Over the course of one year, informed written consent had been acquired from the selected patients.

Inclusion criteria:

Patients between the ages of 20 and 50 of both sexes with ASA-I/II who had been scheduled for elective lumbar spine surgical procedure under general anaesthesia requiring laryngoscopy and endotracheal intubation were enrolled in this study in order to maintain uniformity and to eliminate the effect of surgery-related factors on postoperative myalgia. To obtain a clinically relevant variation in serum potassium levels, it was determined from a previous study [16-20] that 50 patients were required in each group with an 80% power at a 95% confidence interval ($\alpha = 0.05$). The total number of patients had been 100; utilizing an online randomization application, they were randomly divided into two groups of 50 patients each.

Exclusion criteria:

As stated in the introduction, patients who are susceptible to succinylcholine-induced hyperkalemia, those who refuse for participating in research, are nursing or pregnant, have substantial neurological, endocrine, hepatic, or renal dysfunction.

A computer-generated randomization technique was used to divide the 100 patients enrolled into the two categories listed below.

- Group R received intravenous rocuronium (0.06 mg/kg I/V) 60 seconds prior to succinylcholine;
- Group P received intravenous saline as a placebo 60 seconds prior to succinylcholine.

In accordance with hospital protocol, each patient underwent a comprehensive pre-anaesthesia evaluation and series of tests. All patients were fasted for six hours prior to the procedure. The patient's basal pulse rate (bpm), BP (mmHg), and SpO₂ (%) were measured and recorded upon arrival in the operating room. Before inducing anaesthesia, a blood sample was taken from a vein in order to determine the serum potassium level. Then, a Normal Saline infusion of 10-15 droplets per minute was initiated. Subsequent to premedication using Inj. Glycopyrrolate 0.2 mg I.V. along with Inj. Pentazocin 0.5 mg/kg BW as well as pre oxygenation with 100% Oxygen by facemask for 3 minutes, pretreatment was administered with either of the study drugs (the anesthesiologist on the floor as well as researcher consisted uninformed of the injection of study drug). Following 60 seconds of pre-treatment, 5 mg/kg of Thiopentone Sodium was injected intravenously to induce general anaesthesia. Intravenous injection of 2.0 mg/kg BW succinylcholine facilitated tracheal intubation. The occurrence and degree of muscle fasciculations were noted by the observer. [24]

Grade 0- Absolutely no fasciculations.

Grade 1 - Fine fasciculations found on the eyes, neck, face, or fingertips; absence of limb movements.

Grade 2: Moderate fasciculations at more than two sites, or evident limb movements.

Grade 3: Violent or severe, pervasive fasciculations.

General anaesthesia continued on N₂O and O₂ (66%:33%) alongside Halothane (0.5 MAC) as well as Inj. Vecuronium loading (0.1 mg/kg BW) and intermittent (0.02 mg/kg BW) dosages after endotracheal intubation.

Following a five-minute period of succinylcholine injection, another venous blood sample was obtained to determine the serum potassium concentration.

The combined administration of inj. Glycopyrrolate 0.01 mg/kg BW along with inj. Neostigmine 0.05 mg/kg BW reversed the residual muscle relaxant effect at the conclusion of the surgical procedure. After extubation and full recovery, patients were transferred to the recovery area.

The same observer interviewed all patients on the first, second, and third postoperative days to determine the incidence and severity of postoperative myalgia. [24]

Mild- Muscle discomfort or rigidity at a single site, without disability or activity restriction.

Moderate- discomfort in the muscles or rigidity perceived naturally by the patient, which may necessitate analgesic treatment.

Severe- Generalised intense discomfort or incapacitation.

As a rescue analgesic, intravenous administered 1gm of inj paracetamol was administered to patients with moderate to severe myalgia.

Statistical analysis:

The observations were documented and underwent statistical analysis using the student's "t" test, while the chi square test was used for qualitative variables. Observations from both groups were tabulated, and statistical analysis was performed using the appropriate statistical software. $p < 0.05$

was regarded significant, for intergroup comparisons.

Results:

Both study groups had comparable Age (years), Weight (kgs), and gender ratio (%) demographic information. ($P > 0.05$) (Table 1) 74% of patients in group R had no signs of fasciculation (Grade 0), compared to 36% of patients in group P ($P = 0.0001$). In group P, a greater proportion of patients had grade 1 & grade 2 fasciculations than in group R (50% against 24%) & (14% vs. 2%) respectively. ($P > 0.05$) (Table 2)

On the first postoperative day, there was absolutely no difference in myalgia between the two groups ($P = 0.184$). On the second and third postoperative day, a greater proportion of Group P patients had no myalgia or minimal myalgia when compared with Group R ($P < 0.05$). In both categories, only a small number of patients experienced moderate-grade myalgia, which was statistically insignificant. (Table 3 & 4) In both study groups, no significant increase in the serum potassium level was observed. ($P = 0.928$) (Table 5)

Table 1: Demographic Data

S.No.	Parameters	Group R Mean (\pm SD)	Group P Mean (\pm SD)	P value
1.	Age (years)	34.98 \pm 8.26 Mean (\pm SD)	35.26 \pm 9.59 Mean (\pm SD)	0.876(NS)
2.	Weight (kg)	55.74 \pm 9.15 Mean (\pm SD)	56.80 \pm 7.32 Mean (\pm SD)	0.523(NS)
3.	Gender (M: F) (%)	52:48	56:44	0.689(NS)

*NS-Non Significant ($P > 0.05$)

Table 2: Severity and inter-group statistical comparison of fasciculations in two study groups

S. No.	Severity of fasciculations	Group-R		Group-P		Total		P-value
		(n)	(%)	(n)	(%)	(n)	(%)	
1.	Grade-0	37	74	18	36	55	55	0.0001 (S)
2.	Grade-1	12	24	25	50	37	37	0.007 (S)
3.	Grade-2	1	2	7	14	8	8	0.028 (S)
4.	Grade-3	-	-	-	-	-	-	-

*S- Significant ($P < 0.05$)

Table 3: Severity of postoperative myalgia in two study groups

S. No.	Severity of Myalgia	1 st P.O.Day*				2 nd P.O.Day*				3 rd P.O.Day*			
		Group R		Group P		Group R		Group P		Group R		Group P	
		(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
1.	Nil	47	94	43	86	32	64	19	38	23	46	8	16
2.	Mild	3	6	7	14	17	34	27	54	24	48	35	70
3.	Moderate	-	-	-	-	1	2	4	8	3	6	7	14
4.	Severe	-	-	-	-	-	-	-	-	-	-	-	-

*P.O.Day- Post-operative day

Table 4: Inter-group statistical analysis of severity of postoperative myalgia in two study groups

S. No.	Severity of myalgia	1 st P.O.Day		2 nd P.O.Day		3 rd P.O.Day	
		P-value		P-value		P-value	
1.	Nil	0.184 (NS)		0.009 (S)		0.001 (S)	
2.	Mild	0.184 (NS)		0.045 (S)		0.026 (S)	
3.	Moderate	-		0.171 (NS)		0.184 (NS)	
4.	Severe	-		-		-	

*P.O.Day- Post-operative day, NS-Non Significant ($P > 0.05$), S- Significant ($P < 0.05$)

Table 5: Inter-group statistical comparison of serum potassium level (meq/l) in two study groups

S. No.	Serum Potassium(mEq/L)	Group R Mean (\pm SD)	Group P Mean (\pm SD)	P-value
1.	Sample I, Before Induction	4.23 \pm 0.58	4.25 \pm 0.54	0.858 (NS)
2.	Sample II, after 5 min of Succinylcholine	4.44 \pm 0.58	4.45 \pm 0.53	0.928 (NS)

*NS-Non Significant (P>0.05)

Discussion:

In the preponderance of cases requiring general anaesthesia, succinylcholine has proven to be the most effective neuromuscular inhibiting agent for enabling endotracheal intubation. [2] In recent years, however, anesthesiologists have avoided its use due to adverse effects such as fasciculations, postoperative myalgia, and an increase in potassium levels. Due to the fact that it is a cost-effective drug, it continues to be used in a number of developing countries, and numerous studies are ongoing to minimize its adverse effects. A meta-analysis of clinical trials for the prevention of succinylcholine-induced postoperative myalgia revealed that administration of a pre-treatment dosage of different nondepolarizing blocking agents lowered the likelihood and degree of fasciculations and myalgia by about 30%. [25]

In our study, a pre-treatment dosage of 0.06 mg/kg Rocuronium was selected, which was <20% of the ED95 and thus safe and efficacious. [26] This was corroborated by the research conducted by GP Joshi and colleagues. [26]

Abraham V. et al., [18] Kacha et al., [19] Joshi VS. et al., [20] and Singh S. et al., [23] all observed a reduced incidence of fasciculation in the Rocuronium-treated group, similar to the present study.

Depolarizing muscle relaxants like succinylcholine bind to nicotinic acetylcholine receptors at both pre synaptic and post synaptic locations, but the pre synaptic affinity is thought to have a link with fasciculations. [27] If an NDMR is administered prior to succinylcholine, it will attach to the pre synaptic nicotinic acetylcholine receptors, preventing succinylcholine from binding and reducing the incidence of fasciculations. [28] Similarly, Joshi VS et al., [20] Singh S et al., [23] Farhat K et al., [29] and Abbas N et al., [30] reported a lower incidence of myalgia in Rocuronium-pretreated patients than in Vecuronium-pretreated patients. Abraham V et al. [20] discovered no statistically significant difference between postoperative myalgia on the first as well as third postoperative days (P>0.10).

The administration of a single dose of succinylcholine causes a rise in the level of potassium between 0.3 and 0.54 mEq/L within three to five minutes and persisting up to ten minutes. This surge is likely due to potassium escape via cells as a result of neuromuscular

junction depolarization. Although a rise of this magnitude has no significant effect on healthy individuals, it may have deleterious effects in burn injury, enormous trauma, severe intraabdominal infections, metabolic acidosis, spinal cord injury, polyneuropathy, myopathies, and other conditions.

Similar to the current study, Abraham V. et al, [20] Joshi VS. et al., [22] and Farhat K. et al., [24] observed a non-significant increase in serum potassium following pre-treatment using Rocuronium and Normal saline (Placebo).

In contrast to our findings, Singh S et al [25] discovered that following the first 24 hours in postoperative period, the mean K⁺ level was substantially higher in the control group than in the Rocuronium group. (P=0.045).

Conclusion:

Pretreatment with Rocuronium before using Succinylcholine resulted in superior reduction of post-succinylcholine muscular fasciculations and postoperative myalgia, accompanied by a statistically insignificant increase in serum potassium levels.

References:

1. Donati F, Bevan DR. Neuromuscular blocking agents. In: Clinical Anaesthesiology, Barash PG, Cullen BF, Stoelting RK, Cahalan MK and Stock MC (ed). 6th edition. USA, Lippincott Williams and Wilkins, 2009; 520-521.
2. Kato, N., Asakura, Y., Mizutani, M. *et al.* Anesthetic management of electroconvulsive therapy in a patient with a known history of neuroleptic malignant syndrome. *J Anesth* 2007; 21(4): 527-528.
3. Crawford JS. Suxamethonium muscle pains and pregnancy. *Br J Anaesth.* 1971 Jul; 43(7):677-80.
4. Ali AH. Neuromuscular block and its antagonism: clinical aspects. In: Nunn JF, Utting JE, Brown BRJ, eds. *General Anaesthesia*, 5th ed. London: Butterworths 1989; 164-184.
5. Virtue RW. Comparison of gallamine with d-tubocurarine effects on fasciculations after succinylcholine. *Anesth Analg* 1975; 54: 81-2.
6. Collier CB. Dantrolene and suxamethonium-the effect of preoperative dantrolene on the action of suxamethonium. *Anaesthesia* 1979; 34: 152-158.

7. Hatta V, Saxena A, Kaul HL. Phenytoin reduces suxamethonium-induced myalgias. *Anaesthesia* 1992; 47: 664-667.
8. Pinchak AC, Smith CE, Shepard LS, Patterson L. Waiting time after non-depolarizing relaxants alter muscle fasciculations response to succinylcholine. *Can J Anaesth.* 1994; 41: 206-212.
9. Raman SK, San WM. Fasciculations, myalgia and biochemical changes following succinylcholine with atracurium and lidocaine pre-treatment. *Can J Anaesth.* 1997; 44: 498-502.
10. Gupte SR, Savant NS. Post suxamethonium pains and vitamin C. *Anaesthesia* 1971; 26: 436-440.
11. McLoughlin C, Elliott P, McCarthy G, Mirakhor RK. Muscle pains and biochemical changes following suxamethonium administration after six pre-treatment regimens. *Anaesthesia* 1992; 47: 202-206.
12. Kumar M, Talwar N, Goyal R, Shukla U, Sethi AK. Effect of magnesium sulfate with propofol induction of anesthesia on succinylcholine myalgia. *J Anaesth Clin Pharmacol* 2012; 28: 81-85.
13. Shrivastava OP, Chatterji S, Kachhawa S, Daga SR. Calcium gluconate pre-treatment for prevention of succinylcholine-induced myalgia. *Anesth Analg* 1983; 62: 59-62. January 1983 - Volume 62 - Issue 1 - p 59-62
14. Verma RS, Chatterji S, Mathur N. Diazepam and succinylcholine-induced muscle pains. *Anesth Analg* 1978; 57: 295-297.
15. Mingus ML, Herlich A, Eisenkraft JB. Attenuation of suxamethonium myalgias: effect of midazolam and vecuronium. *Anaesthesia* 1990; 45: 834-837.
16. Findlay GP, Spittal MJ. Rocuronium pre-treatment reduces suxamethonium-induced myalgia: comparison with vecuronium. *Br J Anaesth.* 1996 Apr; 76(4):526-9.
17. Martin R, Carrier J, Pirlet M, Claproud Y, Tetrault JP. Rocuronium is the best non-depolarizing relaxant to prevent succinylcholine fasciculations and myalgia. *Can J Anaesth* 1998; 45: 521-525.
18. Abraham V, Kumar AR, Afzal L. Evaluation of post succinylcholine myalgia and intubation conditions with rocuronium pretreatment: a comparison with vecuronium. *Indian J Anaesth* 2008;52: 551-555.
19. Kacha AR, Patel HZ, Engineer SR. Comparison of precurarization with rocuronium bromide and vecuronium bromide for succinylcholine induced postoperative myalgia. *Int J Res Med.* 2012; 1: 21-29.
20. Joshi VS, Todkari KV, Deshpande SG. Comparative study of pre-treatment with rocuronium and vecuronium in postsuccinylcholine fasciculations, intubation condition and myalgia. *J Evol Med Dent Sci* 2016; 38(5): 2319-2324.
21. Motamed C, Choquette R, Donati F. Rocuronium prevents succinylcholine-induced fasciculations. *Can J Anaesth.* 1997 Dec; 44(12):1262-8.
22. Farhat K, Waheed A, Pasha AK, Kazi WA. Prevention of succinylcholine induced muscular effects by pre-treatment with rocuronium. *Pak J Pharmacol* 2012; 29: 25-31.
23. Singh S, Sinha AK, Palaria V, Chauhan AK. Comparison of biochemical changes and myalgia following administration of succinylcholine with or without pre-treatment with rocuronium in patients undergoing tympanoplasty. *Int J Sci Res* 2020; 5(9): 46-48.
24. Yun MJ, Kim YH, Go YK, Shin JE, Ryu CG, Kim W, Paik NJ, Han MK, Do SH, Jung WS. Remifentanyl attenuates muscle fasciculations by succinylcholine. *Yonsei Med J.* 2010 Jul; 51(4):585-9.
25. Pace NL. Prevention of succinylcholine myalgias: a meta-analysis. *Anesth Analg* 1990; 70: 477-483.
26. Joshi GP, Hailey A, Cross S, Thompson-Bell G, Whitten CC. Effects of pre-treatment with cisatracurium, rocuronium, and d-tubocurarine on succinylcholine-induced fasciculations and myalgia: a comparison with placebo. *J Clin Anesth.* 1999 Dec; 11(8):641-5.
27. Bevan DR, Donati F. Muscle relaxants. In: Barash P, Cullen B, Stoelting R eds. *Handbook of Clinical Anesthesia.* Philadelphia, Pa: Lippincott-Raven 1997: 387-397.
28. True CA, Carter PJ. A comparison of tubocurarine, rocuronium, and cisatracurium in the prevention and reduction of succinylcholine-induced muscle fasciculations. *AANA J.* 2003 Feb; 71(1):238.
29. Farhat K, Waheed AK, Bakhtiar S, Pasha AK. Comparative study of succinylcholine and precurarization with rocuronium on muscular effects in patients undergoing surgery under general anaesthesia. *Pakistan Journal of Pharmacology.* 2011 Jan;28(1):33-41.
30. Abbas N, Tariq S, Khan AW, Murtaza G, Naqvi N, Khanzada A. To assess the effects of rocuronium pre-treatment on succinylcholine induced fasciculations and postoperative myalgias. *J Pak Med Assoc.* 2009 Dec; 59(12): 847-50.