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A COMPARATIVE STUDY OF MUSCLE FASCICULATION AND POSTOPERATIVE MYALGIA FOLLOWING ENDOTRACHEAL INTUBATION USING VECURONIUM BROMIDE VS SUCCINYLCHOLINE WITH OR WITHOUT ROCURONIUM PRIMING: A PROSPECTIVE RANDOMISED CONTROLLED TRIAL

Thongram K[1], Kumaragurubaran TR[2], Nongthombam R[3], Singh T[4]

[1] Senior Resident, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India

[2] Assistant Professor, Department of anaesthesiology and critical care, Mahatma Gandhi Medical College & Research Institute , Sri Balaji Vidyapeeth, Puducherry, India

[3] Associate Professor, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur, India

[4] Professor, Department of Anesthesiology, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal, Manipur, India

Correspondence to Kumaragurubaran TR , rkb.sasi@gmail.com

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ABSTRACT

Introduction:

Endotracheal intubation commonly requires neuromuscular blockade for optimal intubating conditions. Succinylcholine remains the gold standard because of its rapid onset and short duration but is associated with muscle fasciculations and postoperative myalgia. Rocuronium pretreatment has been proposed to reduce these adverse effects.

Objective:

To compare the incidence of fasciculation and postoperative myalgia following endotracheal

intubation using succinylcholine alone, succinylcholine with rocuronium priming, and vecuronium alone.

Methods:

This prospective randomized controlled trial included 75 patients of American Society of Anaesthesiologists (ASA) physical status I–II, aged 18–60 years, undergoing elective surgery under general anaesthesia. Patients were randomly allocated into three groups (n=25 each): Group S received succinylcholine 1.5 mg/kg, Group SR received rocuronium priming 0.05 mg/kg followed by succinylcholine 1.5 mg/kg, and Group V received vecuronium 0.1 mg/kg. Primary outcomes were incidence and severity of fasciculations and postoperative myalgia at 6, 12, and 24 hours. Secondary outcomes included intubating conditions and hemodynamic parameters.

Results:

Rocuronium priming significantly reduced fasciculations compared with succinylcholine alone (32.0% vs 60.0%, p=0.013). Fasciculation-like movements were lowest in the vecuronium group (16.0%). Intubating conditions differed significantly among groups, with the best conditions observed in the rocuronium-primed group (p=0.048). Although postoperative myalgia was numerically lower in the rocuronium-primed group, differences at 6, 12, and 24 hours were not statistically significant (p>0.05). Hemodynamic parameters remained clinically acceptable in all groups.

Conclusion:

Rocuronium priming significantly reduces succinylcholine-induced fasciculations and improves intubating conditions. Although postoperative myalgia was numerically lower with rocuronium priming, this difference did not reach statistical significance.

Keywords:

Postoperative myalgia, Rocuronium, Rocuronium priming, Succinylcholine, Vecuronium

INTRODUCTION:

Endotracheal intubation is central to & almost inevitable in most procedures under general anaesthesia and in many of the critical interventions including and not limited to mechanical ventilation, and airway protection in critically ill Patients. Muscle relaxants are frequently employed to facilitate the smooth passage of endotracheal tube through upper airway. Succinylcholine, a depolarizing muscle relaxant is the gold standard for endotracheal intubation due to its quick onset of action and good intubating conditions; the ideal neuromuscular blocking

agent should have a fast onset, brief duration of action, provide profound relaxation and free from haemodynamic changes and other unwanted side effects[(1)]. Succinylcholine allows early establishment of airways and less chances of aspiration. Succinylcholine when used in a dose of 0.5 to 1.5 mg/kg body weight produces excellent muscle relaxation in 30 secs and its effects last for 3 to 5 mins. This short half-life becomes life-saving in the event of difficult intubation or failed induction and rapid sequence induction in patients with full stomach. The usefulness of succinylcholine is limited by a few side effects such as muscle fasciculations, postoperative myalgia, increased serum level of creatinine kinase and potassium, succinylcholine apnea, raised intraocular pressure, extreme bradycardia and malignant hyperthermia. The postoperative myalgia is generalized aches and pain that commonly occurs within 24 hours. The incidence of muscle pain is variable, from 20%-80% receiving succinylcholine[(2)]. The underlying mechanism of muscle damage associated with administration of succinylcholine may involve calcium induced phospholipid degradation with release of damaging products of fatty acid metabolism.

However, rocuronium and vecuronium which are non-depolarizing relaxant have been used in the prevention and reduction of succinylcholine induced muscle fasciculation and found rocuronium a valid alternative for defasciculation[(3)]. Rocuronium has a more rapid onset of action compared to vecuronium and provides good intubation within 60 secs. Rocuronium bromide is a newer, low potency non- depolarising drug with rapid onset time, rapid recovery with cardiovascular stability and no significant histamine release[(4)].

Widely used for the purpose of reducing succinylcholine induced myalgia, rocuronium might have a greater presynaptic activity than other muscle relaxants and reduction of fasciculations in succinylcholine induced myalgia.

Vecuronium bromide is a nondepolarizing neuromuscular blocking agents possessing all of the characteristic pharmacological actions of this class of drugs (curariform). It acts by competing for cholinergic receptors at the motor end plate. The antagonism to acetylcholine is inhibited and neuromuscular block is reversed by acetylcholinesterase inhibitors like neostigmine. The ED90 (dose required to produce 90% suppression of the muscle twitch response with balanced anaesthesia) has averaged 0.057 mg/kg. An initial dose 0.08 to 0.1 mg/ kg generally produces first depression of twitch in approx. 1 min, good or excellent intubation conditions within 2.5 to 3 minutes, maximum neuromuscular blockade within 3 to 5 minutes of injection in most patients[(5)].

METHODOLOGY

This prospective randomized controlled trial was conducted among patients undergoing elective surgeries under general anaesthesia. A total of 75 patients aged between 18–60 years, of either sex, belonging to American Society of Anaesthesiologists (ASA) physical status I and II, were initially planned for inclusion. Institutional ethical committee approval was taken and enrolled patients were also informed fully and consent were taken subsequently for the study.

Study Population

Patients scheduled for elective surgical procedures under general anaesthesia were screened for eligibility.

Inclusion-criteria:

Patients aged 18–60 years, of either sex, belonging to ASA physical status I and II, and posted for elective surgeries under general anaesthesia.

Exclusion-criteria:

Patients with history of contraindications to general anaesthesia, known allergy to study drugs, anticipated difficult airway, recent history of uncontrolled endocrine problem like diabetes mellitus,cardio-vascular diseases, nervous system, hepatic and renal dysfunction were excluded from the study.

Randomization and Group Allocation

Eligible patients were randomly allocated into three groups using restricted block randomization with a block size of six:

- **Group S (n=25):** Received normal saline at 0 min and 1 min, followed by succinylcholine (1.5 mg/kg) at 3 min.
- **Group SR (n=25):** Received rocuronium (0.05 mg/kg) at 0 min, followed by succinylcholine (1.5 mg/kg) at 3 min.
- **Group V (n=25):** Received vecuronium (0.1 mg/kg) at 1 min.

Endotracheal intubation was performed at 4 minutes in all groups. Neuromuscular blockade was maintained with vecuronium (0.1 mg/kg).

Anaesthetic Technique

All patients were premedicated with oral ranitidine 150 mg and alprazolam 0.5 mg on the night prior to surgery. In the operating room, patients were preoxygenated with 100% oxygen for 3 minutes. Intravenous ondansetron (0.1 mg/kg) and butorphanol (0.003 mg/kg) were administered.

Anaesthesia was induced with propofol (2 mg/kg) and maintained with sevoflurane (2 MAC) in oxygen. After induction and loss of corneal reflex, study drugs were administered as per group allocation. Direct laryngoscopy and endotracheal intubation were performed at 4 minutes.

Anaesthesia was maintained with a mixture of 33% oxygen, 66% nitrous oxide, sevoflurane, and intermittent doses of vecuronium.

Outcome Measures

The primary outcomes assessed were:

- Incidence and severity of muscle fasciculations
- Incidence and severity of postoperative myalgia

Postoperative myalgia was assessed at 6, 12, and 24 hours using a standardized grading system (Nil, Mild, Moderate, Severe).

Secondary outcomes included:

- Intubating conditions
- Hemodynamic parameters (heart rate, blood pressure, SpO_2, $ETCO_2$)

Vital parameters were recorded at baseline and at regular intervals (0, 5, 10, and 15 minutes).

Statistical Analysis

Data were analysed using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were expressed as frequency and percentage and analysed using Chi-square test. Continuous variables were expressed as mean ± standard deviation and analysed using one-way analysis of variance (ANOVA). A p-value of <0.05 was considered statistically significant. The patients were allocated to three Groups, Group S, Group SR and Group V following a restricted block randomization using a block size of 6 and study drugs were given as follows

RESULTS

A total of 75 patients were enrolled and randomized equally into three groups of 25 patients each. All participants completed the study and were included in the final analysis.

Baseline demographic characteristics including age, sex, BMI, and ASA physical status were comparable among the three groups, with no statistically significant differences.

Intubating conditions differed significantly among groups (p=0.048). Excellent intubating conditions were observed in 24.0% of Group S, 44.0% of Group SR, and 16.0% of Group V.

Fasciculations were significantly more frequent in Group S compared with the other groups (p=0.013). Fasciculations occurred in 15 patients (60.0%) in Group S, 8 patients (32.0%) in Group SR, and 4 patients (16.0%) in Group V. Moderate fasciculations were observed only in Group S.

At 6 hours postoperatively, mild-to-moderate myalgia occurred in 28.0% of Group S, 12.0% of Group SR, and 24.0% of Group V. At 12 hours, mild myalgia was present in 20.0% of Group S, 8.0% of Group SR, and 8.0% of Group V. At 24 hours, mild myalgia was reported in 20.0% of Group S, 20.0% of Group SR, and 8.0% of Group V. These differences were not statistically significant at any time point (p>0.05).

Hemodynamic parameters were comparable between groups at most time points. Although statistically significant differences were noted at 5 minutes after intubation in heart rate, systolic blood pressure, and diastolic blood pressure, all values remained within clinically acceptable limits. (table 1)

Table 1. Summary of Major Study Findings

Outcome	**Main Finding**	**Statistical Significance**	**Interpretation**
Fasciculation incidence	Lowest in Group V (16%), followed by Group SR (32%), highest in Group S (60%)	Significant (p=0.013)	Rocuronium priming reduced succinylcholine-induced fasciculations
Intubating conditions	Best in Group SR (44% excellent)	Significant (p=0.048)	Rocuronium priming improved intubating conditions
Postoperative myalgia	Numerically lower in Group SR at 6 and 12 h	Not significant (p>0.05)	Trend toward benefit, but not statistically proven
Hemodynamic response	Transient differences at 5 min only	Significant at 5 min	Clinically acceptable in all groups
Overall conclusion	Rocuronium priming beneficial mainly for fasciculation reduction	—	Limited effect on postoperative myalgia

DISCUSSION

Succinylcholine is one of the most commonly used muscle relaxants in clinical practice because of its faster onset, excellent muscle relaxation suitable for intubation and rapid recovery properties. The usefulness of succinylcholine is limited by a few side effects such as muscle fasciculations, postoperative myalgia, increased serum level of creatinine kinase and potassium, succinylcholine apnea, raised intraocular pressure, extreme bradycardia and malignant hyperthermia. For prevention or reduction of succinylcholine induced muscle fasciculations and postoperative myalgia, pre-treatment is given with several agents like Rocuronium, Atracurium, Cisatracurium, Propofol, Thiopentone, Magnesium Sulphate, small dose of Succinylcholine itself. Our study is to compare the incidence of fasciculation and postoperative myalgia after endotracheal intubation with succinylcholine vs succinylcholine with Rocuronium priming and Vecuronium alone and to observe and compare intubating conditions and any side effects or complications during the study in all the groups. Fasciculations are theorised to be caused by occupation of succinylcholine at acetylcholine nicotinic neuronal receptors at the neuromuscular junction. In the present study, the difference in the mean age, weight, sex, ASA grade and haemodynamic variations among these groups were statistically non-significant (P value >0.05), hence these three groups were comparable with respect to age, weight, sex, ASA grade and haemodynamic variations.

There was no statistically significant difference in mean heart rate (bpm) from baseline to 15^{th} minutes except at 5^{th} minutes that is the time of intubation. This is because we have not used any medication as adjuvant for preventing and controlling intubation response and the muscle relaxants used in the three groups have varying response to intubation. Even though the changes in the heart rate show statistically significant difference, all are within clinically acceptable range.

There was no statistically significant difference in mean systolic blood pressure and diastolic blood pressure from baseline to 15^{th} minutes except at 5^{th} minutes for the same reason as cited above. But all the parameters are within clinically acceptable limits even though statistically different. In our study, precurarization with rocuronium followed by succinylcholine and using vecuronium alone did not significantly increase the systolic and mean diastolic blood pressure and heart rate at different time intervals, which is supported by the study of Abhishek Kumar et al.[4] in which they observed no significant differences in systolic and diastolic blood pressure as well as heart rate at different time intervals.

In our study intubating condition was excellent in 6 patients (24.00%) of group S, 11 patients (44.00%) of group RS and 4 patients (16.00%) of group V respectively. Intubating condition

was found good in 17 patients (68.00%) of group S, 14 patients (56.00%) of group RS and 17 patients (68.00%) of group V. Intubating condition was poor in 2 patients (8.00%) of group S, 0 patient (0.00 %) of group SR and 4 patients (16.00%) of group V. The differences in intubating condition between these groups were statistically significant (P=0.048). Comparable observations were made by Rao MH et al[6] in which they found that priming with rocuronium provided excellent intubating conditions with no adverse effects. Similarly V. Abraham et al [1] concluded that precurarization with rocuronium provides better intubating condition then succinylcholine and vecuronium. Vyankatesh J et al[7] and Reyes E.D[8] in their studies observed that Intubating condition was better in precurarization with rocuronium which was in accordance with our study. In our study, fasciculations were observed in 15 patients (60.00%) in group S, in which 2 patients (8.00%) reported moderate fasciculations. In group SR, 8 patients (32.00%) show mild fasciculation while none of the patients show moderate and severe fasciculation. In group V, 4 patients (16.00%) reported mild fasciculation like movement while none of the patients reported moderate to severe fasciculation.

The finding of our study supported the superior efficacy of precurarization with rocuronium for preventing or reducing succinylcholine induced muscle fasciculation compared with succinylcholine but on other hand it was less efficacious than vecuronium. This is directly comparable with the study of V. Abraham et al.[1], Joshi Vyankatesh et al.[7] and Abbas et al[9] also observed that pretreatment with rocuronium significantly reduced succinylcholine induced fasciculations in their respective studies. Similar observations were also reported by Fukano et al [10]. In our study, at 6th hrs post operative peroids, among the group S, 18 patients (72.00%) had no Myalgia, the proportion of mild & moderate myalgia reported in group S was 5 patients (20.00%) & 2 patients (8.00%) respectively. Among the group RS, 22 patients (88.00%) had no Myalgia. The proportion of mild & moderate myalgia in group SR was 3 patients (12.00%) & 0% respectively. Among the group V, 19 patients (76.00%) had no myalgia while the proportion of mild & moderate myalgia was reported in 5patients (20.00%) & 1 patient (4.00%) respectively. There were no significant differences at 6th hrs amongst the study groups (p=0.388). At 12th and 24th hrs in group S, 5 patients (20.00%) had mild Myalgia whereas in group RS and in group V, 2 patients (8.00%) had reported mild myalgia. This finding even though statistically insignificant but clinically, the incidence of myalgia in group SR and group V were much less. This may be due to reduction in sample size from 135 to 75 because of the limited sample size studied during covid pandemic. Similar finding was observed by Kim JH et al. [11] where they also observed less number of myalgia without any statistically significant differences in 60

patients. Similarly Demers-Pelletier J. et al [(12)] observed that rocuronium pretreatment prevents succinylcholine induced postoperative myalgia. Subramaniam.K, Subramaniam B [(13)] observed rocuronium to be a better adjuvant for prevention of postoperative myalgia as compared to d-tubocurarine. JoshiGP et al [(14)] found that rocuronium pretreatment prevents succinylcholine myalgia more effectively as compared to cisatracurium and d tubocurarine.

CONCLUSION:

From this study, we conclude that rocuronium priming reduces succinylcholine induced muscle fasciculation and postoperative myalgia and a very good option for intubations with less time consuming and lesser cost and much reduction in unwanted adverse effects of succinylcholine in the form of fasciculations and postoperative myalgia.

There is no external financial aid

Ethical issues – addressed and approved

The data is available with the first author

There is no conflict of interest

All the authors have significantly contributed

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