Original Research Article

A study to evaluate the effects of rocuronium with different priming intervals on the time of intubation.

Ranjeet Kumar[1], Sudama Prasad[2],Rekha Kumari[3*]

[1]Assistant Professor, Department of Anesthesiology,Pain and critical care, Patna Medical College and Hospital, Patna, Bihar, India

[2]Associate Professor, Department of Anesthesiology,Pain and critical care, Patna Medical College and Hospital, Patna, Bihar, India

[3]Senior resident, Department of Anesthesiology,Pain and critical care, Patna Medical College and Hospital, Patna, Bihar, India

Received: 23-01-2021 / Revised: 28-02-2021 / Accepted: 13-03-2021

Abstract

Background: Succinylcholine cannot be used for rapid sequence induction or intubation (RSI) in several situations due to associated side effects. Rocuronium bromide has faster onset time among nondepolarizing muscle relaxants and can offer a safe alternative for RSI when the priming principle is used. **Aims:** This study was designed to compare the effects of rocuronium with different priming intervals on the time of intubation and intubating conditions. **Materials and Methods:** Ninety patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 20-50 years, of both sexes were divided into three groups of 30 each. Group A patients received a priming dose of 0.06 mg/kg of rocuronium followed by 0.54 mg/kg rocuronium 3 min later. Group B received 0.06 mg/kg followed by 0.54 mg/kg rocuronium 2 min later, and Group C received saline followed by 0.6 mg/kg rocuronium 3 min later. Time of intubation was assessed using train-of-four (TOF) stimuli, and intubating conditions were compared by the Cooper scoring system. **Results:** The onset time of intubation was 57.4 ± 16.3 s in Group A, 104.8 ± 11.5 s in Group B, and 123.9 ± 13 s in group C. Intubating conditions were clinically acceptable in all three groups. **Conclusion:** The 3-min priming interval of rocuronium provides excellent intubating conditions in less than 60 s and can be used in RSI.

Keywords: Intubating conditions, priming, rocuronium, time of intubation

Introduction

Rapid sequence induction or intubation (RSI) using succinylcholine is the most commonly used technique in patients at risk of gastric aspiration.But undesirable side effects associated with succinyl choline,such as muscle fasciculations,myalgia, hyperkalemia,[1] bradyarrhythmias,[2]increased intraocular pressure,raised intracranial pressure,[3] increased intragastric pressure, malignant hyperthermia, and masseter spasm, make it unsuitable in several situations.

This has prompted the use of nondepolarizing muscle relaxants for RSI. But slower onset of action acts as a limiting factor. This limitation can be overcome with various techniques such as the use of high doses of an individual agent, a combination of relaxants, timing principles, or priming technique.[4]

Earlier studies have showed onset of action of rocuronium comparable to succinylcholine with a higher dose, but no clear guidelines are available about the use of priming principle with a safe lower dose as well as the priming interval.

Thus, this study was taken up with the primary objective of evaluating the effects of rocuronium with different priming intervals on the time of intubation and the secondary objective of evaluating the intubating conditions.

**Correspondence*
Dr. Rekha Kumari

Senior resident, Department of Anesthesiology,pain and critical care. Patna Medical College and Hospital,Patna., Bihar, INDIA
E-mail:dr.rekha911@gmail.com

Materials and Methods

This prospective randomized double-blind study was conducted at Department of Anesthesia and Critical Care, at Patna Medical College and Hospital,Patna. The study was approved by the institutional research and ethical committee. The study was conducted between December 2018 and May 2019.This study was conducted in 90 patients at a tertiary care hospital. Patients aged 20-50 years, of both sexes, weighing 50-100 kg, with American Society of Anesthesiologists (ASA) physical status 1 and 2, visiting the hospital for abdominal and peripheral limb surgeries under general anesthesia were included in the study. Exclusion criteria included the following: Patient refusal; pregnancy; significant hepatic, renal, and/or metabolic disorder, and/ or neuromuscular disease; ongoing medications known to influence neuromuscular function; known allergy to rocuronium; and anticipated difficult airway.

Patients were assigned to one of the following three groups A, B, and C randomly according to computer-generated numbers:

Group A: Priming with 0.06 mg/kg of rocuronium followed by 0.54 mg/kg of rocuronium after 3 min of priming interval

Group B: Priming with 0.06 mg/kg of rocuronium followed by 0.54 mg/kg of rocuronium after 2 min of priming interval

Group C: Control group with saline followed by 0.6 mg/kg rocuronium after 3 min interval.

A standard anesthesia protocol was followed. In the operation theater, intravenous cannula was secured in the hand opposite to neuromuscular monitoring and a balanced salt infusion was started. Electrocardiogram (ECG), noninvasive blood pressure (NIBP), and oxygen saturation (SpO_2) were monitored and the baseline values noted. The nerve stimulation technique was explained to the patient

and a supramaximal stimulus was set with a peripheral nerve stimulator.After preoxygenation, groups A and B received a priming dose of rocuronium, while group C received normal saline. The patients were enquired about ptosis, double vision, difficulty in swallowing, and difficulty in breathing. Anesthesia was induced with fentanyl 2 mcg/kg and propofol 2 mg/kg. An intubating dose of rocuronium of 0.54 mg/kg was given to group A after 3min and to group B after 2 min, and 0.6 mg/kg to group C after 3 min of the priming dose. A Supramaximal train-of-four (TOF) stimulus of frequency 1 Hz (T1) was applied over the ulnar nerve at the wrist through surface electrodes every 10 s, and the time for disappearance of T1 of TOF stimuli was noted. The time interval between the intubating dose and loss of T1 of TOF stimuli was considered as the time of intubation. Intubating conditions were graded as excellent, good, or poor based on the Cooper scoring system.

Table 1:Grading system

Grading	Jaw relaxation	Vocal cords	Response to intubation
Excellent	Good	Open	None
Good	Good	Open	Slight diaphragmatic movement or cough
Poor	Moderate	Moving	Severe coughing/bucking

Vital parameters, namely heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and SpO_2 were monitored every 1 min for the first 5 min.

Statistical analysis

A detailed statistical analysis[5] was carried out in the present study. Based on the Rao *et al*. study,[6] to detect a difference of 15 s in time to intubation between the study groups with 1% level of significance and 90% power, a sample size of 30 individuals in each of three groups was chosen. Continuous measurements were presented as mean ± standard deviation (SD), and categorical measurements were presented as number (%). One-way analysis of variance (ANOVA) test was used to measure the time of intubation between the three groups and for comparing intubating conditions among the groups. Significance was assessed at 5% level of significance. Statistical analysis was performed using PASW Statistics, 18.0, SPSS Inc, Chicago, IL, USA. Differences yielding $P < 0.05$ were considered statistically significant.

Results

Table 1 shows the demographic data. All the groups were statistically comparable with respect to age, sex, weight, and ASA physical status. Table 2 shows the comparison of the time of intubation (time interval between intubating dose and loss of T1 of TOF stimuli) among the three groups. The onset time of intubation (loss of T1 of TOF) was 57.4 ± 16.3 s in group A, 104.8 ± 11.5 s in group B, and 123.9 ± 13 s in group C, the control group. The primed group with priming interval of 3 min showed a statistically significant decrease in the onset time of intubation. Intergroup comparison between groups A and B, A and C, and B and C showed $P < 0.001$, which was statistically significant. Table 3 compares the intubating conditions among three groups. Overall excellent to good intubating conditions were obtained in all patients in the three groups. Intergroup comparison between groups A and B, A and C, and B and C showed *P* values of > 0.05, which was statistically insignificant. Hemodynamic variables measured every 2 min for 5 min following intubation showed no statistically significant variation among the three groups.

Table 2: Demographic data

Parameter	Total	Group A	Group B	Group C	*P*
Age	38.8±9.97	38±10.7	38.1±9.2	40.3±10	0.61
Sex (male/female)	49/41	13/17	19/11	17/13	0.138
Weight	61.69±8.64	60.5±8.3	61.2±7.3	63.5±10.1	0.41
ASA PS (I/II)	59/31	21/9	19/11	20/10	0.126

ASA PS: American Society of Anesthesiologists physical status

Table 3: Comparison of times of intubation (time interval between intubating dose and loss of T1 of TOF stimuli)

Time of intubation	Mean±SD	*P*
Group A	57.43±16.3	<0.001
Group B	104.87±11.49	
Group C	123.90±13.19	
Total	123.90±31.24	

SD: Standard deviation, TOF: Train-of-four

Table 4: Comparison of intubating conditions

Intubating conditions	Excellent	Good	*P*
Group A	27 (90%)	3 (10%)	0.53
Group B	26 (86.7%)	4 (13.3%)	
Group C	24 (80%)	6 (20%)	
Total	77 (85.6)	13 (14.4)	

Discussion

RSI is performed to secure a definitive airway in the least amount of time after ablation of protective airway reflexes with the induction of anesthesia. This is the technique most frequently employed for patients with full stomach and at risk of gastric aspiration. Succinylcholine has a proven role in RSI, but can be associated with many untoward effects.

Rocuronium bromide, a steroidal nondepolarizing muscle relaxant is useful for producing rapid onset of action, but onset time and intubating conditions comparable to succinylcholine can be achieved only by administration of 0.9-1.2 mg/kg of rocuronium,[7] which can significantly increase its duration of action.

However, the priming principle can be advocated to shorten the onset time of nondepolarizing muscle relaxants. The priming principle entails a divided-dose technique with a priming dose (10% of

intubating dose), Small enough not to cause any unpleasant side effects and large enough to cause moderate inhibition of neuromuscular transmission.Cooper *et al*.[8] compared the intubating conditions with rocuronium (0.6 mg/kg) and succinylcholine (1 mg/kg) in 50 patients. They found that clinically acceptable intubating conditions were generated in 95% of patients at 60 s and in all patients at 90 s with rocuronium. Intubating conditions were excellent with succinylcholine at both the time intervals. They concluded that rocuronium can be used as a safe alternative to succinylcholine in RSI.

A priming dose of 10% of the standard intubating dose (2 × ED95)[9] and a priming interval of 3-4 min has been recommended as a safe and effective technique. This study was conducted to determine the efficacy of priming with different time intervals on intubation with rocuronium.

Singh *et al*.[10] observed that with 0.6 mg/kg rocuronium and 1.5 mg/kg succinylcholine, the time to achieve maximum blockade was 87.94 s and 65.59 s respectively. Comparable intubating conditions were obtained in the two groups at 60 s. Rao *et al*.[6] used a priming dose of 0.06 mg/kg rocuronium in one group followed by 0.54 mg/kg of rocuronium 3 min later. The control group received saline followed by 0.6 mg/kg of rocuronium after 3 min. The onset time of intubation was 50.6 ± 7.4 s in the priming group and 94.0 ± 11.62 s in the control group, with excellent intubating conditions in both the groups. In accordance with the two studies mentioned above, the dose of 0.6 mg/kg[11]rocuronium with a priming dose of 0.06 mg/ kg [12] (10% of intubating dose) was chosen for our study.

Griffith *et al*.[7] compared the effects of priming and nonpriming by giving one group a priming dose of 0.06 mg/kg rocuronium followed 2 min later by 0.54 mg/kg rocuronium, and giving another group 0.6 mg/kg rocuronium directly. Onset times were 34 ± 6 s in the priming group and 59 ± 14 s in the group without priming.

Based on the results of the above study, we compared two priming intervals of 3 min and 2 min against a control group in our study. We found that the onset time of intubation (loss of T1 of TOF) was 57.4 ± 16.3 s in the priming group with 3 min and 104.8 ± 11.5 s in the priming group with 2 min priming interval. The onset time was 123.9 ± 13 s in the control group. The primed group with a priming interval of 3 min showed statistically significant decrease in the onset time of intubation with rocuronium.

A study was conducted by Naguib *et al*.[13] comparing the effects of priming rocuronium (0.54 mg/kg) with rocuronium (0.06 mg/kg) or mivacurium (0.015 mg/kg). They found the onset time after priming with rocuronium to be 73 s, which was higher compared to our study.

One of the major drawbacks of a priming dose is the occurrence of adverse effects such as weakness, diplopia, dysphagia, generalized discomfort, and breathing difficulties.[9] Aziz *et al*.[9] studied the effects of priming with vecuronium and rocuronium on young and elderly patients. They looked for the presence of muscle weakness by monitoring oxygen saturation, pulmonary function tests, and symptoms of diplopia, dysphagia, and ptosis following priming. They observed greater decreases in oxygen saturation and pulmonary function tests in the elderly (aged 65-73 years) following priming doses of vecuronium and rocuronium when compared to their younger (25-35 years) counterparts.

None of the patients in our study showed evidence of such adverse effects. The absence of subtle symptoms of muscle weakness following priming may be attributed to the smaller priming dose used by us and to the administration of fentanyl 1 min after the priming dose.

Schmidt[14] compared a priming technique (0.06 mg/kg priming dose with a 3 min priming interval) with a bolus application of rocuronium (0.6 mg/kg) on the onset of neuromuscular blockade at the laryngeal adductor and adductor pollicis muscles. The onset times measured at laryngeal adductors (44.7 ± 7.4 s vs 74 ± 23.8 s) and at adductor pollicis (105.4 ± 29.9 s vs 139.2 ± 51.5 s) were significantly shorter in the priming group than in the bolus group. The onset times were significantly shorter at the laryngeal muscles in comparison to the adductor pollicis.

Meistelman[15] studied the onset of neuromuscular blockade with rocuronium at the laryngeal adductor muscles and adductor pollicis in 14 adult patients. With rocuronium 0.25 mg/kg, the onset time was 1.6 ± 0.1 min and 3.0 ± 0.3 min at the laryngeal adductors and adductor pollicis respectively. With 0.5 mg/kg, the onset time was also more rapid at the vocal cords (1.4 ± 0.1 min) than at the adductor pollicis (2.4 ± 0.2 min). They concluded that the onset of action as well as recovery was faster at the laryngeal adductor muscles, but that blockade was less intense than at the adductor pollicis.

The difference in intubation times between our study and the studies mentioned above can be attributed to the site of monitoring of neuromuscular blockade chosen. We chose the adductor pollicis muscle for monitoring neuromuscular blockade in our study for the ease of monitoring.The differences in the onset times among various studies may be attributed to the different modes used (TOF or single twitch), frequency of nerve stimulation, anesthetic drugs, and study population.Rao *et al*.[6] compared the intubating conditions between rocuronium with priming and rocuronium without priming. They found no increase in HR or blood pressure following rocuronium administration.They observed a slight increase in HR and mean arterial pressure (MAP) 1 min post intubation, which was attributed to stress response to intubation.Shorten[16] performed a comparative study in elderly patients given rocuronium 0.9 mg/ kg and patients given vecuronium 0.12 mg/kg, and found no significant change in HR, arterial blood pressure, or plasma epinephrine concentrations in either group. In our study, the hemodynamic variables measured every 2 min for 5 min following intubation showed no Statistically significant variations among the three groups. This was in agreement with the study by Rao *et al*.

We assessed jaw relaxation, position of vocal cords, response to intubation (coughing, bucking, or muscular movements), and the absence of twitches to TOF stimuli just before intubation; intubating conditions were graded as excellent, good, and poor depending on the score. All the patients in our study had excellent to good intubating conditions. This was corroborated by the studies conducted by Naguib *et al*.,[13]Rao *et al*.,[6] and Griffith *et al*.[7]

Conclusion

We conclude that the onset time of intubation after priming with 10% (0.06 mg/kg) of an intubating dose (0.6 mg/ kg) of rocuronium and a priming interval of 3 min was 57.4 ± 16.3 s. This was significantly lower than the other groups with 2 min priming interval (104.8 ± 11.5 s) and without priming (123.9 ± 13 s). Thus, rocuronium with priming can be used as a safe alternative to succinylcholine in RSI.

References

1. Birch AA, Mitchell GD, Playford GA, Lang CA. Changes in serum potassium response to succinylcholine following trauma. JAMA. 1969;210:490-3.
2. Stoelting RK, Peterson C. Heart-rate slowing and junctional rhythms following intravenous succinylcholine with and without intramuscular atropine preanesthetic medication. Anesth Analg. 1975;54:705-9.
3. Minton MD, Grosslight K, Stirt JA, Bedford RF. Increase in intracranial pressure from succinylcholine: Prevention by prior nondepolarizing blockade. Anaesthesiology. 1986;65:165-9.
4. Naguib M, Adbdulatif M, Gyasi HK. Priming with atracurium: Improving intubating conditions with additional doses of thiopental. Anesth Analg.1986;65:1295-9.
5. Suresh KP, Chandrashekar S. Sample size estimation and power analysis for clinical research studies. J Hum Reprod Sci. 2012;5:7-13.
6. Rao HM, Venkatraman A, Malleshwari R. Comparison of intubating conditions between rocuronium with priming and without priming: Randomized and double-blind study. Indian J Anaesth. 2011;55:494-8.

7. Griffith KE, Joshi GP, Whitman PF, Garg SA. Priming with rocuronium accelerates the onset of neuromuscular blockade. J ClinAnesth. 1997;9:204-7.
8. Cooper R, Mirakur RK, Clarke RS, Boules Z. Comparison of intubating conditions after administration of Org 9246 (rocuronium) and suxamethonium. Br J Anaesth. 1992;69:269-73.
9. Aziz L, Jahangir SM, Choudhury SN, Rahman K, Ohta Y, Hirakawa M. The effect of priming with vecuronium and rocuronium on young and elderly patients. Anesth Analg. 1997; 85:663-6.
10. Singh A, Bhatia PK, Tulsiani KL. Comparison of onset time, duration of action and intubating conditions achieved with suxamethonium and rocuronium. Indian J Anaesth. 2004;48:129-33.
11. Fuchs-Burder T, Tassonyi E. Intubating conditions and time course of rocuronium-induced neuromuscular block in children. Br J Anaesth. 1996;77:335-8.
12. Huizinga AC, Vandenbrom RH, Wierda JM, Hommes FD, Hennis PJ. Intubating conditions and onset of neuromuscular block of rocuronium(Org 9426);a comparison with suxamethonium. Acta Anaesthesiol Sc and. 1992;36:463-8.
13. Naguib M.Different priming techniques, including mivacurium, accelerate the onset of rocuronium. Can J Anaesth. 1994; 41:902-7.
14. Schmidt J,Irouschek A, Muenster T, Hemmerling TM, Albrecht S. A priming technique accelerates onset of neuromuscular blockade at the laryngeal adductor muscles. Can J Anaesth. 2005;52:50-4.
15. Meistelman C, Plaud B, Donati F. Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. Can J Anaesth. 1992;39:665-9.
16. Shorten GD, Uppington J, Comunale ME. Changes in plasma catecholamine concentrations and hemodynamic effects of rocuronium and vecuronium in elderly patients. Eur J Anaesthesiol.1998;15:335-41.

Conflict of Interest: Nil
Source of support:Nil