

EFFECTS OF PRIMING ON ONSET TIME AND INTUBATING CONDITIONS WITH ROCURONIUM- A PROSPECTIVE RANDOMISED COMPARATIVE STUDY

Radha Korumbil Raghavan¹, Bindu Meleveetil², Ushakumary Reghunathan³

¹Additional Professor, Department of Anaesthesiology, Government Medical College, Kozhikode, Kerala.

²Associate Professor, Department of Anaesthesiology, Government Medical College, Kozhikode, Kerala.

³Additional Professor, Department of Anaesthesiology, Government Medical College, Kozhikode, Kerala.

ABSTRACT

BACKGROUND

Rocuronium is a newer non-depolarising muscle relaxant with faster onset of action than other non-depolarising muscle relaxants that could be an alternative to succinylcholine in rapid sequence intubation where succinylcholine is contraindicated. Based on onset of action, 0.9-1.2 mg/kg dose of rocuronium may be necessary as an alternative to succinylcholine at the cost of increased clinical duration. In this study, 0.6 mg/kg rocuronium with priming was compared against a single intubating dose of 0.9 mg/kg to know the influence of priming technique on the onset times and intubating conditions.

MATERIALS AND METHODS

A total of 60 patients were randomly allocated to two groups of 30 each. Group A (priming group) received 0.06 mg/kg of rocuronium as priming dose and 0.54 mg/kg rocuronium as intubating dose 3 minutes after priming. Group B (single intubating dose group) received a single intubating dose of 0.9 mg/kg. The onset time of intubation (loss of T1 of TOF stimulation) and intubating conditions were assessed. Continuous measurements were presented as mean±SD using 't' test and categorical measurements were presented as number (%).

RESULTS

Demographic data were comparable with respect to age, sex and weight. The onset time of intubation was 60±13.6 seconds in group A and 60±15.7 seconds in group B. Excellent to good intubation conditions were obtained in both groups.

CONCLUSION

Priming technique hastens the onset of action of rocuronium and with priming we can reduce the dose of rocuronium used for intubation thereby reducing the duration of action.

KEYWORDS

Rocuronium, Priming, Succinylcholine, Non-Depolarising, Rapid Sequence Intubation.

HOW TO CITE THIS ARTICLE: Raghavan RK, Meleveetil B, Reghunathan U. Effects of priming on onset time and intubating conditions with rocuronium- A prospective randomised comparative study. J. Evid. Based Med. Healthc. 2017; 4(7), 351-354. DOI: 10.18410/jebmh/2017/67

BACKGROUND

The rapid securing of the airway is of prime importance in all patients undergoing surgery under general anaesthesia. The protective airway reflexes are blunted in the anaesthetised patients leaving him or her vulnerable to regurgitation of the contents of the stomach and aspiration. Succinylcholine has long been the standard neuromuscular blocking agent used for facilitation of rapid tracheal intubation. When administered intravenously, it produces intubating conditions within 60 seconds followed by a rapid recovery from the blockade. But, undesirable side effects associated with succinylcholine such as muscle

fasciculations, myalgia, hyperkalaemia, bradyarrhythmias, increased intraocular pressure, intragastric pressure, intracranial pressure, malignant hyperthermia and masseter spasm make it unsuitable in several situations.¹⁻³ Its use is either contraindicated or is at best controversial in patients with recent burns, open eye injury, glaucoma, raised intracranial pressures, hyperkalaemia and in patients known to have abnormal variants of the enzyme, plasma cholinesterase. The above side effects and contraindications of succinylcholine had prompted the use of non-depolarising muscle relaxants using various techniques for rapid sequence intubation.⁴ Rocuronium bromide an aminosteroid non-depolarising muscle relaxant has been shown to provide adequate intubating conditions with rapid onset, intermediate duration of action and no obvious side effects. It has the shortest onset time of all the non-depolarising neuromuscular blocking agents currently available.^{5,6} Rocuronium has an onset of action comparable to succinylcholine when used in doses of 0.9-1.2 mg/kg,⁷⁻⁹ but this higher dose increases the duration of action. Therefore, using high dose rocuronium is not desirable for the short and

Financial or Other, Competing Interest: None.

Submission 25-12-2016, Peer Review 02-01-2017,

Acceptance 14-01-2017, Published 21-01-2017.

Corresponding Author:

Dr. Ushakumary Reghunathan,

Harmony, D.P.O. Road,

Malappuram, Kerala-676505.

E-mail: surgeonuk@gmail.com

DOI: 10.18410/jebmh/2017/67



medium duration of surgical procedures. For this reason, various alternative methods were studied with standard intubating dose of rocuronium to achieve comparable onset time and intubating conditions of succinylcholine. In this study, 0.6 mg/kg rocuronium with priming was compared against a single intubating dose of 0.9 mg/kg to know the influence of priming technique on the onset times and intubating conditions. We hypothesised that by using priming principle the onset time of the neuromuscular blockade maybe hastened and we will get comparable intubating conditions with a smaller dose.

MATERIALS AND METHODS

After getting Institutional Ethics Committee approval and written informed consent from all patients, a prospective randomised comparative study was carried out over a period of 12 months on 60 patients of American Society of Anaesthesiologists physical status I and II in the age group of 20-60 years scheduled for elective surgery under general anaesthesia. All patients were randomly allocated into two groups of 30 each. Group A (priming group) and Group B (single intubating dose group) using computer generated random numbers. Patients with anticipated difficult intubation, having medications affecting neuromuscular function, chronic renal and hepatic impairment and BMI >30 were excluded from the study.

All patients were subjected to detailed preanaesthetic evaluation and the procedure of study was explained to them. They were warned of possible symptoms of muscle weakness that could appear after the priming dose, which included difficulty in breathing, difficulty in swallowing, double vision and decreased handgrip strength. Patients were kept nil per oral overnight and premedicated with oral alprazolam 0.5 mg and ranitidine 150 mg night before surgery. In the morning of surgery, ranitidine 150 mg and ondansetron 8 mg was given with sips of water. In operation theatre, monitors like electrocardiography, pulse oximeter and noninvasive blood pressure were attached to all patients and all the baseline parameters were recorded. An IV line was obtained with 18G cannula in the nondominant forearm under local anaesthesia. Intraoperatively, a peripheral nerve stimulator was also used to monitor the neuromuscular transmission. The ulnar nerve was selected for stimulation. After adequate preparation of the area, surface electrodes were applied over the wrist along the course of the ulnar nerve. The negative electrode was placed 3-4 cm proximal to the first one. A supramaximal current of 40mA was selected for simulation.

All patients were preoxygenated for 3 minutes with 100% oxygen. Group A patients received 0.06 mg/kg of rocuronium as priming dose and patients were assessed for possible symptoms of muscle weakness (double vision, difficulty in swallowing and breathing or decrease in handgrip strength). General anaesthesia was then initiated with fentanyl 2 mg/kg and thiopentone 5 mg/kg 3 minutes after the priming dose 0.54 mg/kg of rocuronium was administered. In group B, no priming dose was given and after induction, patients received intubating dose of

rocuronium (0.9 mg/kg). The response of adductor pollicis to train of four was noted independently every 10 seconds until the response to the same became zero (i.e. loss of T1 of TOF stimuli) and the time taken to attain the same was noted. Intubating conditions were assessed 30, 60 and 90 seconds after administration of intubating dose.

Intubating conditions were assessed according to the scoring system proposed by Kreig et al modified by Cooper et al (1992).^{10,11} The parameters taken into consideration were jaw relaxation, vocal cord movement and gross response of the patients to direct laryngoscopy and endotracheal intubation.

Score	Jaw Relaxation	Vocal Cord Movement	Response to Direct Laryngoscopy and Intubation
0.	Poor (impossible)	Closed	Severe coughing or bucking
1.	Minimal (difficult)	Closed	Mild coughing
2.	Moderate (fair)	Moving	Slight diaphragmatic movement
3.	Good (easy)	Open	None

Table 1. Intubating Scoring System

Intubation was carried out only under good and excellent intubation scores and time required to attain the same was noted. Anaesthesia was maintained with oxygen, nitrous oxide and isoflurane. Clinically significant cardiovascular events (changes in blood pressure and/or heart rate 30% above or below baseline values) occurring within 15 minutes after the administration of the intubating dose were also observed. After collection, data was entered in Microsoft Excel and the analysis was done by SPSS 18 software. Continuous measurements were presented as mean±standard deviation (SD) using 't' test and categorised measurements were presented as number (%).

RESULTS

Both groups were comparable with respect to age, sex and weight.

	Group A	Group B	P value
Age	38.7±10.9	40.9±12.9	0.488
Weight	52.9±5.10	52.47±4.7	0.716
Sex	9/21	10/20	0.781

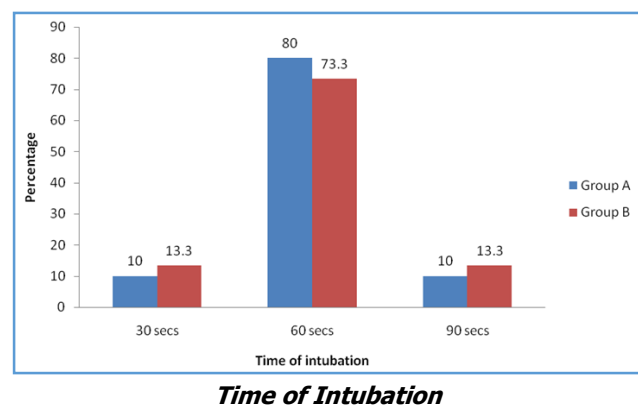
Table 2. Demographic Distribution

The onset time of intubation (time interval between intubating dose and loss of T1 of TOF) was 60±13.6 in group A and 60±15.7 in group B. There was no statistically significant difference between the two groups (p=1.00).

Time of Intubation	Mean±SD	P value
Group A	60±13.6	1.00
Group B	60±15.7	

Table 3. Comparison of Onset of Intubation

SD - Standard Deviation; TOF- Train of Four



Overall, excellent to good intubating conditions were obtained in both groups. Intergroup comparison between group A and B showed p value of 0.781, which was statistically insignificant (Table 4). After administration of intubating dose, neither clinically significant cardiovascular events nor signs were obtained. One patient in group A had difficulty in controlling the tongue and one patient had difficulty in swallowing after administering the priming dose.

Intubating Conditions	Excellent	Good	P value
Group A	21 (70%)	9 (30%)	0.781
Group B	20 (66.7%)	10 (33.3%)	

Table 4. Comparison of Intubating Conditions

DISCUSSION

The rapid sequence induction along with cricoid pressure was introduced as a means to protect airway in patients at risk for regurgitation and aspiration. Succinylcholine has an established role in rapid sequence intubation, but it has many undesirable adverse effects because of its depolarising mechanism of action. Rocuronium with priming could be an alternative to succinylcholine. The priming principle described by Foldes consists of administering a small dose of non-depolarising neuromuscular blocking agent 3 to 6 minutes prior to induction and then administering a second larger dose to facilitate tracheal intubation.¹² Priming technique with rocuronium has been investigated by several authors to reduce the onset time and optimisation of its efficacy.

Griffith et al found that the onset time of rocuronium with priming was significantly shorter than those without priming.¹³ In his study, Susank et al used different neuromuscular blocking agents for priming and he found that priming can facilitate endotracheal intubation by rocuronium in 60 seconds irrespective of the neuromuscular blocking agent used.¹⁴ Rao et al used a priming dose of 0.06

mg/kg followed by 0.54 mg/kg rocuronium in one group and 0.6 mg/kg rocuronium in the other group. The onset time of intubation was 50.6±45s in the priming group and 94.0±11.620 in the control group with excellent intubating conditions in both groups.¹⁵ In a study comparing different priming intervals, Yavascaoglu et al proved that priming with 3 minutes intervals shortened the onset time of rocuronium while a 2-minute interval did not significantly decrease the onset time.¹⁶

In our study, we compared the influence of priming technique on the onset time and intubating conditions of rocuronium against a single-intubating dose. Based on the above said studies, we selected a priming dose of 0.06 mg/kg, a priming interval of 3 minutes with an intubating dose of 0.54 mg/kg and compared against a single intubating dose of 0.9 mg/kg, which was higher than the dose used in these studies. In a study comparing two different doses of rocuronium (0.7 and 0.9 mg/kg) with succinylcholine (1.5 mg/kg) Weiss JH et al found that rocuronium bromide at a dose of 0.9 mg/kg provides intubating conditions similar to succinylcholine 1.5 mg/kg at 1 minute. Intubating conditions at 1 minute following a 0.7 mg/kg were not as good as following 0.9 mg/kg rocuronium or 1.5 mg/kg succinylcholine.¹⁷ McCourt et al found that rocuronium 1 mg/kg and succinylcholine 1 mg/kg have shown excellent intubating conditions at 60s.¹⁸ Sluga M et al compared rocuronium 0.6 mg/kg with succinylcholine 1 mg/kg and they concluded that succinylcholine allows for a more rapid endotracheal intubation sequence and creates superior intubation conditions than rocuronium.¹⁹

In our study, the difference between the priming group and single intubation dose, rocuronium group was not significant statistically in terms of timing of intubation and intubating conditions. This result correlates poorly with the findings of Griffith et al and Rao et al. The reason for those disparities maybe due to the use of large intubating dose (0.9 mg/kg) in single-dose rocuronium.

One of the major drawbacks of priming dose is the occurrence of adverse effects such as visual disturbances, difficulty in swallowing, breathing difficulties, weakness, etc. Aziz et al explained the effects of priming in younger and elderly patients.²⁰ In our study, only 2 patients in priming group had side effects. One had difficulty in swallowing and the other had difficulty in controlling the tongue.

CONCLUSION

Priming technique of rocuronium 0.06 mg/kg with an intubating dose of 0.54 mg/kg provided excellent intubating condition at 60 seconds, which was comparable to a single intubating dose of 0.9 mg/kg. With priming techniques, we can reduce the dose of rocuronium used for intubation thereby reducing the duration of action. So, rocuronium 0.6 mg/kg with priming maybe considered as an alternative to succinylcholine for rapid sequence intubation for short and medium duration surgeries.

One limitation of our study was that we used adductor pollicis muscle for neuromuscular monitoring, which has delayed onset of block compared to adductor muscles of

larynx. So, it appears that intubation maybe performed before complete block is achieved as measured at the thumb.

REFERENCES

- [1] Birch AA Jr, Mitchell GD, Playford GA, et al. Changes in serum potassium response to succinyl choline following trauma. *JAMA* 1969;210(3):490-493.
- [2] Stoelting RK, Peterson C. Heart slowing and junctional rhythms following intravenous succinylcholine with and without intramuscular atropine preanesthetic medication. *Anesth Analg* 1975;54(6):705-709.
- [3] Minton MD, Grosslight K, Stirt JA. Increase in intracranial pressure from succinylcholine: prevention by prior non depolarizing blockade. *Anaesthesiology* 1986;65(2):165-169.
- [4] Naguib M, Brull SJ. Update on neuromuscular pharmacology. *Curr Opin Anaesthesiol* 2009;22(4):483-490.
- [5] Wright PM, Caldwell JE, Miller RD. Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. *Anaesthesiology* 1994;81(5):1110-1111.
- [6] Meistelman C, Plaud B, Donati F. Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscle of the larynx and adductor pollicis in humans. *Can J Anaesth* 1992;39(7):665-669.
- [7] Huizinga AC, Vandenbrom RH, Wierda JM, et al. Intubating conditions and onset of neuromuscular block of rocuronium (ORG 9426): a comparison with suxamethonium. *Acta Anaesthesiol Scand* 1992;36(5):463-468.
- [8] Tryba M, Zorn A, Thole H, et al. Rapid-sequence orotracheal intubation with rocuronium: a randomized double-blind comparison with suxamethonium--preliminary communication. *Eur J Anaesthesiol* 1994;9:44-48.
- [9] De May JC, Debrock M, Rolly G. Evaluation of the onset and intubation conditions of rocuronium bromide. *Eur J Anaesthesiol* 1994;9:37-40.
- [10] Kreig N, Mazur L, Booij LHDJ. Intubation condition and reversibility of a new non depolarizing neuromuscular blocking agents. *Acta Anaesthesiol Scand* 1980;24:423-425.
- [11] Cooper P, Mirakhur RK, Clarke RS. Comparison of intubating conditions after administration of ORG 9426 (Rocuronium) and suxamethonium. *Br J Anaesth* 1992;69:269-273.
- [12] Foldes F. Rapid tracheal intubation with non-depolarising neuromuscular blocking drugs: the priming principle. *Br J Anaesth* 1984;56(6):663.
- [13] Griffith KE, Joshi GP, Whitman PF, et al. Priming with rocuronium accelerates the onset of neuromuscular blockade. *J Clin Anesth* 1997;9(3):204-207.
- [14] Shashank DS, Singh NR, Singh LK. Effects of pretreatment with different neuromuscular blocking agents on facilitation of intubation with rocuronium: a prospective randomized comparative study. *Indian J of Anaesth* 2014;58(3):303-308.
- [15] Rao MH, Venkatraman A, Malleswari R. Comparison of intubating conditions between rocuronium with priming and without priming: randomised and double-blind study. *Indian J Anaesth* 2011;55(5):494-498.
- [16] Yavascaoglu B, Cebelli V, Kelebek N, et al. Comparison of different priming techniques on the onset time and intubating conditions of rocuronium. *Eur J Anaesthesiol* 2002;19(7):517-521.
- [17] Weiss JH, Gratz I, Goldberg ME, et al. Double-blind comparison of two doses of rocuronium and succinylcholine for rapid-sequence intubation. *J Clin Anaesth* 1997;9(5):379-382.
- [18] McCourt KC, Salmela L, Mirakhur RK. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. *Anaesthesia* 1998;53(9):867-871.
- [19] Sluga M, Ummenhofer W, Siegemund M, et al. Rocuronium versus succinylcholine for rapid sequence induction of anaesthesia and endotracheal intubation: a prospective randomized trial in emergent cases. *Anaesth Analg* 2005;101(5):1356-1361.
- [20] Aziz L, Jahangir SM, Choudhury SN, et al. The effect of priming with vecuronium and rocuronium on young and elderly patients. *Anesth Analg* 1997;85(3):663-666.