Comparative Evaluation of Effect of Bolus Injection of Saline with Arm Elevation on the onset Time of Different Dosages of Rocuronium

Garima Anant[1], Vineet Kumar[2]

ABSTRACT

Introduction: Shortening the onset time of neuromuscular blocking drugs is important in some situations. Several protocols have been proposed for this purpose, including the use of the priming principle or timing principle, and administration of large doses but are associated with side effects. This study was designed to evaluate the effect of bolus injection of saline with arm elevation on the onset time of different dosages of rocuronium.

Material and methods: After approval of the Institutional Review Board, this randomized controlled study was conducted in 64 adult ASA I/II patients of 18-60 years age group of either sex scheduled for elective minor surgery. Patients were randomized into 4 groups - Group R6 (n=16) –Patients who received 0.6 mg/kg rocuronium. Group RS6 (n=16) –Patients who received 0.6 mg/kg rocuronium followed by 20 mL saline push over 5 seconds and hand elevation. Group R9 (n=16) –Patients who received 0.9 mg/kg rocuronium. Group RS9 (n=16) –Patients who received 0.9 mg/kg rocuronium followed by 20mL saline- push over 5 seconds and hand elevation. Rocuronium at specified dosages was administered over 2-3 sec into a rapidly running infusion through a T-port in the intravenous (IV) line. In the bolus saline group R6 patients received 0.6 mg/kg rocuronium without saline- push or hand raise, whereas in RS6, 0.6 mg/kg rocuronium followed by 20 mL saline was pushed over 5 seconds into IV line while maintaining the arm elevated vertically. The other group R9 received 0.9 mg/kg rocuronium, and group RS9 was given the same dose of rocuronium followed by 20 ml saline- push over 5 seconds with straight hand elevation.

Results: Our primary outcome, onset time was found to be 89.94 ± 3.45 sec and 77.31 ± 3.09 sec for the Group R6 and RS6 respectively, which was statistically significant with a p value of <0.001. Similarly, onset time was found to be 75.19 ± 2.86 sec and 62.63 ± 2.22 sec for the Group R9 and RS9, which was statistically significant with a p value of < 0.001. Lag time was found to be 38.38 ± 2.87 sec and 31.06 ± 2.84 sec for the Group R6 and RS6 respectively, which was statistically significant with a p value of < 0.001. Similarly, lag time for the Group R9 and RS9 was found to be 32.13 ± 2.78 sec and 24.19 ± 3.23 sec, which was also statistically significant with a p value of < 0.001. 100% clinically acceptable intubation conditions were achieved in all the patients and the intubating conditions were not statistically significant between the groups.

Conclusion: Intravenous bolus injection of saline plus arm elevation shortens the onset time and lag time of rocuronium. 100% clinically acceptable intubation conditions were achieved in all the patients and time to 25% recovery of T1 was found to be comparable between the control and bolus saline groups.

Keywords: Rocuronium, Saline Bolus with Arm Elevation, Onset Time

INTRODUCTION

Muscle relaxation is used to serve various purposes like to provide skeletal muscle relaxation during surgery, mechanical ventilation and to facilitate endotracheal intubation. An ideal neuromuscular blocking agent is one which has brief duration of action, provides profound relaxation and is free from haemodynamic changes. Succinyl choline was once considered to be the most appropriate muscle relaxant to facilitate the endotracheal intubation during induction of anesthesia. However, it can also causes severe hyperkalemia in patients involving burns, denervation or fragile muscle membranes, severe bradycardia after a second dose of succinylcholine, increases in intracranial pressure, intragastric pressure or intraocular pressure, cardiac arrest, etc. serious side effects.[1-4] Rocuronium is a desacetoxy analogue of vecuronium, a steroidal non-depolarising muscle relaxant with an onset time (after 3-4 times 95% effective dose) not different from that of succinylcholine. It has a rapid to intermediate onset (depending on dose) and intermediate duration of action. Shortening the onset time of neuromuscular blocking drugs is important in situations like in patients with full stomach requiring rapid sequence induction of anaesthesia. Several methods have been proposed for this purpose, including use of the priming principle or timing principle, and administration of large doses and non-pharmacological techniques.[5-7] The onset of neuromuscular blocking drugs depends partly on factors such as circulation time and muscle blood flow.[8] The time taken for delivery of the drug from the peripheral intravenous catheter to the central circulation is one of the factor that influences the onset time. The onset time of vecuronium is accelerated if it is administered via pulmonary artery catheter.[9] American Heart Association recommends that during resuscitation, arm should be elevated during drug administration so that gravity aids delivery to the central circulation.[10]

We designed our study to comparatively evaluate the effect of bolus injection of saline with arm elevation on the onset time of different dosages of rocuronium.

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MATERIAL AND METHODS

After approval of the Institutional Review Board, this randomized controlled study was conducted in 64 adult ASA I/II patients of 18-60 years age group of either sex scheduled for elective minor surgery. Patients with history of cardiac, respiratory, hepatic and/or renal failures, neuromuscular disease, BMI > 30 kg/m2, inflammation or infection over injection site, diabetes, pregnant and lactating women, on medication that might interfere with neuromuscular transmission, history of allergy to muscle relaxants were excluded from the study. Patients were randomized into 4 groups - Group R6 (n=16) –Patients who received 0.6 mg/kg rocuronium. Group RS6 (n=16) –Patients who received 0.6 mg/kg rocuronium followed by 20 mL saline push over 5 seconds and hand elevation. Group R9 (n=16) – Patients who received 0.9 mg/kg rocuronium. Group RS9 (n=16) –Patients who received 0.9 mg/kg rocuronium followed by 20 mL saline- push over 5 seconds and hand elevation. Standard anaesthesia protocol was followed.

Monitoring included electrocardiography, capnography, pulse oximetry, non-invasive blood pressure and TOF-Watch. IV fentanyl at 2mcg/kg was given and patients were preoxygenated with 8-9 liters of oxygen by using face mask with Bain's circuit. General anaesthesia was induced using propofol 1.5 –2.5 mg/kg BW. Patient's lungs were then be ventilated using a facemask with 66% nitrous oxide in oxygen and isoflurane 1% W/V. Rocuronium at specified dosages was administered over 2-3 sec into a rapidly running infusion through a T-port in the intravenous (IV) line. In the bolus saline group R6 patients received 0.6 mg/kg rocuronium without saline- push or hand raise, whereas in RS6, 0.6 mg/kg rocuronium followed by 20 mL saline was pushed over 5 seconds into IV line while maintaining the arm elevated vertically. The other group R9 received 0.9 mg/kg rocuronium, and group RS9 was given the same dose of rocuronium followed by 20 ml saline- push over 5 seconds with straight hand elevation. Evoked responses to train-of-four stimulation were measured every 10-s at the adductor pollicis muscle along with single twitch stimulation every 10-s. Assessment with single twitch height was done and any twitch height depression of its control value was noted as the " lag time". The time from end of injection of initial dose of muscle relaxant to the maximal depression of twitch height, along with TOF count of 1 or less was noted as the " onset time". After T1 block reached 95%, clinical correlation was assessed in-relation to tracheal intubating conditions along with Cormack and Lehan grading. After intubation, the lungs were mechanically ventilated to maintain an end-tidal carbon dioxide tension of 35 -40 mmHg. After this TOF monitoring was done every 5 min, along with single twitch height –TOF score more than 3 or more and time to 25% recovery of T1 was noted as the "duration of the drug". At this point, the study was finished.

Primary outcome: Onset time- defined as the time until T1 block reaches 95%. **Secondary outcomes:** Lag time- defined as the time from the start of rocuronium injection until the first decrease in T1, Tracheal intubating conditions, Cormack and Lehane grading of the glottic view, Time to 25% recovery of T1 were noted.

STATISTICAL ANALYSIS

At the end of the study, the quantitative variables were expressed in terms of Mean ± SD and compared using Kruskal Wallis/ ANOVA test and also Wilcoxon/ unpaired t-test/ Bonferroni test. A p-value <0.05 was considered significant.

RESULTS

This study was conducted in 64 ASA I or II adult patients who were randomly allocated into 4 groups: Group R6 (n=16) – in which .6mg/kg rocuronium was given, Group RS6 (n=16) – in which 0.6 mg/kg rocuronium was given followed by 20 ml saline push over 5 sec and hand elevation, Group R9 (n=16) – in which 0.9 mg/kg rocuronium was given and Group RS9 (n=16) – in which 0.9 mg/kg rocuronium was given followed by 20 ml saline push over 5 sec and hand elevation. Demographic profile of all the groups was comparable with each other.

Assessment with single twitch height was done and any twitch height depression of its control value was noted as the " lag time", measured in seconds. Lag time was found to be 38.38 ± 2.87 sec and 31.06 ± 2.84 sec for the Group R6 and RS6 respectively, which was statistically significant with a p value of < 0.001. Similarly, lag time for the Group R9 and RS9 was found to be 32.13 ± 2.78 sec and 24.19 ± 3.23 sec, which was also statistically significant with a p value of < 0.001. Also, on comparing all the 4 Groups together the difference came out to be statistically significant with a p value of < 0.001, as shown in Fig 1. A trend of decreasing lag time with use of saline bolus and with increasing the dose was seen.

The time from end of injection of initial dose of muscle relaxant to the maximal depression of twitch height, along with TOF count of 1 or less was noted as the " onset time", measured in seconds. Onset time was found to be 89.94 ± 3.45 sec and 77.31 ± 3.09 sec for the Group R6 and RS6 respectively, which was statistically significant with a p value of <0.001. Similarly, onset time was found to be 75.19 ± 2.86 sec and 62.63 ± 2.22 sec for the Group R9 and RS9, which was statistically significant with a p value of < 0.001. Also, on comparing all the 4 Groups together, the difference was statistically significant with a p value of <0.001 as shown in Fig 2. A trend of decreasing onset time with use of saline bolus and with increasing the dose was seen.

After T1 block reached 95%, clinical correlation were assessed in-relation to tracheal intubating condition (Krieg et al 1980) which had 3 parameters of laryngoscopy, vocal cords and coughing. Each having points 1 to 4 and total score of 3 to 12. The intubating conditions were rated excellent, good, poor and bad depending on the total score.

Intubating conditions were excellent in 87.50% in Group R6

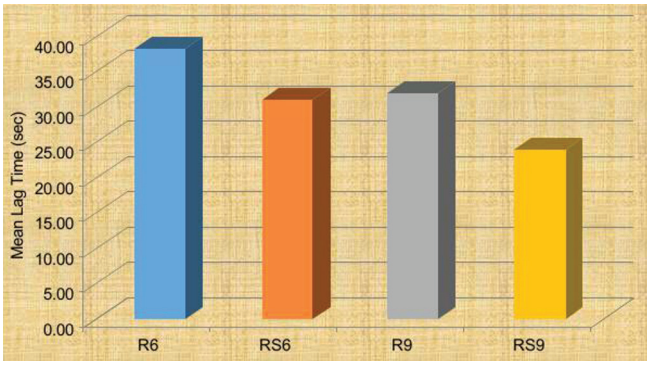

Figure-1: Mean lag time (sec) [p value <0.001]

and RS9 and 93.75% in Group R9 and RS9 respectively, and were good in 12.50% in Group R6 and RS6 and 6.25% in Group R9 and RS9. 100% clinically acceptable intubation conditions were achieved in all the patients and the intubating conditions were not statistically significant between the groups.P value of 0.5 between Group R6 and RS6, and Group R9 and RS9. P value of .272 between Group R6 and R9, and Group RS6 and RS9.

Cormack Lehane grading of the glottis view was assessed at the time of laryngoscopy and was noted. CL Grading between Group R6 and RS6 was comparable with a p value of 0.355, and between Group R9 and RS9 was also comparable with a p value of 0.334, between Group R6 and R9 was also comparable with a p value of 0.223 (Fig 3).

After intubation, TOF monitoring was done every 5 min, along with single twitch height –TOF score more than 3 or more and time to 25% recovery of T1 was noted as the " duration of the drug". Clinical duration of the intubating dose was found to be comparable and statistically not significant between the Group R6 and RS6, and Group R9 and RS9 with a p value of 0.482 and 0.416. However, it was statistically significant between the Group R6 and R9, Group RS6 and RS9 with a p value of < 0.001 as shown in Fig 4.

DISCUSSION

In our study, we evaluated the effect of bolus injection of saline with arm elevation on the onset time and lag time of different dosages of rocuronium. The time from end of injection of initial dose of muscle relaxant to the maximal depression of twitch height, along with TOF count of 1 or less was noted as the " onset time". Onset time was found to be 89.94 ± 3.45 sec and 77.31 ± 3.09 sec for the Group R6 and RS6 respectively. Similarly, onset time was found to be 75.19 ± 2.86 sec and 62.63 ± 2.22 sec for the Group R9 and RS9 respectively, which was found to be statistically significant with a p-value of <0.001. The bolus saline group had a shorter onset time of neuromuscular block at the adductor pollicis muscle of about 12 seconds.

We suggest that bolus saline and arm elevation caused more rapid drug delivery to the central circulation and hence shortened the onset time. These were found to be comparable with previous studies. The circulation time to the target organ and its blood flow partly determine the onset time of the neuromuscular block. For example, onset time is faster when a neuromuscular blocking drug is injected directly into the pulmonary artery rather than into a peripheral vein. Iwasaki et al[9] compared the onset times of vecuronium neuromuscular block administered into either the central circulation or a peripheral vein. The latent onset of neuromuscular block occurred sooner in patients given vecuronium into the central vein than when administered into a vein on the hand also the onset of block was found to be faster when vecuronium was administered into the pulmonary artery than into the right atrium. Emerman et al[11] investigated the effect of peripheral bolus injection on circulation times during cardiac arrest. Measurements of circulation times were made following injection of indocyanine green dye both with and without a bolus of 20 mL saline flush into a peripheral vein of mongrel dogs. They concluded that a bolus injection of 20 mL of saline enhances dye circulation times and peak levels during cardiac arrest in this animal model. Neumar et al[10] in 2010 American Heart Association Guidelines for

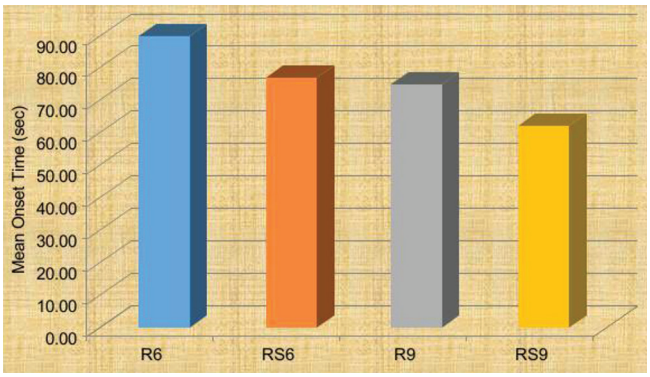

Figure-2: Mean onset time (sec) [p value < 0.001]

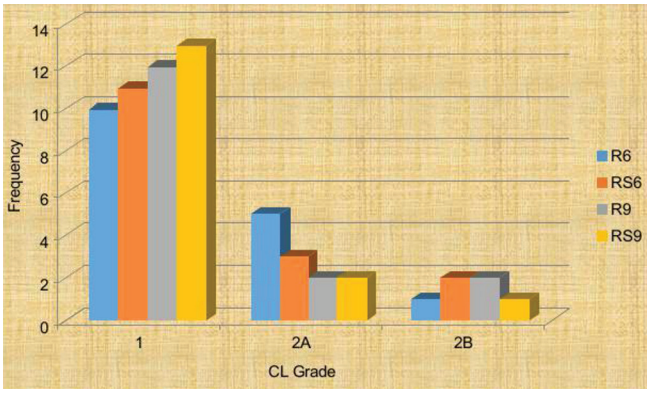

Figure-3: Cormack Lehane Grading.

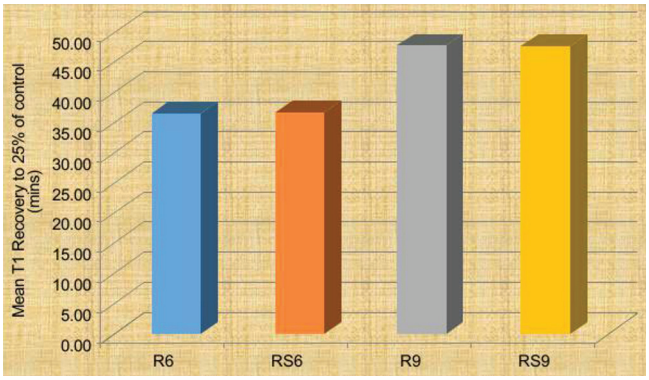

Figure-4: Time to 25% recovery of T1 (min)

Cardiopulmonary Resuscitation and Emergency Cardiovascular Care recommended if a resuscitation drug is administered by a peripheral venous route, it should be administered by bolus injection and followed with a 20-mL bolus of IV fluid to facilitate the drug flow from the extremity into the central circulation. Briefly elevating the extremity during and after drug administration theoretically may also recruit the benefit of gravity to facilitate delivery to the central circulation but has not been systematically studied.

Assessment with single twitch height was done after administering muscle relaxant and any twitch height depression of its control value was noted as the " lag time". Lag time was found to be 38.38 ± 2.87 sec and 31.06 ± 2.84 sec for the Group R6 and RS6, and for the Group R9 and RS9 was found to be 32.13 ± 2.78 sec and 24.19 ± 3.23 sec, respectively. The bolus saline group had lag time shortened by about 7 sec which was found to be statistically significant with a p- value of <0.001. These results were found to be comparable to previous studies.

Fuches -Buder et al[12] compared intubating conditions and time course of rocuronium induced neuromuscular block in children and found the lag time to be 37 ± 12 sec for 0.6 mg/kg and 33 ± 14 sec for 0.9 mg/kg. Wierda et al[13] studied the time course of action and intubating conditions following vecuronium, rocuronium and mivacurium and found the lag time to be 25 ± 8 sec following 0.6 mg/kg of rocuronium. Zhou et al[14] compared onset and offset of action and tracheal intubating conditions after rapacuronium and rocuronium and found the lag time with 0.6 mg/kg of rocuronium to be 44 ± 16 sec. Nitahara et al[15] studied the effect of bolus injection of 20 ml saline with arm elevation on the onset time of vecuronium administered via a peripheral vein and found that bolus injection of saline plus arm elevation resulted in shorter onset time and shorter lag time of neuromuscular block by vecuronium. We concluded the same from our study.

As cardiac output and systemic vascular resistance were not measured in our study, we are unable to draw conclusions on a possible change in cardiac output after bolus injection of 20 ml saline.

In our study, we used TOF-Watch monitor with acceleromyography and evoked responses to train-of-four stimulation measured every 10 sec at the adductor pollicis muscle along with single twitch stimulation every 10 sec. Feldman et al[16] studied the effects of increasing rate of ulnar nerve stimulation from 0.1 Hz to 1 Hz. Onset time was decreased at all doses by about 50% when stimulation was increased from 0.1 Hz to 1 Hz. They also demonstrated the inverse relationship between onset time and dose when using TOF stimulation which was less obvious at 0.1 Hz stimulation. These results show that rocuronium is present in the neuromuscular junction in a concentration that can produce complete neuromuscular block as early as 31 sec after administration, but that the effects are not seen at this time if slow rates of stimulation are used.

These results emphasize the need for care in comparing onset times in studies with different modes of stimulation. An effect which is not obvious at 0.1 Hz maybe partly revealed by TOF stimulation every 20 sec but only fully revealed when higher rates of stimulation are used.

Intubating conditions were excellent in 87.50% in Group R6 and RS9 and 93.75% in Group R9 and RS9 respectively, and were good in 12.50% in Group R6 and RS6 and 6.25% in Group R9 and RS9. 100% clinically acceptable intubation conditions were achieved in all the patients. Cooper et al[17] compared intubating conditions after administration of Org 9426 (rocuronium) 0.6mg/kg at 60 or 90 sec and compared the data with those obtained after suxamethonium 1 mg/kg. Intubating conditions after Org 9426 were found to be clinically acceptable (good or excellent) in 95% of patients at 60 sec and in all patients at 90 sec. Magorian et al[18] compared rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Intubation conditions were good or excellent in 100% of patients with rocuronium in doses of 0.6 and 0.9 mg/kg.

Rocuronium has an intermediate duration of action even upto the doses of three times ED95. In

our study, after intubation, TOF monitoring was done every 5 min, along with single twitch height –TOF score more than 3 or more and time to 25% recovery of T1 was noted as the " duration of the drug". Time to 25% recovery of T1 was found to be 39.79 ± 2.23 and 36.83 ± 2.48 minutes for the Group R6 and RS6, and 47.89 ± 2.21 and 47.74 ± 1.93 minutes for the Group R9 and RS9, respectively. Our results on the duration of action matches with those conducted previously. Foldes et al[19] found the clinical duration of intubation dose of 0.6 mg/kg to be 40 ± 3.2 min. Magorian et al[18] found the clinical duration of action of 0.6 mg/kg to be average 37 minutes and 53 minutes for 0.9 mg/kg of rocuronium. Wierda et al[13] found the clinical duration of action of 0.6 mg/kg rocuronium to be 28 ± 9 min. Kumar et al[20] found the time to recovery of T1 to 25% of 0.6 mg/kg with desfurane to be 36 ±8.3 min and with isoflurane to be 31 ± 8.2 min respectively. Lin et al[21] compared the neuromuscular action of rocuronium with vecuronium and found the clinical durations of action of 0.6 mg/kg rocuronium to be 44.2 ± 13.2 min.

In our study, none of the patients had any adverse reaction on administration of rocuronium which can be transient hypotension, tachycardia, arrhythmia, hiccups, pruritus, nausea, wheeze and allergic/hypersensitivity reactions. Our study had a few limitations. Firstly, the anaesthetist who recorded the time course of the rocuronium induced block was not blinded to the group assignment of the patient and he was monitoring the TOF-Watch. However, this could have been overcome by another researcher administering rocuronium with or without bolus injection of saline and arm elevation. Such blinding could have reduced the potential bias in this study. Secondly, intubation conditions were assessed using scoring given by Krieg et al.[22]

CONCLUSION

From our study we conclude that the bolus saline group had a shorter onset time of neuromuscular block at the adductor pollicis muscle of about 12 sec. the bolus saline group had a shorter lag time of about 7 seconds. · 100% clinically acceptable intubation conditions were achieved in all the patients. · Time to 25% recovery of T1 was found to be comparable between the control and bolus saline groups.

We recommend bolus injection of saline plus arm elevation to shorten the onset time of neuromuscular blocking drugs. This is a simple method that requires no additional equipment or drugs and avoids the side effects associated with other methods like priming principle, timing principle or administering large doses. Hence, a 20-ml syringe of saline is therefore the only piece of equipment necessary to shorten the onset time of rocuronium.

REFERENCES

1. El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. Anesth Analg. 2010;110:1318–25.
2. Kararmaz A, Kaya S, Turhanoglu S, Ozyilmaz MA. Effects of high-dose propofol on succinylcholine-induced fasciculations and myalgia. Acta Anaesthesiol Scand. 2003;47:180– 4.
3. Levine M, Brown DF. Succinylcholine-induced hyperkalemia in a patient with multiple sclerosis. J Emerg Med. 2012;43:279–82.
4. Al-Khafaji AH, Dewhirst WE, Cornell CJ Jr, Quill TJ. Succinylcholine-induced hyperkalemia in a patient with mucositis secondary to chemotherapy. Crit Care Med. 2001;29:1274–6.
5. Foldes FF. Fine tuning the priming principle. Anesthesiology 1985;63:560–1.

6. Koh KF, Chen FG. Rapid tracheal intubation with atracurium:the timing principle. Canadian Journal of Anesthesia. 1994;41:688–93.
7. Han TH, Martyn JA. Onset and effectiveness of rocuronium for rapid onset of paralysis in patients with major burns: priming or large bolus. British Journal of Anaesthesia. 2009;102:55–60.
8. Donati F. Onset of action of relaxants. Can J Anaesth. 1988;35:S52-8.
9. Iwasaki H, Igarashi M, Kawana S, Namiki A. Accelerated onset of vecuronium neuromuscular block with pulmonary arterial administration. Canadian Journal of Anesthesia. 1994;41:1178–80.
10. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, et al. Part 8: Adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122:S729–67.
11. Emerman CL, Pinchak AC, Hancock D, Hagen JF. The effect of bolus injection on circulation times during cardiac arrest. Am J Emerg Med. 1990;8:190-3.
12. Fuchs-Buder T, Tassonyi E. Intubating conditions and time course of rocuronium-induced neuromuscular block in children. Br J Anaesth. 1996;77:335-8.
13. Wierda JM, Hommes FD, Nap HJ, van den Broek L. Time course of action and intubating conditions following vecuronium, rocuronium and mivacurium. Anaesthesia. 1995;50:393-6.
14. Zhou TJ, White PF, Chiu JW, Joshi GP, Dullye KK, Duffy LL, Tongier WK. Onset/offset characteristics and intubating conditions of rapacuronium: a comparison with rocuronium. Br J Anaesth. 2000;85:246-50.
15. Nitahara K, Sugi Y, Shigematsu K, Kusumoto G, Abe S, Higa K. Effect of bolus injection of 20 ml saline with arm elevation on the onset time of vecuronium administered via a peripheral vein: a randomised controlled trial. Anaesthesia. 2013;68:904-7.
16. Feldman SA, Khaw K. The effect of dose and the rate of stimulation on the action of rocuronium. Eur J Anaesthesiol Suppl. 1995;11:15-7.
17. Bevan DR, Fiset P, Balendran P, Law-Min JC, Ratcliffe A, Donati F. Pharmacodynamic behaviour of rocuronium in the elderly. Can J Anaesth. 1993;40:127-32.
18. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Anesthesiology. 1993;79:913-18.
19. Foldes FF, Nagashima H, Nguyen HD, Schiller WS, Mason MM, Ohta Y. The neuromuscular effects of ORG9426 in patients receiving balanced anesthesia. Anesthesiology. 1991;75:191-6.
20. Cooper R, Mirakhur RK, Clarke RS, Boules Z. Comparison of intubating conditions after administration of Org 9246 (rocuronium) and suxamethonium. Br J Anaesth. 1992;69:269-73.
21. Lin PL, Liu CC, Fan SZ, Chao A, Shin SC, Tai YT. Comparison of neuromuscular action of rocuronium, a new steroidal non-depolarizing agent, with vecuronium. Acta Anaesthesiol Sin. 1997;35:127-31.
22. Krieg N, Mazur L, Booij LH, Crul JF. Intubation conditions and reversibility of a new non depolarizing neuromuscular blocking agent, Org-NC45. Acta Anaesthesiol Scand. 1980;24:423-5.

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