

Comparison of Different Doses of Rocuronium for Endotracheal Intubation

Neena Raizada¹, Gaurav², Manoj Kumar Yadav³, R. B. Singh⁴, T. Prabhakar⁵

ABSTRACT

Introduction: Rocuronium is an intermediate acting NDMR with rapid onset of action. The aim of this prospective, randomized, double blind study was to assess and compare the time of onset, duration of action and intubating conditions with three different doses of rocuronium bromide (0.6 mg/kg, 0.9 mg/kg, 1.2 mg/kg).

Material and Methods: The anaesthesia was induced with injection propofol (till apnea appear). After 60 sec, non-depolarizing muscle relaxant rocuronium bromide was administered intravenously. Patients were randomly allocated into three groups according to dose of Rocuronium (0.6 mg/kg, 0.9 mg/kg and 1.2 mg/kg). Jaw relaxation, vocalcord position, motor response to intubation and overall intubating conditions were assessed.

Results: Excellent intubating conditions were seen in 50, 70% and 90% of the patients after 0.6 mg/kg, 0.9mg/kg, 1.2 mg/kg of Rocuronium respectively: P<0.05. Onset of action and duration of action were dose dependant.

Conclusion: Rocuronium bromide in a dose of 1.2 mg/kg IV has rapid onset of action, longer duration and excellent intubating conditions in comparison to 0.9 mg/kg and 0.6 mg/kg dose at 60 seconds. So it can be used for intubation in emergency intubating conditions and where succinylcholine is contraindicated.

Keywords: Anesthesia, Intubation Conditions, Onset of Action, Duration of Action, Rocuronium

INTRODUCTION

The introduction of neuromuscular blocking drugs into clinical practice represents one of the most significant advances in the development of anaesthesiology and has revolutionized the practice of anaesthesia¹.

Although, currently succinylcholine is the only available muscle relaxant for rapid tracheal intubation, But, succinylcholine has a number of undesirable side effects like muscle fasciculation, myalgia, hyperkalaemia bradyarrhythmias increased intra-ocular tension, increased intracranial tension² increased intragastric pressure, anaphylaxis, malignant hyperthermia and masseter spasm. Hence, it is not suitable in situations like neuromuscular disorders, burns, acute head injury, intracranial bleed, open eye injury, spinal cord injury³ cerebrovascular accidents and renal diseases. Therefore need exists for a nondepolarising muscle relaxant with a rapid onset of action.

Rocuronium is good alternative to suxamethonium⁴ as it produce rapid onset of action in both elective and emergency intubation procedures, thus avoiding the various side effects of Suxamethonium.

Hence the present study was designed to compare the different doses of Rocuronium [(2xED₉₅ (0.6 mg/kg); 3xED₉₅ (0.9 mg/kg); 4xED₉₅(1.2 mg/kg)] to assess the intubating condition at 60 seconds and hemodynamic changes during and after intubation and duration of action of Rocuronium.

MATERIAL AND METHODS

This study was done at Rural Institute of Medical Sciences, Saifai, Etawah for a period of one year. After taking institutional ethical committee approval, written informed consent from the patients was taken. Sixty patient's aged 18 to 60 year and ASA grade 1 and 2, MPS 1 and 2 were randomized into three groups

Group A - Includes 20 patients receiving 0.6mg/kg Rocuronium

Group B - Includes 20 patients receiving 0.9mg/kg Rocuronium

Group C - Includes 20 patients receiving 1.2mg/kg Rocuronium

All patients underwent a thorough Pre Anesthetic Check (PAC) which included history of present complaints, past illness, general and systemic examination and routine and specific investigations depending on the age, complaints and examination findings of the patient. Tablet Ranitidine 150 mg and tablet Alprazolam 0.25 mg was given night before surgery and 2 hours prior to the time of surgery. All the patients were kept fasting for at least 6 hour before surgery. Patients were taken on the operation table and multipara monitor was connected. Preoperative heart rate and blood pressure were noted. The other arm on which vein was not taken was fixed to armrest and site of ulnar nerve stimulation at medial side of wrist near proximal crease was chosen. It was shaved and cleansed with spirit. Prior to the induction of anaesthesia, patients were premeditated with inj.midazolam 0.05 mg/kg, inj. glycopyrrolate 0.001 mg/kg, fentanyl 1mcg/kg, inj. ondansetron 0.1 mg/kg. All patients were preoxygenated with 100% oxygen for a period of the three minutes through Bains circuit. Patients was induced with inj Propofol 2mg/kg. At this point the train of four stimuli was done and its basal reading noted Four supramaximal stimuli were given

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prior to the injection of neuromuscular blockade followed by every 30 seconds after the drug has been administered. Each stimulus in the train causes the muscles to contract and fade and response provides the basis of evaluation. The intubation was done with PVC cuffed endotracheal tube of appropriate size at a fixed time that is at 60 seconds in all three groups. The intubation was done by one person only in all the cases and he was aware of the muscle relaxant used and the time interval chosen. After checking for the bilateral air entry, the tube was fixed and attached to close circuit. The patients were maintained on oxygen and nitrous oxide in 33%:66% ratio, Isoflurane 0.5-1% and muscle relaxant Rocuronium on arrival of two twitch response to Train of four stimulation. All the patients were observed for onset time of muscle relaxant under study, its duration of action, Intubating conditions at the time of intubation, hemodynamic variables and side effects/ complications. For onset time and duration of action of drug, peripheral nerve stimulator (MICROSTIM PLUS) was used. All four modes of stimulation i.e. Single twitch, Train of four, Titanic stimulation and Double burst stimulation are present on this. Just after the induction of the patient, the small silver electrodes were applied to the stimulation site and four successive stimuli of Train of four were delivered at 2 Hz i.e. one stimulus at 0.5 seconds. The resultant four twitches of the adductor pollicis muscle were observed visually. The train of four stimulation was then given at every 10 seconds after the injection of muscle relaxant to the loss of all four twitches. The Train of four stimulation was then given every five minutes till the recovery of second twitch response. The time from the injection of muscle relaxant to the recovery of second twitch response was taken as the duration of action. This was followed by supplementation of muscle relaxant with rocuronium bromide 0.15 mg/kg bolus for maintenance. Onset of action was considered as the time taken from completion of injection of the study drug to abolition of three responses to the train of four stimuli (90% block). The intubating conditions were judged clinically at fixed time interval i.e. at 60 seconds in all three groups., after the injection of study drug with the help of (Copenhagen Consensus Conference)^{5,6} rating scale

The vital parameters like pulse rate, systolic and diastolic blood pressure were recorded at fixed time intervals i.e. before intubation, immediately after intubation, then at 15 minutes after intubation with the help of vital sign monitor. All the patients were observed for various side effects of Rocuronium like, bradycardia (values less than 20% of baseline), tachycardia (values more than 20% of baseline), hypotension (values less than 20% of baseline mean arterial pressure), hypertension (values more than 20% of baseline mean arterial pressure), anaphylactic reaction, rash, exanthema, urticaria and bronchospasm. Pre-extubation Train of four stimuli was done and only after appropriate ratio was obtained >0.7, patients were administered reversal with injection Neostigmine 0.05 mg/kg and injection Glycopyrrrolate 0.005mg/kg. Oropharyngeal suction was done and patient was extubated when fully awake and fulfilled the criteria of extubation

STATISTICAL ANALYSIS

The results were expressed a mean±SD and percentages. The Chi-square test was used to compare the categorical variables between the groups. The one way analysis of variance ANOVA with Tukey's post hoc tests was used to compare the continuous variables. The repeated measures of analysis of variance were used to compare the effect of time and time to group interaction on continuous variables. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

The demographic profile of patients was comparable in all the groups. Fig.1 shows the comparison of intubating condition among the groups. Intubating condition was found to be excellent in most of the patients of Group A (50%) and in majority of the patients of Group B (75%) and Group C (90%). However, the difference was nearly significant (p=0.05).(Chi-square test)

Fig 2 shows the comparison of onset and duration of action among the groups. Onset of action was taken as time for disappearance of T2 twitch and was mentioned in seconds, whereas duration was defined as time from onset of action to time to reappearance of T2 twitch. Duration of action was mentioned in minutes. There was significant (p=0.0001) difference in the time to onset of action among the groups. The post hoc analysis revealed that duration of action also differed significantly (p=0.0001) among the groups others

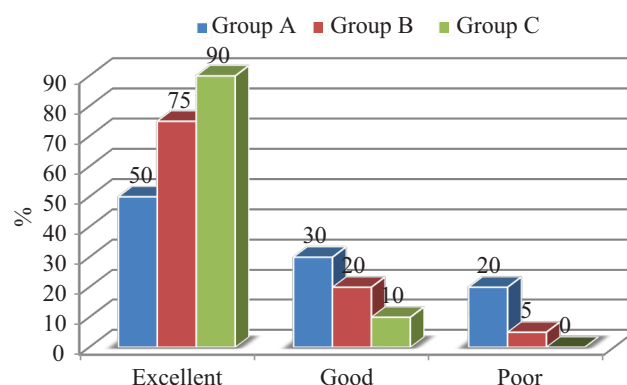


Figure-1: Comparison of intubating condition among the groups

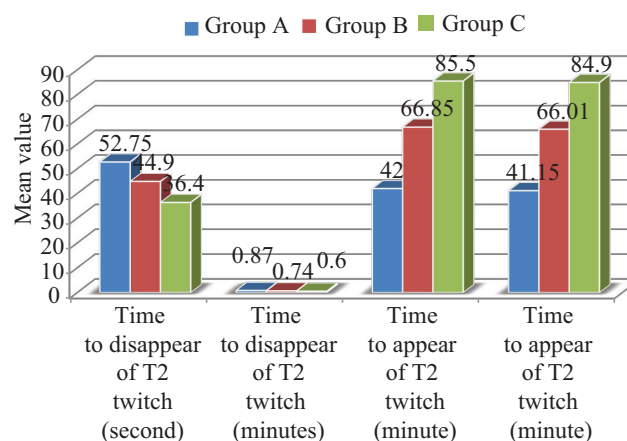


Figure-2: Comparison of onset and duration of action among the groups

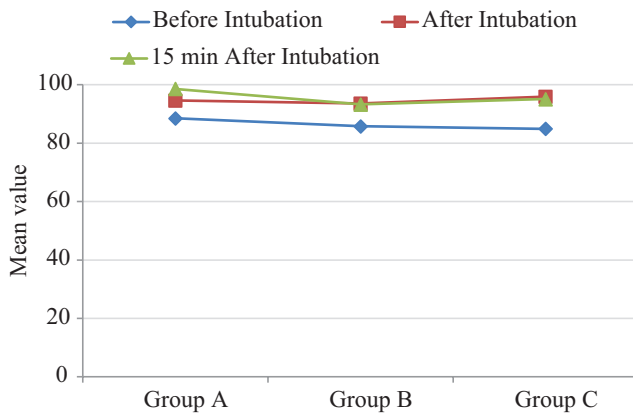


Figure-3: Comparison of pulse rate.

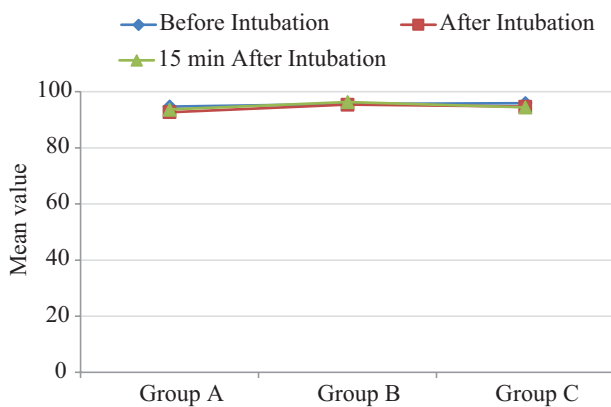


Figure-4: Comparison of MAP

group (ANOVA test used)

Fig.3 shows the comparison of pulse rate (per minute) among the groups across time periods. There was no significant ($p > 0.05$) difference in the pulse rate among the groups at before Intubation, after Intubation and 15 min after Intubation. The repeated measures of analysis of variance revealed that there was significant effect of time in the change in pulse rate in the groups ($F=36.71$, $p=0.0001$) and no significant effect of Time X Group interaction ($F=1.21$, $p=0.30$).

Figure-4 shows the comparison of MAP among the groups across time periods. There was no significant ($p > 0.05$) difference in the MAP among the groups at before Intubation, after Intubation and 15 min after Intubation. The repeated measures of analysis of variance revealed that there was no significant effect of time in the change in pulse rate in the groups ($F=1.06$, $p=0.34$) and no significant effect of Time X Group interaction ($F=0.41$, $p=0.79$). (ANOVA test used)

DISCUSSION

In our study at the dose of 0.6 mg/kg (group A) 50% patient had excellent intubating condition 30% good and 20% poor. At the dose of 0.9 mg/kg (group B) 75% patient had excellent intubating condition 20% good and 5% poor and at dose of 1.2 mg/kg (group C) 90% patient had excellent 10% good intubating condition. We saw here on increasing the dose of Rocuronium bromide excellent intubating condition increase with higher dose (Fig1).

Dr Chanda Khatri et al (2016)⁷ compared three different

doses (0.3, 0.6, and 0.9 mg/kg) rocuronium bromide for endotracheal intubation. In group 0.3 mg/kg intubating conditions at 60 seconds were poor in 65% and intubation was impossible in 35%. In group 0.6 mg/kg intubating conditions were excellent in 60% and satisfactory in 40%. In group 0.9 mg/kg intubating conditions were excellent in 85% and satisfactory in 15%, which is similar to our study. Cooper R et al (1993)⁸ (0.6 mg/kg) found clinically acceptable (good or excellent) in 95% of patients at 60 seconds and in all patients at 90 seconds. These observations are similar to that of our study. There were no significant differences in intubating condition in males and females in all three groups. R Devi et al (2014)⁹ study two different dose of rocuronium bromide 0.6 mg/kg (group A) and 0.9 mg/kg (group B) found in group A 44% Excellent and 56% good intubating condition and in group B 88% excellent and 12% good. which is similar to our result. Vijay Kumar et al (2015)¹⁰ found Intubating conditions clinically were excellent in 16 cases (53%), good in 12 cases (40%), and fair in 2 cases (7%) respectively in (0.6 mg/kg) Group-A. In (0.9 mg/kg) group-B excellent in 29 cases (97%) and good in 1 case (3%). which is similar to our study. Bunburaphong P et al (2001)¹¹ evaluated the intubating conditions at 1 minute after 0.3, 0.6 and 0.9 mg/kg of rocuronium in elective, elderly patients. They obtained excellent or good conditions in 50% at rocuronium 0.3 mg/kg, compared with 95% at 0.6 mg/kg, and 85% at 0.9 mg/kg of rocuronium respectively. But excellent conditions were 5% (0.3 mg/kg), 30% (in 0.6 mg/kg) and 45% (0.9 mg/kg). Their conclusion was rocuronium 0.6 or 0.9 mg/kg is adequate for intubation at 1 minute. We also found that on increasing the dose of rocuronium bromide, number of patients having excellent intubating conditions increased.

Somboonviboon W et al (2000)¹² conducted a randomized controlled trial study to evaluate the intubating conditions at 1 minute after 0.3, 0.6 and 0.9 mg/kg of rocuronium. Excellent or good conditions were observed in 77.8% with rocuronium 0.3 mg/kg compared to 94.4% and 97.2% at 0.6 and 0.9 mg/kg of rocuronium, respectively. Excellent conditions were achieved at 1 minute in 16.7%, 52.8% and 77.8% after 0.3, 0.6 and 0.9 mg/kg of rocuronium respectively.

Clinical relaxation usually requires 75%-95% neuromuscular blockade. In the present study the onset of action was considered as the time taken from completion of injection of the study drug to abolition of three responses to train of four stimulus (90% block).

The mean onset of action at dose 0.6 mg/kg was 52 seconds, at 0.9 mg/kg was 44 seconds and at 1.2 mg/kg was 36 seconds. We find here that with increase in the dose of rocuronium bromide, onset of action decreases. Various studies have reported different onset times of Rocuronium depending on the dose employed.

The present study concurs with the findings of the studies of Alvarez -Gomez JA et al (1994)¹³, who have also reported the onset time similar to the present study. They all used 0.6 mg/kg Rocuronium Bromide for endotracheal intubation found that onset of action within 60 second.

The present study also concurs with the finding of the studies of Naguib M, Cynthia AL et al (2005)¹⁴ who have also reported the onset time similar to the present study at three different doses taken in study. Onset time at dose 0.6 mg/kg was in range 48-156 second and at dose 0.9 mg/kg onset time was in range 48-144 second and at dose of 1.2 mg/kg onset time of action was in range 36-38 second.

De May JC et al(1994)¹⁵ observed that onset time in 0.6 mg/kg group was longer in comparison to that of 0.9 mg/kg group, which is similar to observation of our study.

The faster onset of action of Rocuronium has been attributed to its low potency. This necessitates a higher dose, which ensures the presence of more relaxant molecules in the bloodstream and thus due to a higher concentration gradient, the transport towards the bio phase is faster.

The duration of action of the initial intubating dose in the present study was considered as the time taken from the onset of action to the recovery of the second twitch in the train –of –four and subsequent doses were supplemented at the recovery of the second twitch in train of four.

In the present study duration of action of dose 0.6 mg/kg was 41.15 minute and at dose 0.9 mg/kg was 66.01 minute and at dose of 1.2 mg/kg was 84.90 minute

Our findings also correlate with the findings of Foldes FF et al (1991)¹⁶ who used 0.6mg/kg of rocuronium and found duration of action 40 minutes.

.In the study by Fuch-Buder T et al (1996)¹⁷ duration of action was 21±4 min. in 0.6 mg/kg group and 34±11 min. in 0.9 mg/kg group. As this study was carried out in children having shorter duration of action than of our study.

E Abouleish et al(1996)¹⁸ used Rocuronium (org 9426) for caesarean section they used Rocuronium bromide at dose 0.6 mg/kg and found that duration of action 32.7 minute which is similar to present study at 0.6 mg/kg dose.

In the study by P Sudha et al(2015)¹⁹ duration of action of dose 0.6 mg/kg was 37.9±6.1 minutes and that of 0.9 mg/kg was 49.3±8.7 minutes which is similar to our study at dose 0.6 mg/kg and 0.9 mg/kg.

An ideal neuromuscular blocking agent should produce cardiovascular stability. The findings of the present study correlates with the study by Hudson ME et al (1998)²⁰ with Rocuronium in a dose of 0.6 mg/kg wherein they concluded that no changes in heart rate occurred with the given dose of Rocuronium.

This observation also correlates with the study by Nitschman P et al (1994).²¹Rocuronium in a dose of 0.9 mg/kg produced no change in heart rate.Schramm et al (1996)²² studied the heart rate changes with Rocuronium in dose 0.6 mg/kg and found no significant change in heart rate.

In group-A mean arterial pressure before intubation was 94.75 and after 92.70 and 15 minute after intubation is 93.70.

In Group B mean arterial pressure before 95.70 and after intubation 95.40 and after 15 minute intubation is 96.35 and in Group C mean arterial pressure before intubation 95.95 and after intubation 94.40 and 15 minute after intubation 94.45 which was comparable to the pre induction level and there was clinically no significant change in p value.

There was clinically no significant difference in the blood pressure in three groups throughout the study period.This correlates with the study of Levy JH et al (1994)²³ who determined the haemodynamic and histamine release of Rocuronium when administered in increased doses under N₂O/O₂-sufentanil anaesthesia and found no difference in blood pressure in doses up to 1.2mg/kg which is similar to our result

Khuenl-Brady KS et al²⁴ also stated that rocuronium did not show changes in mean arterial pressure of clinical significance.

CONCLUSION

Rocuronium bromide in a dose of 1.2 mg/kg IV has rapid onset of action and excellent intubating conditions as compared to 0.9 mg/kg and 0.6mg/kg dose at 60 seconds so it can be used for emergency intubation and where succinylcholine is contraindicated.

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REFERENCES

1. LeVasseur R, Desai SP. Ebenezer Hopkins Frost (1824-1866): William T.G. Morton's first identified patient and why he was invited to the Ether demonstration of october 16, 1846. *Anesthesiology* 2012; 117:238-42
2. Stoelting RK, Peterson C. Heart slowing and junctional rhythms following intravenous succinylcholine with and without intramuscular atropine preanaesthetic medication. *Anesth Analog* 1975; 54:705-9.
3. Stevenson PH, Birch AA. Succinylcholine induced hyperkalemia in patient with a closed head injury. *Anesthesiology* 1979; 51:89-90.
4. Savarese JJ, Caldwell JE, Lien CA, Miller RD. Pharmacology of muscle relaxants and their antagonists. In: Miller, (Editor), 6th ed. Philadelphia Churchill Livingstone; 2004; 1:490
5. Thwaites AJ, Edmonds S, Tomilinson A, Kendell JB and Smith I: Double blind comparison of sevoflurane vs propofol and succinylcholine for tracheal intubation in Children; *British J anaesthesia* 1999;83: 410-14.
6. Agoston S: Onset time and evaluation of intubating conditions, rocuronium in perspective; *Eur J Anaesth [suppl]* 1995 11:31-7.
7. Dr Chanda Khatri,Dr Kishore Khatri,dr. Vijaylaxmi jain, Comparison of Onset, Duration of Action and Intubating Conditions of Three Dosages 0.3 mg/kg,0.6 mg/kg,0.9 mg/kg of Rocuronium Bromide; *international Journal of Science and Research*. 2016;5:729-733.
8. Cooper RA, Mirakur RK, Maddineni VR, Neuromuscular effects of rocuronium bromide (Org 9426) during fentanyl and halothane anaesthesia. *Anaesthesia*, 1993; 48: 103-105.
9. Usha Devi R, Srinivas V. Y, B. T. Shivaramu, Vasundhara Vadaguru Mallikarjuna, Bangalore G. Sanjay, Divya Rani. Intubating Conditions with two different Doses of Rocuronium Bromide for Caesarean Section: A comparative clinical study. *Journal of Evolution of Medical and Dental Sciences* 2014;3: 12947-12956

10. Vijay Kumar M, Heggeri, Aparna S, Harbishettar, Ajit Kumar Deka, Tejwant Rajkhowa. Intubating conditions of two different doses of rocuronium at 60 seconds: by clinical Assessment; and with T.O.F Response of Adductor Pollicis Muscle; journal of clinical and diagnostic Research. 2015;9:24-28.
11. Bunburaphong P, Werawatganon T, Panyarachun K, Vimala J, Chainongbua J, Tungamornsatit J. Intubating conditions after three different doses of rocuronium in the elderly. *J Med Assoc Thai.* 2001;84:S244-50.
12. Somboonviboon W, Bunburaphong P, Whanna O, Juajarungjai S, Sukvivat K. Intubating conditions after three different doses of rocuronium. *Med Assoc Thai.* 2000; 83:850-55.
13. Alvarez-Gomez JA, Fabregat J, Estelles ME, Brugger AJ, Aguilar R, Perez F. Speed of intubation using a new neuromuscular blocker: Rocuronium bromide (ORG 9426). *Rev Esp Anesthesiol Reanim* 1994; 41: 3-6.
14. Naguib M, Cynthia AL. Pharmacology of muscle relaxants and their antagonists, Chapter 13 in Miller RD (ed) *Anesthesia*, 6th edition, Elsevier-Churchill Livingstone, 2005; 494-495 pp.
15. De Mey JC, Debrock M, Rolly G. Evaluation of the onset and intubation conditions of rocuronium bromide. *Eur J Anaesthesiol Suppl.* 1994; 9: 37-40.
16. Foldes FF, Nagashima H, Nguyen HD, Schiller WS, Mason MM, Ohta Yoshio. The neuromuscular effects of ORG 9426 in patients receiving balanced anesthesia. *Anesthesiology* 1991; 75: 191-196.
17. Fuchs- Buder T, Tassonvi E. Intubating conditions and time course of rocuronium-induced neuromuscular block in children. *Br. J. Anaesth.* 1996;77:335-8.
18. Abouleish E, Abboud T, Lechevalier T, Zhu, J, Chalian A, Alford K. Rocuronium (Org 9426) for caesarean section. *Br. J. Anaesth.* 1994; 73: 336-341.
19. Sudha P, Manju B, Comparison of the effect of two different doses of Rocuronium on intubating condition. *International surgery journal.* 2016;3:582-585.
20. Hudson ME, Rothfield KP, Tullock WC, Firestone LL. Haemodynamic effects of vocuronium bromide in cardiac surgical patients. *Can J Anaesth* 1998;45:139-143.
21. Nitschmann P, Oberkogler W, Hertsig M, Schwarz S. Comparison of haemodynamic effects of Rocuronium bromide with those of Vecuronium in patients undergoing CABG surgery. *Eur J Anaesthesiol* 1994; 9:113-115.
22. Schramm WM, Strasser K, Bartunek A, Gilly H, Spiss CK. Effects of Rocuronium and Vecuronium on intracranial pressure, mean arterial pressure and heart rate in neurosurgical patients. *Br J Anaesth* 1996;77: 607-611.
23. Levy JH, Davis G, Duggan J, Szlam F. Determination of the haemodynamic and histamine release of Rocuronium (ORG 9426) when administered in increased doses under N2O/O2 – Sufentanil anesthesia. *Anesth Analg* 1994; 78: 318-321.
24. Khuenl-Brady KS, Puhlinger F, Koller J, Mitterschiffthaler F. Evaluation of the time course of action of maintenance doses of rocuronium (Org 9426) under halothane anaesthesia. *Acta Anaesthesiol Scand.* 1993; 37: 137-139.

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