DOI: https://doi.org/10.3329/medtoday.v38i1.87849

ORIGINAL ARTICLE OPEN ACCESS

Effects of Different Doses of Rocuronium for Facilitation of Endotracheal Intubation among the Patients Undergoing General Anaesthesia

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Abstract

Introduction: *Endotracheal intubation is an integral part of airway management duringgeneral anesthesia. With the advancement of anesthesia, there have always been a search of an ideal muscle relaxants which can provide ideal intubating conditions in short duration with minimal side effects. Rocuronium is an intermediate acting Non-depolarising Muscle Relaxant (NDMR) with rapid onset of action. The aim of this prospective observational study was to assess and compare the time of onset of action and intubating conditions with three different doses of rocuronium bromide (0.6 mg/kg, 0.75 mg/kg, 0.9 mg/kg).* ***Material and methods:*** *This study was conducted to compare and evaluate effect of three different doses of Rocuronium bromide for endotracheal intubation in ASA I & II patients aged 18-60 years of either sex. Patients were randomly allocated into three groups according to dose of Rocuronium (Group A - 0.6 mg/kg of Rocuronium bromide, Group B - 0.75 mg/kg of Rocuronium bromide & Group C – 0.90 mg/kg of Rocuronium bromide). Jaw relaxation, vocal cord position, motor response to intubation and overall intubating conditions were assessed.* ***Results:*** *Laryngoscopy and endotracheal intubation in each group were assessed by* ***Cooper*** *[1] criteria. Good to excellent intubating conditions were seen in 51%, 100% and 100% of the patients after 0.6 mg/kg, 0.75mg/kg, 0.9 mg/ kg of Rocuronium respectively. Onset of action were dose dependant.* ***Conclusion:*** *Lower, safe and sufficient dose of rocuronium bromide 0.75 mg/kg IV can produce good to excellent intubating conditions with rapid onset of action in contrast of a dose of 0.60 mg/kg IV and 0.90 mg/kg IV.*

Keyword: *Rocuronium, Intubating condition.*

Number of Tables: 07; Number of References: 15; Number of Correspondences: 05.

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Introduction:

Rocuronium is a non-depolarizing neuromuscular blocker widely used to induce muscle relaxation during genera[l] anaesthesia for both elective and emergency surgeries. Among the non- depolarizing neuromuscular blockers available in the market, rocuronium is popular for its rapid onset of action and reversibility by

Received: 16 August 2025 *Accepted revised version:* 19 November 2025

sugammadex[2]. This steroid-based muscle relaxant has become a safer drug of choice in clinical settings for endotracheal intubation during general anesthesia. Endotracheal intubation is a critical component of general anesthesia to protect the airway from possible regurgitation and maintenance of adequate oxygenation. Endotracheal intubation requires relaxation of the laryngeal muscles with complete vocal cord paralysis during emergency surgery where rocuronium at a dose of 1.2 mg/kg was found non-inferior to facilitate first attempt intubation in comparison to suxamethonium 1 mg/kg intravenously[3].The time between drug administration and achieving sufficient muscle relaxation for intubation should be minimized to reduce the risk of silent regurgitation and aspiration. Parikh[4] explained the physiochemical properties of rocuronium where they narrated rocuronium is 5-7 times less potently bind with choline receptor than vacuronium thus easily can be reversed by sugammadex in emergent situation but its onset of action is fast enough which is comparable to suxamethonium even at as low dose as 0.6 mg/kg. An ideal neuromuscular blocking agent should have a rapid onset, short duration, induce profound relaxation, and be free from histamine release, anaphylaxis, and hemodynamic instability. Optimal intubating conditions by rocuronium is dose dependent. Achievement of this optimal level is important to prevent the potential risk of airway trauma. Rocuronium acts as an ideal muscle relaxant for adult patients undergoing general anaesthesia at a dose of 0.9 mg/kg where increased dose (1.2 mg/kg) poses risk of haemodynamic depression and reduced dose (0.6 mg/kg) poses risk of inadequate relaxation. Although risk of anaphylaxis from rocuronium due to its histamine releasing property, should always be keep in mind as histamine release is agent specific phenomenon rather than dose dependence[5]. Poor intubating conditions, such as resistance to laryngoscope insertion or patient reaction to intubation, must be avoided to ensure patient safety. A failed intubation, which may occur for several reasons including inadequate muscle relaxation during the RSI procedure, can lead to silent regurgitation and may result in severe injury or fatality[6]. In recent years, rocuronium has emerged as a preferred alternative for rapid sequence induction (RSI) at doses ranging from 0.6 to 1.2 mg/kg. Tran[7] discussed detail in their cochraine meta-analysis about the key advantages of rocuronium which lies in its fast onset, intermediate duration of action, and minimal hemodynamic effects, at several doses with differet induction agents. 1 mg/kg rocuronium when given with alfentanil showed no difference in onset time of action between suxamethonium and rocuronium, rather it provides a longer duration of action lasting 37 to 72 minutes, and has the benefit of being reversible with an antidote. Use of etomidate as induction agent and rocuronium as muscle relaxant was found promising by Tran[7] in emergent situation where maintenance of haemodynamic stability was challenging and suxamethonium use was hazardous due to potential risks of hyperkalemia and raised intra-cavitary pressure. The only major contraindication of use of rocuronium routinely is a potential chance of allergy to the drug though its allergent property is less if compared with atracurium. The prevalnce of allergy to rocuronium was more in paediatric population as the regression model showed the odds ratio 9.17 (0.59-141.00, 95% CI) while used as sole muscle relaxant with total intravenous anaesthesia[8]. Paediatric people generally need more dose of rocuronium for facilitation of intubation. 0.6 mg.kg-1 rocuronium was sufficient for tracheal intubation in 60 seconds in adult and elderly patients. It was, however, insufficient for clinically acceptable tracheal intubation conditions in 60 seconds in 100% of children[9]. This increased dose may explain the more prevalence of allergic phenomenon in children than adult or elderly. Thus a suspicion remain about the agent specific and dose independent nature of rocuronium for allergic menifestations. In another study, Shukla[10] explored the efficacy of rocuronium in facilitating endotracheal intubation when sufficient time was allowed for the muscle relaxant to take effect. They concluded that if a 90-second interval was provided between the induction of general anesthesia and intubation—following a proper pre-oxygenation protocol—administering 0.6 mg/kg of rocuronium was sufficient to achieve optimal intubating conditions. This dosage provided adequate jaw relaxation, complete vocal cord paralysis, and effective suppression of the cough reflex, all of which are critical for a smooth and successful endotracheal intubation. Their findings highlight that, with appropriate timing, a relatively low dose of rocuronium can provide excellent intubating conditions, reducing the need for higher doses that may increase the risk of adverse effects. Rocuronium has been recognized as a valuable neuromuscular blocking agent since its introduction in 1994. It possesses many of the qualities expected of an ideal short-acting muscle relaxant for intubation. Administered at doses as low as 0.6–0.9 mg/kg, it works effectively when combined with induction agents such as propofol or thiopental in adult patients undergoing general anesthesia. Rocuronium offers a fast onset of action, typically within 60 seconds, while presenting a lower risk of adverse events in adult patients, such as hypersensitivity. These attributes have been confirmed in various studies[11].

Materials and Methods:

This Prospective observational study was conducted in Department of Anaesthesia Pain Palliative and Intensive Care, Dhaka Medical College Hospital, Dhaka from September 2021 to August 2024 (3 years). The adult patients who are selected to elective surgery under General Anaesthesia were selected after fulfilling inclusion and exclusion criteria. Inclusion Criteria were patients give informed consent for this study, patients aged between 18 and 60 years, ASA physical status I or II, Mallampati class I or II, patients scheduled for elective surgery under General Anaesthesia requiring endotracheal intubation. Exclusion Criteria were presence of neuromuscular disease, hepatic and renal impairment, reactive lung disease, pregnancy, upper limb surgery, history of allergy to study drugs.

Results:

Observations and results after data processing and analysis of this prospective observational study is presented in this section. This study included 99 eligible patients in DMCH scheduled to undergo elective surgeries under general anaesthesia with endotracheal intubation. Based on inclusion and exclusion criteria, patients were enrolled and divided into three groups after randomization. Group A (n=33) received 0.6 mg/kg rocuronium i.v. after induction, Group B (n=33) received 0.75 mg/kg rocuronium i.v. after induction, Group C (n=33) received 0.9 mg/kg rocuronium i.v. after induction. Data were collected on a pre- formed sheet. Analysis was done using SPSS v24 and MS Excel, and results were presented in tables, bar diagrams, and graphs. Categorical data (e.g., sex, ASA class) were shown as frequency and percentage using $\chi 2$

analysis, while numerical data (e.g., MAP, age, BMI) were presented as mean ± SD using ANOVA test. Data were analyzed with a 95% confidence interval and a 5% margin of error, with $p < 0.05$ considered statistically significant. Hypothesis testing was done at 80% power.

Table I: Demographic characteristics of the studied patients

Characteristics	Group A n=33	Group B n=33	Group C n=33	P value
Age in years	32.48±10.97	37.76±8.59	34.36±7.91	
Sex				
Male	17 (51.5)*	16(48.5)	16(48.5)	0.96
Female	16(48.5)	17(51.5)	17(51.5)	
Weight in kg	54.24±7.53	54.42±5.09	56.58±5.04	0.22

*percentages in paranthesis

Table I showing study participants are statistically equivalent in terms of demographic (Age, Sex, weight) charecteristics ($p > 0.05$). $\chi 2$ test was done to compare categorical variables (Sex) and ANOVA test was done to compare the numerical variables (age, weight).

Table II: Study patients categorized by time for onset and duration of action of different doses of rocuronium

Variables Onset of action	Group A (n=33)	Group B (n=33)	Group C (n=33)	Level of significane (p value) between groupA and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
(seconds)	99.42±7.54	70.00±2.35	60.42±1.77	0.00*	0.00*	0.00*
Duration of action (minutes)	24.67±1.19	30.33±1.16	41.09±1.04	0.00*	0.00*	0.00*

* Highly significant

Table II showing there are significant differences in time for onset of action of different doses of rocuronium. Group A (0.6 mg/kg) needed highest time (99.42±7.54) for onset of neuromuscular blockade

Table III: Study patients categorized by intubating conditions

Variables	Group A (n=33)	Group B (n=33)	Group C (n=33)	Level of significane (p value) between group A and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
Intubation score	5.27±2.02	8.24±1.25	8.24±1.20	0.00**	0.00**	0.769
TOF twitches elicited after 60 seconds of rocuronium injection	1.39±0.49	0.21±0.42	0.00±0.00	0.002*	0.00**	0.00**

* Significant

** Highly significant

Table III showing intubation score was significantly lower ($p < 0.05$) and TOF twitches elicited after 60 seconds of rocuronium injection were significantly higher ($p < 0.05$) among the participants of group A in comparison to group B and group C. ANOVA was done to test the significance of difference of variables to assess intubating condition.

Table IV: Mean arterial pressure (MAP) Profile of Studied Patients

Timepoint	MAP (mm of Hg)			Level of significane (p value) between group A and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
	Group A (n=33)	Group B (n=33)	Group C (n=33)			
Baseline	89.00±5.14	89.73±5.61	89.88±6.57	0.920	0.084	0.139
After induction	85.24±5.29	86.88±5.46	86.21±5.05	0.726	0.498	0.783
After intubation	97.00±5.78	96.94±6.91	95.91±7.40	0.593	0.287	0.360
1 min after intubation	93.61±5.88	96.48±6.97	94.85±6.61	0.453	0.405	0.986
3 min after intubation	89.15±6.07	92.27±6.05	88.42±6.71	0.624	0.028*	0.421
5 min after intubation	86.33±5.21	88.94±5.84	85.97±6.58	0.502	0.207	0.535

* Significant

Table IV shows that the distribution of mean arterial pressure across various timepoints was similar ($p > 0.05$), with the exception of a significant difference observed between Group A and Group B ($p<0.05$) three minutes after intubation. ANOVA was used to assess the significance of mean arterial pressure differences at each timepoint.

Table V: Heart Rate (HR) Profile of Studied Patients

Timepoint	HR (beats per minute)			Level of significane (p value) between group A and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
	Group A (n=33)	Group B (n=33)	Group C (n=33)			
Baseline	89.58±11.21	88.48±10.32	90.30±8.12	0.216	0.114	0.347
After induction	93.58±11.22	92.48±10.38	94.33±8.18	0.220	0.076	0.364
After intubation	107.52±11.27	96.82±10.43	99.42±8.25	0.314	0.015*	0.201
1 min after intubation	109.64±11.11	94.09±9.53	95.39±8.35	0.203	0.021*	0.273
3 min after intubation	107.21±11.17	90.97±9.67	90.48±8.21	0.303	0.041*	0.300
5 min after intubation	98.30±11.03	87.15±10.24	85.27±7.72	0.419	0.024*	0.194

* Significant

Table V shows that heart rates several minutes after intubation were significantly lower ($p < 0.05$) in Group C compared to Group A. ANOVA was used to evaluate the significance of heart rate differences at each timepoint.

Table VI: SpO2 Profile of Studied Patients

Timepoint	SpO2 (%)			Level of significane (p value) between group A and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
	Group A (n=33)	Group (n=33) B	Group C (n=33)			
Baseline	98.15±1.17	97.61±1.09	97.67±1.11	0.515	0.603	0.898
After induction	99.36±1.03	99.61±0.86	99.48±091	0.067	0.258	0.424
After intubation	99.52±0.67	99.67±0.54	99.70±0.53	0.080	0.044	0.724
1 min after intubation	99.64±0.78	99.64±0.78	99.73±0.67	1.000	0.278	0.278
3 min after intubation	99.00±1.46	98.42±1.37	98.48±1.18	0.783	0.444	0.631
5 min after intubation	97.82±1.16	97.91±1.26	97.85±1.06	0.611	0.567	0.286

Table VI shows that the distribution of SpO2 among the

participants of all groups across various timepoints were similar (p > 0.05). ANOVA was used to assess the significance of SpO2 differences at each time point.

Table VII: Perioperative adverse events among the study participants

Adverse effects	Group A (n=33)	Group B (n=33)	Group C (n=33)	Level of significane (p value) between groupA and group B	Level of significane (p value) between group A and group C	Level of significane (p value) between group B and group C
Tachycardia	22 (66.7)**	10 (30.3)	12 (36.4)	0.006*	0.026*	0.794
Hypertension	5 (15.2)	0 (0.0)	0 (0.0)	0.053	0.053	0.500
Bradycardia	0 (0.0)	0 (0.0)	2 (6.1)	0.500	0.492	0.492

* Significant.

** Percentage in parenthesis

Table VII demonstrates that tachycardia was significantly more prevalent (p < 0.05) in participants of Group A compared to Group B and Group C. No significant differences in other adverse effects were observed among the groups.

Discussion:

This study recruited 99 patients divided into three groups of 33 participants in each to evaluate intubating properties of different doses of rocuronium. In this study, three different doses of rocuronium (0.6mg/kg, 0.75mg/kg and 0.9mg/kg) were used for muscle relaxation before endotracheal intubation and various parameters like time for onset of action of rocuronium, intubating conditions (jaw relaxation, vocal cord position, response to intubation), TOF response and vital parameters (HR, SBP, DBP, MAP, SpO2) were compared. In terms of demographic profile (age, sex, weight) all participants of these groups were equally distributed. The onset of action of neuromuscular blockade were studied clinically by observation of cessation of spontaneous breathing and electrically by peripheral nerve stimulator (STIMPOD® TOF watch). Intubation score was derived from Cooper[1] and his colleagues' research work. Intubation score was found fair to good among the participants of group A and good to excellent among the participants of group B and group C. No difference was observed in terms of intubation score among the participants of group B and group C. Train-of-four (TOF) stimulation of ulnar nerve after 60 seconds of rocuronium injection elicits 1.39 ± 0.49 twitches which signifies 80% to 90% neuromuscular receptor blockade occurred within one minute after 0.6 mg/kg rocuronium injection. On the other hand, 0.75 mg/kg and 0.9 mg/kg injection of rocuronium caused near about 100% receptor blockade within one minute. There was significant difference in onset time among the three groups. Group C (0.9 mg/kg) showing fastest onset 60.42±1.76 seconds compared to Group B (0.75 mg/kg) (70.00±2.34sec) and Group A (0.6 mg/kg)(99.42±7.54 sec). The duration of action was also prolonged in group C (41.09±1.04) than group B (30.33±1.16) and group C (24.67±1.19). The intergroup differences in terms of onset and duration of action of rocuronium was highly significant (p=0.00). Tran[7] reported an onset time 89.0 ± 33.0 sec. after 0.6mg/kg and 75.0 ± 28.0 sec after 0.9mg/kg rocuronium. Their results aligned with the findings of this study. On the other hand, Heggeri[12] reported an onset time of 3.0 minutes after 0.6mg/kg rocuronium. However, Weirda[13] reported an onset time of 172.0 sec after rocuronium 0.6mg/kg. The research conducted by Cheng[14] indicated that a dose of 0.9 mg/kg of rocuronium produces intubating conditions that are similar to those obtained with suxamethonium at 1.5 mg/kg, particularly when used alongside alfentanyl and thiopentone. Conversely, a lower dose of 0.6 mg/kg of rocuronium was deemed inadequate. The current study supports their conclusions. Another study found that rocuronium 0.6 mg/kg with thiopentone 6mg/kg provides good to excellent intubating conditions at 80 seconds and found that rocuronium is safe for mother and foetus[15]. Heart rate was significantly higher (p <0.05) immediately after intubation among the group A (107.52±11.27) patients in comparison to group B (96.82±10.43) and group C (99.42±8.25) However, difference between group B and group C were not significant (p > 0.05) in any time point. Systolic blood pressure was higher among the patients of group A after intubation due to less obtunded laryngeal reflex. In contrast, SBP among patients of group B and group C were stable. Mean arterial pressure and SpO2 was stable among the participants of all groups and difference of these variables were not significant. Few adverse events occurred during the study. In Group C (0.9 mg/kg), 2 patients (6%) developed bradycardia one and three minutes after intubation, both of whom were treated with 0.6 mg of intravenous atropine. In Group A, 5 patients (15%) developed hypertension, defined as an increase in SBP of more than 20% from baseline, immediately after intubation, and were treated with intermittent intravenous boluses of fentanyl (0.5 μg/kg). Tachycardia occurred in 13 patients (39%) in Group C, 10 patients (30%) in Group B, and 23 patients (70%) in Group C, immediately, one minute, and three minutes after intubation, all treated with 5–10 mg of intravenous labetalol. No allergic reactions or critical incidents were reported during the study.

Conclusion:

Rocuronium 0.6 mg/kg dose may not be sufficient to achieve ideal intubating conditions within 60 seconds. However, when comparing Groups B and C, there was no significant difference in intubating parameters, indicating that a dose of 0.75 mg/kg is both safe and effective for achieving optimal intubating conditions. Therefore, 0.75 mg/kg rocuronium appears to be the lower, safer dose that can reliably provide the necessary muscle relaxation for intubation without compromising cardiovascular stability or TOF response.

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