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Comparison of Rocuronium in Two Different Doses with Succinyl Choline – Onset Time, Duration of Action and Intubating Conditions

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Abstract

Background: *Rocuronium Bromide is an ewer, low potency non-depolarising neuromuscular blocking agent. Patients often require an endotracheal intubation technique during emergencies or electively to protect against aspiration, increased intracranial pressure, or to facilitate intubation. Traditionally succinylcholine has been the most commonly used muscle relaxant for this purpose because of its fast onset and short duration; unfortunately, it can have serious side effects. Rocuronium has been suggested as an alternative to succinylcholine for intubation The aim of this study was to compare tracheal intubating conditions, onset time, duration of action of rocuronium 0.9 mg/kg, 0.6 mg/kg and succinylcholine 1.5 mg/kg during induction of anaesthesia.*

Methods and findings: *This prospective, randomized, double – blind study was carried out in seventy-five ASA grade (I – II) adults, aged 18-65 years of either sex, who were scheduled to undergo various surgeries under general anaesthesia. Patients were divided into three groups. Group I received succinyl choline 1.5 mg/kg intravenously (n=25), Group II received rocuronium0.6mg/kg intravenously (n=25), Group III received rocuronium 0.9 mg/kg intravenously (n=25) after induction with propofol. Intubation was attempted on fading of all four twitches of adductor pollicis muscle, evoked after train of four stimulation of ulnar nerve using a peripheral nerve stimulator at every 15 seconds after injection of muscle relaxant. Onset time, duration of action and intubating conditions were assessed.*

Results: *Excellent intubating conditions were obtained in 84 %, 56 % and84 % of the patients after administration of succinyl choline 1.5 mg/kg, rocuronium 0.6 mg/kg and rocuronium 0.9 mg/kg respectively; P 0.032. Acceptable intubating conditions (excellent and good grade combined) were obtained in all patients. Onset time and duration of action were significantly more in rocuronium group 0.9 mg/kg (111.00±19.3 sec and 45.60±6.87 min respectively) as compared to rocuronium 0.6 mg/kg (195.72±34.62 sec and 27.04±6.79 min respectively) while succinyl choline group (64.92±10.91 sec and 8.64±2.23 min respectively).*

Conclusion: *Rocuronium has anintermediate duration of action. Onsettime of rocuronium is reduced with increase in dose from 0.6 mg/kg to 0.9 mg/kg. Rocuronium provides clinically acceptable intubating conditions comparable to that of succinyl choline.*

Keywords: *Anaesthesia, intubating conditions, rapid sequence induction, succinylcholine, rocuronium.*

Introduction

In the present day practice, muscle relaxation is used for two purposes 1) To facilitate endotracheal intubation 2) To provide surgical relaxation. The ideal neuromuscular blocking agent for intubation should have a fast onset, brief duration of action, provide profound relaxation and be free from hemodynamic changes. Since then, Succinylcholine has been the 'gold standard' neuromuscular relaxant for tracheal intubation with its rapid onset and short duration of action. . However, some people cannot use this medication as it can cause serious salt imbalances or reactions, so an equally effective medication without these side effects would be advantageous. One possible alternative medication is rocuronium, a muscle relaxant with fewer side effects but longer duration of action.

The intermediate acting amino steroid, rocuro-nium became available as a non-depolarising muscle relaxant in l995. Rocuronium offers the fastest onset of action, taking about 60 - 90 seconds for complete block to develop with doses of 0.6 - 0.9 mg/kg. It has been shown to have rapid onset of action believed to be primarily due to its low potency and has an intermediate duration of action.

The present study was designed to compare the intubating conditions as a primary outcome and onset time and duration of action as a secondary outcome after using rocuronium in two different doses i.e.; 0.6mg/kg ($2xED_{95}$) and 0.9 mg/kg ($3xED_{95}$) and a standard dose of succinylcholine (1.5 mg /kg) for intubation in adults. Doses equivalent to twice the ED_{95} are generally considered to be the optimal dose of non-depolarizing relaxants for intubation [1, 4]

Materials and Methods

After approval by local ethics committee and written informed consent of the patients; a prospective randomized, double blind study was conducted in seventy five patients of either sex, aged between 16-65yearsof ASA grade I-II and Mallampati grade 1-2 undergoing elective surgery requiring general anaesthesia and tracheal intubation. Patients were excluded from study if they had 1) patients with neuromuscular disorder 2) Anticipated difficult intubation eg; obesity, increased thyromental distance, mallampatti grade 3 or 4, pregnancy etc. 3) Patients receiving medications known to influence neuromuscular function 4) Hepatic or renal disease 5) History of allergic reaction to rocuronium. Seventy- five patients were randomly allocated into three groups (25 patients each). Group I received succinylch-oline 1.5 mg/kg intravenously Group II received rocuronium 0.6 mg/kg intravenously, Group III received rocuronium 0.9 mg/kg intravenously. All patients were kept nil per orally 8 hrs prior to surgery. All patients were premedicated with intramuscular injection of pethidine 1mg/kg and promethazine 0.5 mg/kg 45 minutes before induction of general anaesthesia. An intravenous access was established and 500m1 of ringer lactate was infused in premedication room. Inj. Midazolam 0.02mg/kg intravenously 5 minutes before induction given. Once the patient was sedated, monitors like pulse oximeter, non-invasive blood pressure and ECG monitor was attached and vital parameters were evaluated.

Patients were pre oxygenated with 100% oxygen for three minutes. Induction was done with Propofol 1-2 mg/kg IV till loss of eyelash reflex followed by muscle relaxant of the designated dose. Before administration of muscle relaxant, the supramaximal stimulus was determined with help of single twitch stimulation using peripheral nerve stimulator, by placing electrodes over the fore-arm just proximal to the wrist. Four successive stimuli of train of four were delivered at 2 Hz. The resultant four twitches of adductor pollicis muscle were observed visually. The time was noted. The train of four stimulation was then delivered at every 15 seconds after the injection of muscle relaxant till fading of all four twitches. Time from injection of muscle relaxant to the fading of all four twitches was taken as time of onset of action of muscle relaxant. At this time trachea was intubated. The intubating conditions were assessed clinically with the help of four

point scale given by cooper et al which is as follows.

Table 1; Grading system for intubation by Cooper et al (1992)[18,19]

Score	Jaw Relaxation	Vocal Cords	Response to intubation
0	Poor(impossible)	Closed	Severe coughing
1	Minimal(difficult)	Closed	Mild coughing
2	Moderate	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None

Total Score Excellent (8-9),Good (6-7), Fair (3-5), Poor (0-2)

Cuffed tracheal tubes of 7 and 8 mm size were used in female and male patients respectively. Tracheal intubation and grading of the intubating conditions was performed by an experienced anaesthetist unaware of the dose and type of muscle relaxant. Intubating conditions were evaluated by a qualitative scoring system described by Cooper et al[13]. Intubating conditions were considered as excellent (all variables are excellent), good (all variables were either excellent or good) or poor (the presence of a single variable listed under poor) . Excellent or good intubating conditions were regarded as clinically acceptable; poor intubating conditions were regarded as clinically not acceptable. Blood pressure, heart rate (HR) and Spo_2 were monitored. Time for reappearance of twitch height to 25 % of initial response, from the injection of relaxant was noted and it represented the duration of action of relaxant. Maintenance of anaesthesia was done with O2, N2 O and further doses of muscle relaxant. Volatile anaesthetics are known to potentiate the effects of NDMRs.[18] At the completion of surgery, reversal of neuromuscular blockade was achieved with atropine 0.02 mgkg-1 iv and neostigmine 0.05 mgkg-1 iv. Patients were extubated with the appearance of all four twitches on train of four stimulation visually. The baseline characteristics were analysed using descriptive statistics and ANOVA. Intubating conditions were analysed using chi-square test. Onset time and duration using ANOVA. P value <0.05 is considered significant. Descriptive statistics in the form of mean, standard deviation, frequency and percentages have been calculated for interval and categorical variables, respectively. To see a significant difference among the groups, one way analysis of variance (ANOVA) with post-hoc Bonferroni test has been applied to interval variables and chi-square tests for categorical variables.

Results

Table 2 Patient data

	Group I (n=25)	Group II (n=25)	Group III (n=25)	P
Age (years)	35 .52 ± 13.34	36.32 ± 9.89	39.88 ± 11.76	0.382
Weight (kg)	51.00± 8.05	51.00 ± 7.12	48.40 ± 7.19	0.369
Height(cm)	161.28± 6.29	159.60 ± 4.08	158.48 ± 7.12	0.209
Sex (M/F)	8.17 ± 1.978	5.20 ± 1.978	4.21 ± 1.978	0.372

Demographic data of this study correlate well with each other.

Table 3 Intubating conditions.

Intubating condition		Group I	Group II	Group III	P
Acceptable	Excellent	21 (84%)	14(56%)	21(84%)	0.032
	Good	4 (16%)	11(44%)	4 (16%)	
Fair		0(0)	0(0)	0(0)	
Poor		0(0)	0 (0)	0 (0)	
Total		25	25	25	

The intubating conditions were excellent in 84 % of patients (21out of 25) and good in remaining l6%of patients (4 out of 25) in group I and so acceptable in 100% of patients at 60-70 seconds with succinylcholine 1.5 mg/kg. The intubating conditions were excellent in 56% of patients (14 out of 25)and good in remaining 44% of patients (11 out of 25) in group II and so acceptable in100%of patients at 60-70 seconds with rocuronium 0.6mg/kg. The intubating conditions were excellent in 84% of patients (21 out of 25) and good in remaining 16% of patients (4 out of 25) in group III and so acceptable in 100%of patients at 60-70 seconds with rocuronium 0.9 mg/kg. The chi squared value was6.908.The corresponding P value is0.032, indicating a significant difference between the three groups in the number of patients with excellent intubating condition. There was no difference in the number of patients with excellent intubating conditions at 60-70 seconds after administering succinylcholine 1.5 mg/kg and after administering rocuronium 0.9 mg/kg i.e.; group I and III

Onset of action

The mean time to achieve maximum block i.e. Onset time of action of succinylcholine 1.5mg/kg was 64.92±10.91seconds and of rocuronium 0.6mg/kg was 195.72±34.62 seconds and of rocuronium 0.9mg/kg was111±19.13 seconds, which is almost half of the value in group II.

Table 4 Onset time (secs)

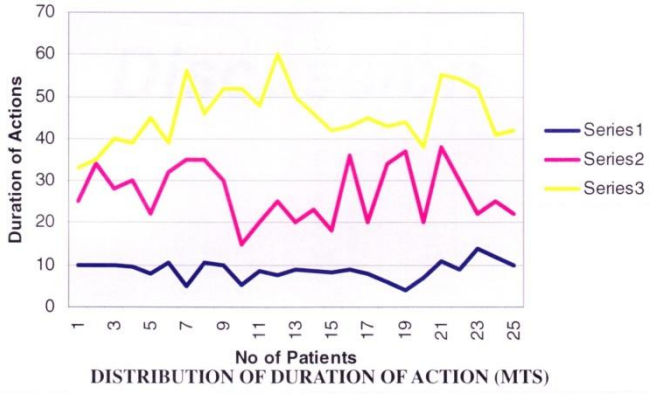
Groups	Mean	Standard deviation	P Value
I	64.92	10.91	
II	195.72	34.62	0.000
III	111.00	19.13	

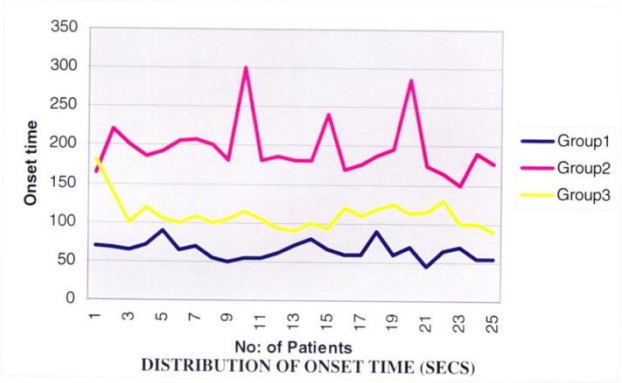
ANOVA was used. p - 0.000 indicating a highly statistically significant difference between the groups. To determine which of the groups were different, Bonferroni correction was used. There was a statistically significant difference between the three groups (P-0.000). There is a dose dependent decrease in the onset time with rocuronium. The onset time of rocuronium was significantly longer than succinyl choline.

Table 5 Duration of Action (minutes)

Groups	Mean	Standard deviation	P Value
I	8.64	2.23	
II	27.04	6.79	0.0000
III	45.60	6.87	

In group I patients who received succinylcholine l.5mg/kg, duration of action was shorter 8.64±2.23 minutes. In group II patients who received rocuronium 0.6mg/kg, duration of action was 27.04±6.79 minutes. In groups III patients who received rocuronium 0.9 mg/kg, duration of action was 45.60±6.87minutes.ANOVA was used. P = 0.000indicating a highly statistically signifi-cant difference between the groups. To determine which of the groups were different, bonferroni between all the three groups P = 0.000.The duration of action of rocuronium was significantly longer than that of suxamethonium. There is significantly prolonged duration of action when dose of rocuronium is increased from 0.6mglkg to 0.9mg/kg.





Discussion

Rocuronium bromide is a low potency non-depolarising muscle relaxant with intermediate duration of action.The aim of our present study was to compare intubating conditions using rocuronium 0.6 mg/kg with those of succinylcholine 1 mg/kg.

Primary and secondary outcomes

Succinylcholine creates better intubation conditions than rocuronium 0.6 mg/kg for both excellent and clinically acceptable intubation conditions after induction. At a dose of 0.9mg/kg, the condition was better. The number of failed intubations was nil, with a statistically significant difference between the three groups in the number of patients with excellent intubating condition, with no clinically or statistically significant difference between rocuronium 0.9 mg/kg and succinylcholine.

Based upon previous works [8,13,15,16,19], rocuronium was given in a bolus dose of 0.6 mg/kg (2 x ED95) and in a dose of 0.9 mg/kg (3 × ED 95) in the present study. All patients could be intubated at 60 sec with succinylcholine. This is similar to the reports of previous works.

As a secondary outcome, onset time and duration of action was studied among the three groups. Though the onset time was significantly more with rocuronium 0.6 mg/kg and 0.9 mg/kg as (195.72±34.62 sec) and (111.00±19.13sec) respecttively than with succinylcholine (64.72± 10.91 sec), the quality of neuromuscular block at larynx was comparable with intubation score of 7-9.Therefore, onset time is complementary to information provided by intubation score. It is very important to note that all the patients in rocuronium group were intubated with good to excellent intubating conditions, when there was no diaphragmatic activity. This perhaps may be acceptable even in emergency tracheal intubation in those patients in whom succinylcholine is contraindicated because of presence of other problems. In the study conducted by R. Cooper et al[13,15,18] 95% patients had developed clinically acceptable intubating conditions at 60 sec with rocuronium 0.6 mg/kg, when the patients were induced with thiopentone 5mg/kg and fentanyl 1-3 g/kg. In 1998, Stoddart compared intubating conditions of rocuronium 0.6 mg/kg with succi-nylcholine 1 mg/kg in 60 children undergoing tonsillectomy. Onset time was 92±41 sec & 42±11 sec with rocuronium & succinylcholine respect-ively. This faster development of clinically acceptable intubating conditions may be attributed to use of opioids in their induction regimen. In a study conducted by Susan Woelfel, clinical duration was found to be 26.7±1.9 min with rocuronium to be 0.6 mg/kg. Fuchs – Buder observed it be 21±4 min whereas Stoddart observed a clinical duration of 24.2±6.6 min with same dose. Present study confirmed that rocuronium is an intermediate acting muscle relaxant. It was observed that the clinical duration of action of rocuronium 0.6 mg/kg was 27.04±6.79min, 0.9 mg/kg was 45.60±6.87min there were no significant haemodynamic changes in both the groups

One of the most frequently used modificationin the rating scale as tool for assessment of intubating conditions, was introduced by Krieg et al in 1980 in which a numeric value is assigned to signify the quality of intubating conditions. Cooper [17] modification of this rating scale was used in present study. In another study by Sparr et al[16], intubating conditions after using succinylcholine I mg/kg was compared with intubating conditions after using rocuronium 0.6mg/kg in elective cases. 45 seconds later, all patients were intubated .It was found that clinically acceptable intubating conditions (good or excellent) appeared in all patients given succinyl choline and in 96% of patients given rocuronium. In the present study; clinically acceptable intubating conditions appeared in all patients; which was in accordance with prior studies.

Magorian et al [13] compared the duration of action of rocuronium in doses of 0.6mg/kg,0.9mg/kg and 1.2 mg/kg with that of succinylcholine in the doses of lmg/kg. It was found to be 37 minutes, 53 minutes, 73minutes for rocuronium 0.6 mg/kg,0.9 mg/kgand l.2mg/kg respectively and duration of

action of succinylcholine 1 mg/kg was 9 minutes. In our study, duration of action of rocuronium 0.9mg/kg,0.6mg/kg and succinylcholine 1.5 mg/kg are 45.6 minutes, 27.04 minutes and 8.64 minutes respectively and in accordance with prior studies. He also evaluated the intubating conditions. Intubating conditions were clinically acceptable in all the patients, a finding which was not different in the present study. Onset time of rocuronium 0.9 mg/kg appeared to beshorter than onset time of rocuronium 0.6 mg/kg and so there was a dose dependent decrease in onset time with rocuronium. Increasing the dosage of rocuronium from 0.6mg/kg to 0.9 mg/kg nearly halved the onset time. Increasing the dose from 0.6mg/kgto 0.9mg/kg doubles the clinical duration which is similar to the finding in the present study. Thus they found that a dose of rocuronium equal to or larger than 0.6mg/kg provided acceptable conditions at 60 seconds after administration of the drug, which is consistent with present study. In this study, excellent intubating conditions appeared only in 84% of patients with succinyl choline 1.5 mg/kg at 60 seconds. With rocuronium 0.6mg/kg, excellent intubating conditions were got in 56% of patients only at 60 seconds. With rocuronium 0.9mg/kg, excellent intubating conditions seen in 84% of patients at 60 seconds. So itwas clear that, after 0.9 mg/kg rocuronium; better intubating conditions were got similarto that with succinyl choline.

Our study has several limitations. First, monitoring the adductor pollicis is not a useful measure for evaluating the neuromuscular block at the laryngeal, diaphragm, and masseter muscles as the diaphragm recovers faster than hand muscles after succinylcholine. Pansard *et al*. [18] demonstrated that diaphragm recovery occurs 2 min earlier than adductor pollicis recovery at all levels of twitch height recovery. second, our results were obtained in young, healthy and normal weight patients. Increasing age, obesity and pre-existing lung disease would make patients more vulnerable to desaturation. There are clinical situations in which "acceptable" conditions for tracheal intubation ina patient with increased intracranial pressure and a full stomach might increase morbidity. Our findings have clinical relevance in patients with unanticipated difficult airway. The faster return to spontaneous ventilation with the 0.6 mg/kg dose increases the margin of safety in the event of a "Cannot Intubate, Cannot Ventilate" situation compared with the 0.9 mg/kg dose. Anotherlimitation of this study was that rocuronium is slightly less effective than succinylcholine for creating excellent and acceptable intubation conditions. Rocuronium should therefore only be used as an alternative to succinylcholine when it is known that succinylcholine should not be used and a more prolonged intubation is expected. Future research in this field is very essential especially regarding priming of rocuronium and sugammadex for reversal.

It was concluded from this study that rocuronium bromide has an intermediate duration of action. Clinically acceptable intubating conditions were comparable between rocuronium and succinylcholine. Rocuronium has an onset time longer than succinyl choline .Onset time of rocuronium is reduced with increase in dose from 0.6 mg/kg to 0.9 mg/kg. Rocuronium at a dose of 0.6 mg/kg provides acceptable intubating conditions at 60-70 seconds, comparable with succinyl choline at a dose of 1.5 mg/kg. The duration of action of rocuronium is significantly longer than succinyl choline. Rocuronium at a dose of 0.9 mg/kg has a longer duration of action than at a dose of 0.6mg/kg.

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