

A Clinical Evaluation of the Intubating Conditions using two Different Doses of Rocuronium and its Comparison with Succinylcholine for Rapid Sequence Induction: A Prospective Single Blind Study

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ABSTRACT

Introduction: Succinylcholine is the gold standard for rapid sequence induction. However its use is associated with many adverse effects so the search for an ideal neuromuscular blocking agent was done. Rocuronium is the only drug currently available which has the onset of action similar to that of succinylcholine and is devoid of any adverse effects that are commonly seen with succinylcholine. So the aim of this study was to evaluate rocuronium as a muscle relaxant using two different doses for rapid sequence endotracheal intubation and compare it with succinylcholine.

Material and Methods: Ninety patients were divided into three groups of 30 each. Groups A received injection succinylcholine at 1.5 mg/kg, Groups B and C received rocuronium 0.6 mg/kg and 0.9 mg/kg respectively. Onset of action of relaxant, intubation conditions, intubation score and duration of action were compared.

Results: The onset time was significantly shorter with succinylcholine 1.5 mg/kg in comparison to rocuronium 0.9 mg/kg and 0.6 mg/kg. Intubating conditions were excellent with succinylcholine 1.5 mg/kg and rocuronium 0.9 mg/kg in comparison to rocuronium 0.6 mg/kg.

Conclusion: Rocuronium in the dose of 0.9 mg/kg should definitely be given preference over succinylcholine in conditions, where the use of succinylcholine is hazardous.

Keywords: Neuromuscular Blocking Agents, Intubating Conditions, Rocuronium, Succinylcholine, Rapid Sequence Induction.

INTRODUCTION

Rapid sequence induction (RSI) is a method of achieving rapid control of the airway whilst minimizing the risk of regurgitation and aspiration of gastric contents.¹ The time interval from the suppression of protective reflexes by induction, to accomplishment of intubation, is a critical period, during which regurgitation and tracheobronchial aspiration of acidic gastric contents can occur.² Intravenous induction of anaesthesia and use of a faster onset muscle relaxant, with application of cricoid pressure, is swiftly followed by the placement of an endotracheal tube.

The ideal neuromuscular blocking agent for RSI should have a fast onset, brief duration of action, should provide profound relaxation and should be free from any haemodynamic changes.¹

Succinylcholine is the gold standard for rapid sequence induction. However its use is associated with many adverse effects. Because of these side effects, the search for an ideal neuromuscular blocking agent, focused on nondepolarizing

type of relaxants, which has a rapid onset time and offers good to excellent intubating conditions similar to that of succinylcholine was done. Among the non depolarizing muscle relaxants vecuronium and atracurium were presented as an attractive alternative to succinylcholine. However neither of these has the onset time as short as succinylcholine. Rocuronium bromide is 2 morpholino 3 - disacetyl 16 N - allyl pyrrolidino derivative of vecuronium.³ It is a newer non - depolarizing muscle relaxant that was introduced in 1994. It is the only drug currently available which has the rapidity of onset of action similar to that of succinylcholine and is devoid of any adverse effects that are commonly seen with succinylcholine. So, it can be safely used for RSI, when succinylcholine is contraindicated.

In the light of above background, the present study was designed to compare the onset of action, intubating conditions, duration of action, haemodynamic effects and adverse effect (if any) of rocuronium with that of succinylcholine in adult patients undergoing elective surgeries.

The aim of the present study was to evaluate clinically rocuronium as a muscle relaxant using two different doses for rapid sequence endotracheal intubation and compare it with succinylcholine.

MATERIAL AND METHODS

After approval from the institutional ethical committee this prospective, randomized, single blind study was conducted in the department of anaesthesiology, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India. A total of 90 patients of either sex, with ASA grade I or II, aged 18 years - 60 years were enrolled for the study. The patients were randomly assigned using "computer generated random number table" to one of the following groups:

Group A (n=30): Were scheduled to receive Succinylcholine 1.5 mg/kg intravenously.

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Group B (n=30): Were scheduled to receive Rocuronium 0.6 mg/kg intravenously.

Group C (n=30): Were scheduled to receive Rocuronium 0.9 mg/kg intravenously.

Anesthesia technique: Pre-anesthetic checkup was done and patient was informed about the procedure. Tab. alprazolam 0.5 mg was given evening before surgery and at 5 Am in the morning with a sip of water. IV line was secured with 18 Gauge IV cannula and IV fluid was started. The patient was connected to all the standard monitors to record pulse rate, O₂ saturation, NIBP and ECG. Premedication with inj. Midazolam 0.05 mg/kg body weight before the procedure was given. At this point of time, the Digistim III (Mainline Medical Inc., Georgia, US) peripheral nerve stimulator was connected to the patient. It was used to observe the twitch response of the thumb (abduction and extension) every second, after injection of the study drugs to establish their onset of action. The lead wire with the black plug was plugged into the black jack located on the rear panel of the instrument and the lead wire with the red plug was plugged into the red jack located adjacent to the black jack.

Gelled electrodes were placed in line, over the posterior interosseous nerve, which is a continuation of the deep branch of radial nerve. The distal (negative) electrode was placed on the extensor aspect of the wrist in between the styloid processes of the radius and ulna. The proximal electrode (positive electrode) was placed 5 cm proximal over the posterior aspect of the forearm.

Next, the instrument was adjusted to provide supramaximal stimulation (SMS) which is defined as the level at which additional stimulation current does not increase twitch response. This setting can be approximated by adjusting the control knob to the level where any further increase in stimulus current would not increase the level of the twitch response. The reading on the digital display was noted and this baseline setting was maintained throughout the procedure. The machine was then turned off.

After pre oxygenation for 3 minutes, with 100% oxygen, anaesthesia was induced with injection propofol 2.0 mg/kg. The peripheral nerve stimulator was immediately switched on and set to SMS which was noted earlier. Each patient then received the calculated dose of the respective muscle relaxant intravenously as a single bolus dose according to the allocated group. The time of injection of the muscle relaxant was noted. Simultaneously, the twitch response of the thumb was also noted, till it completely ceases.

Complete cessation of twitch response of the thumb marked the onset of action of the drugs. The onset of action of the drug was taken from the injection of the neuromuscular blocking agent to complete cessation of twitch response of the thumb. Sixty seconds after injection of neuromuscular blocking agent, direct laryngoscopy was performed and intubating conditions were assessed according to four point scale of Cooper et al.⁴ scoring system:

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Poor (impossible)	Closed	Severe coughing or bucking
1	Minimal (difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None
Total score	Excellent (8-9), Good (6-7), Fair (3-5), Poor (0-2)		

Scoring of intubating conditions

Orotracheal intubation was not done, if the intubating condition score was less than 6 and the patient was ventilated for another thirty seconds. If the intubating condition score still remained less than 6, even after ninety seconds of injection of neuromuscular blocking agent, the patients was further ventilated and intubation condition score was assessed every 30 seconds until good to excellent intubating condition score was achieved and then intubated.

All the patients were intubated with a well lubricated, appropriate sized poly vinyl chloride cuffed endotracheal tube. Bilateral air entry was checked and the tube was firmly secured and controlled ventilation was started. Anaesthesia was maintained with 30% oxygen, 70% nitrous oxide, isoflurane as volatile anaesthetic and an intermittent muscle relaxant.

Monitoring of vital parameters such as heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation were recorded at fixed intervals, i.e., before premedication, after induction, before intubation and then at 5, 10, 20, 30 minutes following intubation.

The clinical duration of action of the study drugs, i.e., the time from administration of the relaxant to the first appearance of spontaneous respiration was also noted.

At the end of surgery, all anaesthetics were stopped, 100% oxygen was given and oropharyngeal suction was done. After returning of respiratory efforts residual neuromuscular blockade was reversed by injection neostigmine 0.04 mg/kg and Injection glycopyrrolate 0.02 mg/kg intravenously.

When respiration became normal and tidal volume was adequate, extubation was done. After extubation, patients were oxygenated with 100% for 5 minutes and then shifted to postoperative ward.

STATISTICAL ANALYSIS

All the results were compiled, compared and analysed statistically by using the statistical package for the social science (SPSS 22.0, IBM, New York, USA). The data was compiled using Microsoft Excel Sheet (Windows 2007). For each variable the mean and standard deviation were calculated. One way ANOVA was performed for multiple comparisons followed by Tukey - post hoc test for pair wise comparisons. *P*-value <0.05 was considered significant and <0.001 was considered highly significant.

RESULTS

All the three groups were comparable in the terms of Age,

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)	p-value
Age (Years)	41.70±17.8	37.30±16.0	39.37±17.20	0.874
Body Mass Index	23.49±2.6	22.92±3.12	24.30±2.57	0.349
Gender (M/F)	12/18	19/11	15/15	0.655
ASA (I/II)	24/06	26/04	24/06	0.805
Duration of surgery (Minutes)	97.83±9.5	97.0±7.8	105.116±10.4	0.450

Table-1: Comparison of demographic data

Variables	group A	group B	group C	p-value
Onset of action (Sec)	47.60±3.76	77.40±5.32	58.37±4.82	<0.001
Duration of action(min)	5.40±1.14	27.70±5.32	46.60±4.27	<0.001
Intubation Score(At 60 sec)	9	4	8	<0.001
Excellent Intubation condition (At 60 sec)	100%	0%	93.33%	<0.001

Table-2: Comparison of onset, duration of action, intubation score and intubation conditions

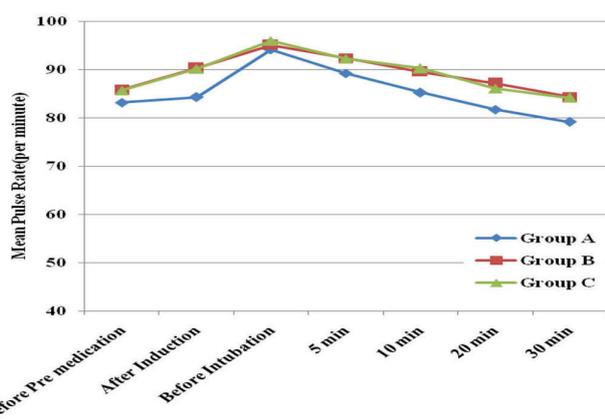


Figure-1: Comparison of Mean Arterial Pressure (MAP) in Group A, Group B and Group C

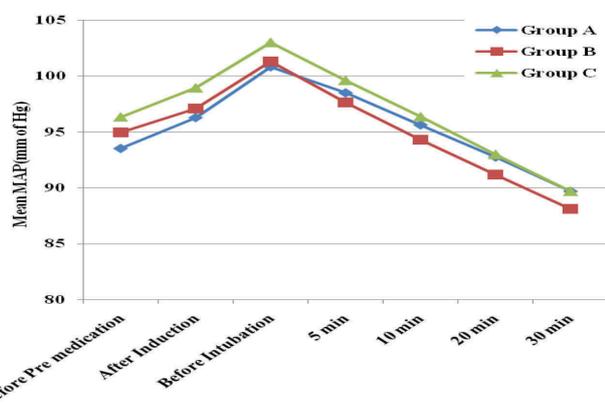


Figure-2: Comparison of Mean Systolic Blood Pressure in Group A, Group B and Group C.

Gender, Body Mass Index, ASA Grade and duration of surgery and no statistically significant difference was found (p -value >0.05) (Table-1).

The mean onset of action of the drug in group A was 47.60 ± 3.76 seconds, in group B was 77.40 ± 5.32 seconds and in group C was 58.37 ± 4.82 seconds. The difference in the mean onset of action of the drugs, was statistically highly significant (p -value <0.01) (Table-2).

The mean duration of action of the drug in group A was 5.40 ± 1.14 minutes, in group B was 27.70 ± 3.67 minutes and in group C was 46.60 ± 4.27 minutes. The difference in the

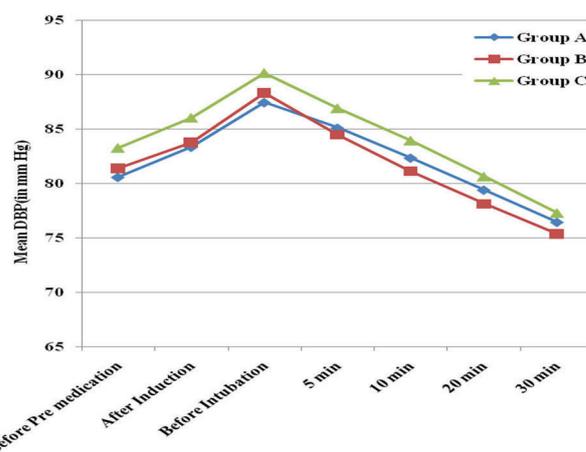


Figure-3: Comparison of Mean Diastolic Blood Pressure (DBP) in Group A, Group B and Group C.

mean duration of action of the drugs was statistically very highly significant (p -value <0.001) (Table-2).

The median intubating score in group A was 9, in group B was 4, and in group C, it was 8 at 60 seconds (Table-2).

Mean pulse rate was comparable in all the three groups on starting of procedure. Pulse rate changes during the entire intraoperative period were statistically not significant in all the three groups (p -value >0.05) (Figure-1).

Mean systolic blood pressure was comparable in all the groups on starting of procedure. Systolic blood pressure changes during the entire intraoperative period was statistically not significant in all the three groups (p -value >0.05) (Figure-2).

Mean Diastolic blood pressure was comparable in all the groups on starting of procedure. Diastolic blood pressure changes during the entire intraoperative period was statistically not significant in all the three groups (p -value >0.05) (Figure-3).

DISCUSSION

Although succinylcholine is the gold standard for rapid sequence induction rocuronium has been shown to possess most of the properties of an ideal muscle relaxant such as nondepolarizing type of mechanism of action, rapid onset of action, short duration of action, rapid recovery, noncumulative, free from cardiovascular side effects, no histamine release, pharmacologically inactive metabolites

etc.

Onset of Action

In our study, the mean onset of action of succinylcholine was 47.60 ± 3.76 seconds. The result concurs with the studies of Mishra MN et al.² Shukla A et al.³, Sluga M et al. Hemmerling TM et al. Parikh K et al. Magorian T et al. Sutradhar B et al. and Chavan SG et al.⁵⁻¹⁰ However contrasting results were found in studies by Cooper RA et al.⁴, Singh A et al. Venkateswaran R et al., and Laurin EG et al.¹¹⁻¹³ which can be explained due to different doses used.

In our study, the mean onset of action of rocuronium in the dose of 0.6 mg /kg was 77.40 ± 5.32 seconds. This result corroborates with studies by Shukla A et al., Cooper RA et al., Sluga M et al.³⁻⁵ Parikh K et al., Magorian T et al.⁷⁻⁸ Singh A et al.¹¹, and Puhlinger F K et al.¹⁴ However conflicting results were found in studies by Mishra MN et al.² Hemmerling TM et al.⁶ Chavan SG et al.¹⁰ and Venkateswaran R et al.¹² In the present study, the mean onset of action of rocuronium in the dose of 0.9 mg/kg, was 58.37 ± 4.82 seconds. This result concurs with the study done by Hemmerling TM et al.⁶ However, contrasting results were found in studies of Magorian T et al.⁸ and Chavan SG et al.¹⁰ The difference in results in various studies may be due to different methods of detecting the onset of neuromuscular blockade.

Duration of Action

The mean duration of action of the drug in group A was 5.40 ± 1.14 minutes, in group B, was 27.70 ± 3.67 minutes and in group C it was 46.60 ± 4.27 minutes. The difference in the mean duration of action of the drugs was statistically highly significant (p - value < 0.001).

In our study, the mean duration of action of succinylcholine was 5.40 ± 1.14 min. This result concurs with the studies done by Shukla A et al.³ Parikh K et al.⁷ Chavan SG et al., Singh A et al., Venkateswaran R et al.¹⁰⁻¹² and. Penchalaiah C et al.¹⁵ However, conflicting result was seen in studies of Cooper RA et al.⁴ Magorian T et al. and Sutradhar B et al.⁸⁻⁹ In the present study, the mean duration of action of rocuronium in the dose of 0.6 mg /kg, was 27.70 ± 3.67 . This result concurs with the studies done by Shukla A et al., Cooper RA et al.³⁻⁴ Parikh K et al.⁷ Chavan SG et al. Singh A et al.¹⁰⁻¹¹ Puhlinger K et al. Penchalaiah C et al.¹⁴⁻¹⁵ Schultz P et al. and Naguib M et al.¹⁷⁻¹⁸ However, confliction is seen in study of Magorian T et al.⁸

In the present study, the mean duration of action of rocuronium in the dose of 0.9 mg/ kg, was 46.60 ± 4.27 min. It matches with the results of the studies done by Cooper RA et al.⁴ Hemmerling TM et al.⁶ Magorian T et al.⁸ Chavan SG et al.¹⁰ Penchalaiah C et al.¹⁵ and Schultz P et al.¹⁷

Intubating Conditions

Intubating conditions are more dependent on the degree of neuromuscular block at the laryngeal adductors than that at the adductor pollicis.¹⁶ Total blockade of the larynx or diaphragm may not be necessary for acceptable intubating conditions. The onset of relaxant is much quicker in the muscles that are required to achieve good intubating conditions, than in the usually monitored muscle.¹⁹

Thus, in the present study, excellent intubating conditions were achieved in all the patients, using succinylcholine at 60 second in the dose of 1.5 mg/ kg. This result is approximately comparable to the results in the studies by Mishra MN et al., Shukla A et al.²⁻³ Parikh K et al. Magorian T et al.⁷⁻⁸ and Penchalaiah C et al.¹⁵ However, in the study done by Mc Court KC et al.²⁰ only 80% of the patients achieved excellent intubating condition.

In the present study, excellent to good intubating conditions were not achieved in any of the patients, at 60 second with 0.6 mg/ kg dose of rocuronium.

This finding corroborates with the studies done by Mishra MN et al.² Cooper RA et al.⁴ Parikh K et al.⁷ Puhlinger FK et al., Penchalaiah C et al., and Naguib M et al.¹⁴⁻¹⁶

However, our results conflicts with the results of Shukla A et al.³ and Mc Court KC et al.²⁰ who had fair intubating conditions in 25% and 20% of the patients respectively.

In the present study, excellent to good intubating conditions were achieved in 93.33% of the patients at 60 second with 0.9 mg/kg dose of rocuronium. This finding corroborates with the studies by Magorian T et al.⁸ Penchalaiah C et al.¹⁵ and Naguib M et al.¹⁸ However, in the study conducted by Mc Court KC et al.²⁰ only 58.2% of patients had excellent intubating condition. Factor, which can be attributed to the difference in intubating conditions may be that the relaxation of laryngeal muscles occurs before the adductor pollicis of the thumb.

Haemodynamic Effects

An ideal neuromuscular blocking agent should produce cardiovascular stability. In the present study, the haemodynamic changes with succinylcholine in the dose of 1.5 mg/kg were compared to the haemodynamic changes with rocuronium in the dose of 0.6 mg/kg and 0.9 mg/kg.

The finding of the present study is in agreement with the studies of Shukla A et al., Cooper RA et al.³⁻⁴, Penchalaiah C et al.¹⁵ Nitschmann P et al., and Levy JH et al.²¹⁻²²

However, there was an increase in heart rate and mean arterial pressure following administration of the study drugs, in all the three groups which is consistent with the study done by Booth et al.²³ who reported that during the first minute following injection of rocuronium, heart rate increased by 36%. Theself et al.²⁴ reported, that there was rise in mean arterial pressure following administration of succinylcholine, which was explained on the basis of stimulation of autonomic ganglion. Furthermore clinically insignificant increase in haemodynamic parameters was due to response to laryngoscopy and endotracheal intubation, which subsided to near pre medication value ten minutes after intubation.

Adverse Effects

No adverse reactions like bradycardia, tachycardia, hypotension, hypertension, bronchospasm, laryngospasm, cutaneous flushing, urticaria, anaphylactic reactions, were observed in any patient belonging to all the three groups. Similar results were found in the studies done by Shukla A et al.³ Parikh K et al.⁷ and Penchalaiah C et al.¹⁵ Although

fasciculations were reported as the only adverse effect in 95% of the patients in succinylcholine group.

CONCLUSION

From the study, it can be concluded that succinylcholine has a short onset time when compared to rocuronium at different doses and provides excellent intubating conditions within sixty seconds of drug administration. Rocuronium, in dose of 0.9 mg/kg, also provides excellent intubating conditions within sixty seconds of drug administration, but at the cost of prolonged duration of neuromuscular blockade and significant drug cost. However, with, rocuronium, in dose of 0.6 mg/ kg, it is mandatory to wait for ninety seconds to achieve intubating conditions similar to that of succinylcholine.

Thus, rocuronium in the dose of 0.9 mg/kg is a good alternative to succinylcholine for rapid sequence induction, in adult patients, in situations where succinylcholine is contraindicated and when there is no anticipated difficult airway.

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