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A comparative study to evaluate the optimum intubating dose of rocuronium bromide versus succinylcholine chloride as an ideal intubating muscle-relaxing agent

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ABSTRACT

Background: Rocuronium bromide is a new amino steroidal neuromuscular blocking agent which is structurally related to vecuronium and its onset time and intubating conditions are comparable with succinylcholine and without the undesirable side effects. **Aims and Objectives:** This study was planned to evaluate the ideal intubating dose of rocuronium bromide by comparing intubating conditions achieved by its different doses of rocuronium bromide and to consider rocuronium as an ideal intubating muscle relaxing agent, in place of succinylcholine chloride for elective long surgeries. **Materials and Methods:** This study was conducted on 120 patients who fulfilled the eligibility criteria. These patients were randomized into four groups of 30 each by block randomization technique. Each group received rocuronium bromide 0.6 mg/kg, 0.9 mg/kg, 1.2 mg/kg, and succinylcholine chloride 1 mg/kg, respectively. **Results:** Out of all the three doses of rocuronium bromide 0.9 mg/kg produced a similar intubating condition as succinylcholine chloride in the dose of 1 mg/kg without undue prolongation of the neuromuscular blockade. **Conclusion:** Rocuronium bromide can be used as an alternative to succinylcholine as an ideal intubating muscle relaxing agent.

Key words: Rocuronium bromide; Succinylcholine chloride; Neuromuscular blockade

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INTRODUCTION

Endotracheal intubation is a development without which general anesthesia cannot be considered safe for any major surgery, particularly head and neck, thoracic, and abdominal surgeries. Hence, the search began for a relaxant which had a rapid onset and short duration of action. Out of all the relaxant succinylcholine have been the drug of choice for intubation since its introduction in 1952.[1]

Succinylcholine chloride within the dose of 1 mg/kg provides excellent intubating conditions in 60–90 s with a short duration of action on the diaphragm and adductor muscles of the larynx involved in respiration and airway protection.[1]

Unfortunately, succinylcholine chloride has many side effects such as an increase in intragastric, intracranial, and intraocular pressure, rhabdomyolysis with hyperkalemia, changes in cardiac rhythm including bradycardia and cardiac arrest, malignant hyperthermia in susceptible individuals and also life-threatening increase in serum potassium levels are noticed in patients with burns, trauma, injuries, or upper motor neuron lesion.[2,3]

Therefore, it is contraindicated in patients with a head injury, eye injury, patients having a recent history of burns, and patients

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with injuries. Considering the side effects and contraindications, efforts were made to seek out a newer neuromuscular blocking agent with a comparable fast onset and shorter duration of action but without the associated side effects of succinylcholine chloride. Non-depolarising neuromuscular blocking agents such as pancuronium, vecuronium, and atracurium are used for endotracheal intubation, but they take a much longer time to achieve favorable intubating conditions.[3]

Rocuronium bromide, introduced in 1994 is a new amino steroidal neuromuscular blocking agent. It is structurally related to vecuronium and its onset time and intubating conditions are comparable with succinylcholine and without the undesirable side effects.[4,5]

With this background, the following study has been conducted with the primary objectives of (a) to evaluate the ideal intubating dose of rocuronium bromide by comparing intubating conditions achieved by different doses of rocuronium bromide and (b) to consider rocuronium as an ideal intubating muscle relaxing agent, in place of succinylcholine chloride for elective long surgeries. Secondary objectives were (a) to observe the hemodynamic changes after administration of both the muscle relaxants and (b) to check for any adverse effects or abnormal response to the drugs.

Aims and objectives

a) To evaluate the ideal intubating dose of rocuronium bromide by comparing intubating conditions achieved by different doses of rocuronium bromide
b) To consider rocuronium as an ideal intubating muscle relaxing agent, inplace of succinylcholine chloride for elective long surgeries.

Secondary objectives

a) To observe the hemodynamic changes after administration of both the muscle relaxants
b) To check for any adverse effects or abnormal response to the drugs.

MATERIALS AND METHODS

After getting the Institutional Ethics Committee's approval this randomized controlled study was conducted. One hundred and twenty patients scheduled for elective surgeries under general anesthesia were selected for this study (Fig. 1).

Inclusion criteria

a. Patients scheduled for elective surgeries under general anesthesia
b. Patients in the age group of 18–60 years
c. Patients with physical status ASA-I and ASA-II
d. Patients with Mallampati score-I and II.

Exclusion criteria

a. Patient's refusal to be included in the study
b. Allergic to any study drug
c. Patients with physical status ASA more than II
d. Patients with an anticipated difficult airway
e. Patients suffering from renal or cardiovascular issues

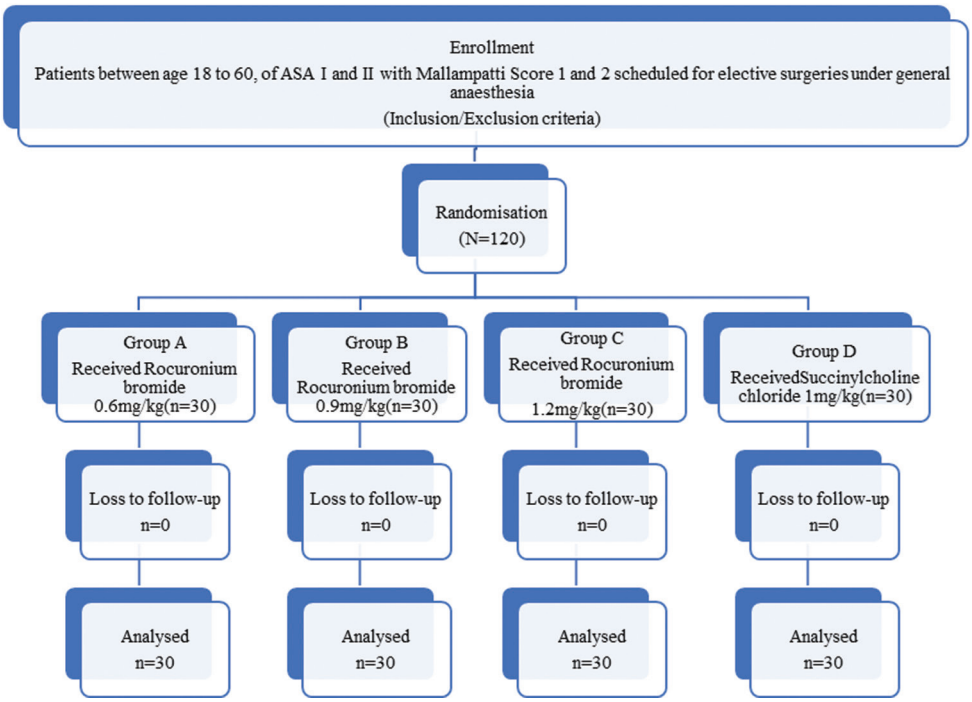

Figure 1: CONSORT diagram

f. Patients with a history of malignant hyperthermia
g. Pregnancy.

Preoperatively informed, written consent was obtained from these patients. These patients were randomized into four groups of 30 each by block randomization technique.

- Group A/Group 1 received rocuronium bromide 0.6 mg/kg (n=30)
- Group B/Group 2 received rocuronium bromide 0.9 mg/kg (n=30)
- Group C/Group 3 received rocuronium bromide 1.2 mg/kg (n=30)
- Group D/Group 4 received succinylcholine chloride 1 mg/kg (n=30).

In all patients, baseline vital parameters were recorded. History regarding previous anesthesia, surgery, any significant medical illness, medications, and allergy were recorded. A complete physical examination and airway assessment were done. Following laboratory investigations were done: Hemoglobin % urine- albumin and sugar, blood- urea, sugar, creatinine, liver function tests, E.C.G., and chest X-ray. Patients were premedicated with an injection of glycopyrrolate 10 μg/kg and injection of fentanyl 2 μg/kg and injection of midazolam 15 min before surgery. Then pulse, blood pressure, oxygen saturation, and ECG were noted as pre-induction data.

In group A/group1, patients were induced with injection of propofol 2 mg/kg slowly followed by rocuronium bromide 0.6 mg/kg i.v. In group B/group 2 patients were induced with injection of propofol 2 mg/kg slowly followed by rocuronium bromide 0.9 mg/kg i.v. Group C/group 3 is induced by injection of propofol 2 mg/kg slowly followed by rocuronium bromide 1.2 mg/kg i.v. and in group D/group 4 they were induced by succinylcholine chloride 1 mg/kg.

In all the groups, jaw relaxation and vocal cord relaxation were considered for atraumatic laryngoscopy at 60 s or if needed 75 s and then 90 s.

During laryngoscopy, cardiovascular response was assessed, from the time of intubation and 2, 5, and 10 min, and then every 10 min pulse, blood pressure, and spO_2 were recorded.

Intubating conditions were assessed using the criteria of Cooper et al.[6] The three items of this score are as follows:

a. Ease of laryngoscopy (along with jaw relaxation)
b. Aspect of vocal cords
c. Response of the diaphragm to tracheal intubation.

These offer a four-point scale. The appropriate values were selected and then added up to a total numeric score of a maximum of 9.[6,7]

A total score of 8–9 is rated as excellent; 6–7 is rated as good; 3–5 is rated as fair; 0–3 is rated as poor intubating conditions.

Good and excellent conditions were taken to be "clinically acceptable" by Cooper et al. Anesthesia was maintained using a closed circuit with a circle absorber having 50% N_2O and 50% O_2. After clinical recovery from the intubating dose of muscle relaxant, the period of study will be over and the anesthesia was maintained by O_2, N_2O, and sevoflurane and a further dose of muscle relaxant.

After completion of the surgery, reversal of neuromuscular blockade was achieved with injection of neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg i.v. after satisfactory recovery and the patient was extubated.

The following observations were recorded:

a. The mean onset of neuromuscular blockade and duration of action were calculated for all the four groups
b. The heart rate, systolic pressure, and diastolic pressure were recorded before induction, during intubation, and 1 min, 3 min, and 5 min after intubation and compared between the four groups
c. Intubating conditions were scored by a scoring system used by Mirakhur et al.[8-10] The scores for jaw relaxation, vocal cord position, and response to intubation and the total scores are compared between the three groups.

Statistical analysis plan

All recorded data were entered using MS Excel software and analyzed using SPSS software to determine the statistical significance. Analysis of Variance was used to study the significance of the mean of various study parameters among the three groups. Student's "t" test was used to compare the two groups on mean values of various parameters. The P-value taken for significance is 0.05. The study was conducted on 120 patients randomly allocated into four groups as given below.

Sample size

The sample size was calculated assuming a standard deviation of 10 and type 1 error of 5, a confidence interval of 95%, and the power of the study at 80%. Thirty patients were in each group, therefore a total of 120 patients were considered for this study.

RESULTS

A total of 120 patients undergoing elective surgery were recruited for this study. There was no significant difference between the distribution of age and sex among the four study groups.

Vocal cord position

Regarding vocal cord position, the closed status (score 0) was seen in three cases in Group 1, whereas no such case had been encountered in Group 2, Group 3, and Group 4. The mean score for vocal cord position was significantly higher in Groups 2, 3, and 4 (2.8±0.43, 3±02, 9±0.25, respectively) compared to Group 1 (i.e. 1.6±0.67) (Table 1).

Jaw relaxation

On analyzing the jaw relaxation, it was impossible to open in three cases and open with difficulty in 13 cases in Group 1. These kinds of problems did not occur in Group 2 and Group 3 and only one case in Group 4. Statistical analysis showed that the mean score for jaw relaxation was significantly less in Group 1 than in Groups 2, 3, and 4 (Table 2).

Response to intubation

With regard to response to intubation, two cases had severe coughing or bucking, and 14 cases had moderate coughing in Group 1. However, these untoward events occurred less in Group 2, Group 3, and Group 4 (Table 2). The mean score for response to intubation was significantly higher in Groups 2, 3, and 4 when compared to Group 1 (2.54±0.41, 3±0, 2.9±0.25. and 1.5±0.89, respectively).

Intubation score

The analysis of intubation scores to asses condition at intubation showed that the higher doses result statistically significant increase in ease of intubation when compared to succinylcholine.

Acceptable intubating conditions (excellent and good) were observed in all thirty patients in groups 2, 3, and 4. Six patients had poor intubation scores, nine patients had fair intubation scores in group 1. No significant difference in groups 2, 3, and 4.

Statistical analysis revealed that mean heart rate, systolic blood pressure, and diastolic blood pressure during intubation in Group 1 was significantly higher than in Group 2, Group 3, and Group 4 (Figures 2 and 3).

The analysis showed that the onset of blockade is inversely proportional to the dose of rocuronium. The onset time for the intubating dose was significantly lower in groups 3 and 4 (62.3±13.37, 57.2±6.11) and between groups 1 and 2 (98.5±18.34, 68.5±17.82) (Table 3).

The duration of neuromuscular blockade increases as the dose increases. The duration of action of the intubating dose was significantly higher in Group 3 (56.2±5.97 min) when compared to Groups 1, 2, and 4 (24.0±3.57, 39.7±4.14, and 5.23±1.07 min) (Table 3).

DISCUSSION

In the present study, we compared different doses of rocuronium with the current practice drug in use, i.e., succinylcholine chloride in the patient requiring induction of anesthesia and endotracheal intubation for elective surgeries.

We studied three different doses of rocuronium (0.6 mg/kg, 0.9 mg/kg, and 1.2 mg/kg) along with succinylcholine chloride 1 mg/kg was used for intubation and various parameters such as onset time, duration of neuromuscular

Table 1: Distribution of study participants according to vocal cord position (n=120)

Group	0-closed	1-closing	2-moving movement	3-open relaxed	Mean±SD
Group 1	1	11	16	2	1.6±0.81
Group 2	0	0	10	20	2.8±0.43
Group 3	0	0	0	30	3±0
Group 4	0	0	5	25	2.9±0.25

Table 2: Distribution of study participants according to Jaw relaxation and response to intubation (n=120)

Parameter	Group 1	Group 2	Group 3	Group 4
Jaw relaxation				
Impossible to open	3	0	0	1
Open with difficulty	13	0	0	0
Moderate opening	9	8	0	0
Easy to open	5	22	30	29
Mean±SD	1.6±0.67	2.67±0.48	3±0	2.8±0.38
Response to intubation				
Severe coughing	2	1	0	1
Moderate coughing	14	0	0	1
Slight diaphragm movement	8	7	0	0
No movement	6	22	30	28
Mean±SD	1.5±0.89	2.54±0.41	3±0	2.9±0.25

Table 3: Distribution of study participants according to onset and duration of first dose (n=120)

	Mean			
Parameter	**Group A**	**Group B**	**Group C**	**Group D**
Onset (Seconds)	98.5±18.34	68.5±17.82	62.3±13.37	57.2±6.11
Duration (minutes)	24.0±3.57	39.7±4.14	56.2±5.97	5.23±1.07

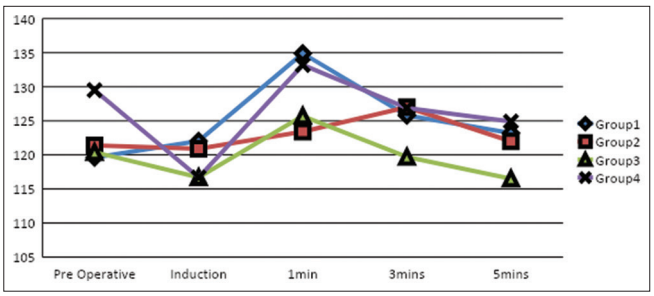

Figure 2: Distribution of study participants according to systolic blood pressure (n=120)

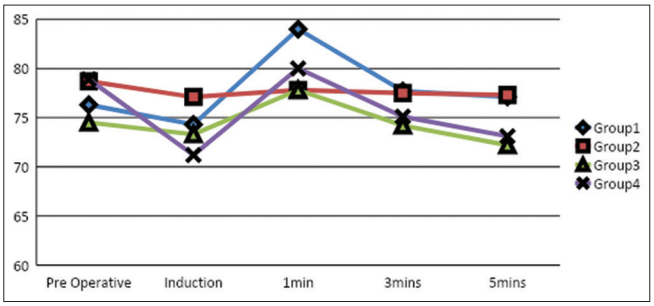

Figure 3: Distribution of study participants according to diastolic blood pressure (n=120)

blockade, intubating conditions and hemodynamic changes were compared. Intubating conditions were compared using Cooper et al.,[6] criteria. The onset time and duration of the neuromuscular blockade were studied by laryngoscopy, hemodynamic response, and ventilatory parameters.

A study done by Hanskirkegaard–Nielson, James E, and Peter D Berky, on 80 subjects concluded that after induction with fentanyl, propofol and rocuronium (1.04 mg/kg) gave 95% successful intubation and were similar to succinylcholine group. The endotracheal tube could be passed through the vocal cords of all the patients enrolled for the study and they also concluded that rocuronium bromide 1 mg/kg can be safely used for almost all emergent cases as an intubating drug and provide intubating conditions similar to succinylcholine.

In our study, there was a significant difference in onset of time among the four groups. Group 3 showed the fastest onset compared to the others. Even though the onset of time is faster in Group 3 there is a prolongation of the duration of neuromuscular blockade for the first dose of rocuronium and this is an added disadvantage to this group.

Good to excellent conditions have been reported within 60 s following 0.6–1.2 mg/kg, intubating conditions as observed by Mirakhur et al.,[9] Cooper et al.,[10] and Huizinga et al.,[11] were good or acceptable in 95% of patients at 60 s and all patients at 90 s. The average intubating time reported by Mirakhur et al. was 89 s.[12-14]

However, in our study, we observed excellent to good conditions in 46.6% in Group 1, and 100% in Groups 2, 3, and 4. Our observations in rocuronium are very close to that observed by the above authors.

It is expected to have an onset time possibly as rapid as that of succinylcholine but unlike succinylcholine, rocuronium has little or no cardiovascular side effects and does not cause histamine release. Thus, it is an ideal muscle relaxant for rapid sequence induction of anesthesia and may be preferable to succinylcholine in compromised patients in whom cardiovascular effects are to be avoided. Rocuronium is currently being used for rapid sequence induction, as an alternative to succinylcholine. It has a rapid onset of action, less than a minute for complete neuromuscular blockade with doses of 0.9–1.2 mg/kg.[5]

Intubating conditions were good to excellent for rocuronium at the 0.9 mg/kg dose (100%), and 1.2 mg/kg dose (100%), whereas rocuronium at 0.6 mg/kg dose had the least number of excellent to good conditions and the most poor or not possible assessment.

There were important changes or intergroup differences in blood pressure and heart rate. Patients receiving 0.6 mg/kg were more likely to experience moderate coughing and bucking after tracheal tube insertion.

The higher dose of rocuronium (0.9–1.2 mg/kg) produces ideal intubating conditions but the duration of action is very much prolonged at 1.2 mg/kg. No further improvement in intubating conditions was achieved by increasing the dose of rocuronium from 0.9 to 1.2 mg/kg. Therefore out of all the three doses of rocuronium bromide 0.9 kg produced a similar intubating condition as succinylcholine chloride in the dose of 1 mg/kg without undue prolongation of the neuromuscular blockade.

Limitations of the study

However, our study has some limitations too, for example,

a. Less availability and higher cost of sugammadex in case of failed intubation but unavailability did not cost the

patient's well-being

b. Non-availability of a neuromuscular monitor but the recovery time did not get prolonged but caused observer bias for determining the offset
c. The cases did not include emergency patients so the effectiveness of the emergency is not known
d. As the sample size was small the effect on the entire population is not known.

CONCLUSION

Among the three doses of rocuronium bromide used for endotracheal intubation in the study, this can be concluded that, rocuronium bromide in the dose of 0.9 mg/kg and 1.2 mg/kg produced acceptable intubating conditions in 60 s and out of all the three doses of rocuronium bromide 0.9 kg produced as similar intubating condition as succinylcholine chloride in the dose of 1 mg/kg without undue prolongation of the neuromuscular blockade.

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Author's contributions:
PB- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, manuscript preparation, and submission of article; **AM-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **SC-** Design of study, statistical analysis, and Interpretation**; NM-** Review manuscript, analysis, and manuscript revision.

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