EVALUATION OF INTUBATING CONDITIONS WITH AND WITHOUT PRIMING DOSE OF ROCURONIUM BROMIDE

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ABSTRACT

BACKGROUND

The beneficial effects of priming technique with rocuronium in reducing the onset time for intubation compared to non-priming technique inspired us to conduct a study in which we compared the onset time for intubation and intubating conditions.

AIMS

The study compares the intubating conditions between priming and non-priming techniques with 2xED95 dose of rocuronium bromide. The following parameters were compared. 1. The onset time for intubation, 2. Intubating conditions.

METHODS AND MATERIAL

The present study was carried out in the Department of Anaesthesiology, Govt. Chengalpattu Medical College, Chengalpattu, Tamilnadu in 80 patients of either sex of ASA grade I and II between the ages of 18 and 60 years. These patients were systematically randomized into groups of 40 each, Group I (Priming group) – Receiving rocuronium bromide with priming and Group II (Control group) - Receiving rocuronium bromide without priming. Neuromuscular monitoring was done by stimulating the ulnar nerve.

STATISTICAL ANALYSIS

The data was analysed by statistical software SPSS 17.0 and XLSTAT 2013. Independent student 't' test was used to find the significance in continuous data between the two groups. Chi-square test was used to analyse categorical data.

RESULTS

Priming with 10% of the intubating dose of rocuronium bromide prior to the large intubating dose significantly reduces the onset time for intubation and the intubating conditions were excellent in both priming and non-priming technique of rocuronium bromide.

CONCLUSION

Priming technique with rocuronium bromide has beneficial effects in reducing the onset time for intubation compared to the non-priming dose; at the same time intubating conditions were comparable to the bolus injection of non-priming dose of rocuronium bromide.

KEYWORDS

Rocuronium, Priming, Neuromuscular Monitoring, Intubating Conditions.

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INTRODUCTION

During anaesthesia facilitation of endotracheal intubation is achieved by administration of neuromuscular blocking agents. The understanding of neuromuscular blockers pharmacology was greatly improved and the muscle relaxants have become an important component of many anaesthetics and facilitated the growth of surgical field into new areas and with the use of innovative techniques.[1]

The only rapidly acting muscle relaxant was succinylcholine, a depolarizing muscle relaxant. There are a number of side effects associated with the use of succinylcholine like muscle fasciculation, myalgia, hyperkalaemia,[2] dysrhythmias,[3] malignant hyperthermia, masseter spasm, increased intraocular intracranial and intragastric pressures.[4] The self-taxing technique may minimize these side effects, but it was not always effective, hence not commonly practiced.

In terms of facilitating rapid endotracheal intubation, rocuronium bromide is the first non-depolarizing muscle relaxant considered to be the replacement for succinylcholine, but at a higher dose. High dose regimens are associated with a prolonged duration of action and potentially increased cardiovascular side effects.[5]

Priming is the principle by which a small sub-paralyzing dose of the non-depolarizing muscle relaxant (About 10% of the intubating dose) be given 2 to 4 minutes before a large loading dose has been shown to accelerate the onset of neuromuscular blockade for most non-depolarizing muscle relaxants by 30 to 60 seconds for endotracheal intubation.[6]

The present study was undertaken to evaluate the efficacy of the priming principle using Rocuronium Bromide in reducing the onset time for endotracheal intubation and to evaluate the intubating conditions in comparison to the bolus dose of rocuronium bromide without priming.

METHODS AND MATERIAL

After getting the approval by the Ethical Committee, study was conducted on 80 patients who underwent general anaesthesia

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with endotracheal intubation. It is a comparative prospective randomized controlled study.

Inclusion Criteria

1. Age 18 – 60 years of both sex.
2. ASA I and II
3. MPC I and II
4. Elective surgeries.

Exclusion Criteria

1. Age <18 years and >60 years.
2. ASA III and IV.
3. Patients with neuromuscular disorders.
4. Pregnancy, Hepatic and Renal disease.
5. Allergy to Rocuronium.
6. Patients receiving drugs that interfere with neuromuscular transmission.

Patients were systematically randomized into two groups of each.

Group I–Priming Group– Patients receiving rocuronium 0.6 mg/kg with priming.

Group II–Control Group- Patients receiving rocuronium 0.6 mg/kg without priming.

Preoperative Evaluation

Age, weight, height, vital parameters, history of previous anaesthesia and surgery, significant medical illness and medications and allergies were recorded in all patients. Complete physical examination, airway assessment followed by laboratory investigations was done.

Haemoglobin, PCV, Total WBC count, Differential WBC count, ESR, Urine albumin and sugar, Blood urea, serum creatinine, liver function tests, ECG, X-ray chest, Blood grouping and typing and other relevant investigations.

Anaesthesia Protocol

Preoperative visit was done to allay the anxiety and to explain the anaesthetic procedure to the patients and to obtain the informed consent. Inj. Glycopyrrolate 0.2 mg IM was given 45 minutes prior to induction and patient was shifted to operation theatre. After establishing IV line multiparameter monitoring with ECG, NIBP, SpO_2, temperature started.

Neuromuscular monitor was connected. The electrodes of the neuromuscular monitor were applied to volar aspect of the wrist, so as to stimulate the ulnar nerve whose motor point is located at 1.5 to 2.5 cm proximal to the pisiform bone on the lateral aspect of the flexor carpi ulnaris tendon. The distal electrode (negative) was placed about 1 cm proximal to the point, at which the proximal flexor crease of the wrist crosses the radial side of the flexor carpi ulnaris tendon and the proximal electrode (Positive) was placed 2.5 cm proximal to the distal electrode.[7] The electrical stimulation normally elicits finger flexion and thumb adduction. The polarity of the electrodes is less crucial when both the electrodes are close to each other at the volar side of the wrist; however, placement of the negative electrode distally elicits the greatest neuromuscular stimulation.

Inj. Midazolam 0.03 mg/kg IV and Inj. Fentanyl 2 µg/kg IV given 10 minutes before the priming dose. Total intubating dose (0.6 mg/kg) of rocuronium was diluted to 5 mL with normal saline. For group I patients, 0.5 mL of this solution was mixed with 1.5 mL saline to make it to 2 mL. In group II patients, 2 mL of normal saline was used instead of the priming dose.

Patients were pre-oxygenated for three minutes; IV injection of the priming dose 0.06 mg/kg (10% of the intubating dose) of rocuronium bromide or normal saline 2 mL was given 3 minutes before intubating dose as per randomization. The priming dose and the priming interval were chosen based on the reports of previous studies.[8,9,10,11,12]

Induction was with propofol 2 mg/kg IV, given 2.5 minutes after the priming dose or saline. Following loss of consciousness, the ulnar nerve was stimulated at the wrist using peripheral nerve stimulator. The current strength was progressively increased and then single twitch was elicited. When the maximal thumb adduction obtained the current strength was noted and 1½ times the current strength was used for eliciting Train-of-Four Stimuli.

Intubating dose of rocuronium bromide was given 3 minutes after priming dose over a period of 5 seconds. Patient was ventilated with 100% oxygen. TOF was elicited every 10 seconds and thumb adduction assessed visually. Trachea was intubated after the disappearance of the T1 of the TOF stimuli.

Time interval between the intubating dose and the loss of T1 of TOF stimuli was considered as the onset time of rocuronium bromide.

After the loss of T1 of the TOF stimuli, the trachea was intubated by an anaesthesiologist who was blinded to the study and drug preparation. Intubating conditions were noted and the intubation score recorded using an intubation scoring system described by Cooper et al and graded as excellent, good, fair and poor according to the score.

Heart rate and blood pressure were recorded at baseline, immediately after intubation, 1 minute and 5 minutes after endotracheal intubation. Anaesthesia was maintained with 33% oxygen and 67% nitrous oxide using closed circuit system and controlled ventilation.

OBSERVATION

The following Data Were Collected in this Study

1. Demographic profile such as age in years, sex, weight in kgs.
2. Onset time for intubation in seconds.
3. Intubating conditions by Cooper scoring system (Table 1, Table 2).
4. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure at baseline, intubation, 1 minute after intubation and 5 minutes after intubation.

STATISTICAL METHODS

The data was analysed by statistical software SPSS 17.0 and XLSTAT 2013. Independent student 't' test was used to find the significance in continuous data between the two groups. Chi-square test was used to analyse categorical data.

RESULTS

The two groups were comparable with respect to the age, weight and sex. There was no statistical difference between the two groups in demographic profile.

The mean onset time for intubation (Table 3) in group I was 60.0±14.5 seconds and in group II was 91.0±13.9 seconds.

There was statistically significant difference between the two groups ($p<0.0001$).

The mean score for jaw relaxation (Table 4) in group I was 2.9±0.3 and in group II was 2.8±0.4. There was no statistically significant difference between the two groups (p>0.05).

The mean score for vocal cord position (Table 5) in group I was 2.9±0.2 and in group II was 2.8±0.3. There was no statistically significant difference between the two groups (p>0.05).

The mean score for intubation response (Table 6) was 2.9±0.1 in both the groups. There was no statistically significant difference between the two groups (p>0.05).

The mean intubation score (Table 7) was 8.8±0.5 in group I and 8.6±0.7 in group II. There was no statistically significant difference between the two groups (p>0.05).

In group I 95% of the patients had excellent intubating conditions, while in group II 90% of the patients had good intubating conditions (Table 8). There was no statistically significant difference between the two groups (p>0.05).

Mean heart rate (Table 9), systolic blood pressure (Table 10), diastolic blood pressure (Table 11), mean arterial blood pressure (Table 12) at baseline, intubation, 1 minute after intubation and 5 minutes after intubation all were comparable. There was no statistically significant difference between the two groups.

Score	Jaw Relaxation	Vocal Cords	Intubation Response
0	Poor Relaxation	Closed	Severe coughing
1	Minimal Relaxation	Closing	Mild coughing
2	Acceptable Relaxation	Intermediate	Diaphragmatic coughing
3	Well Relaxed Jaws	Abducted/No Movement	No coughing

Table 1: Scoring of Intubating Conditions

Intubation Score	Grade
8-9	Excellent
6-7	Good
3-5	Fair
0-2	Poor

Table 2: Grading of Intubation Score

Group	Range	Mean±SD	t–value	p-value
I	40–100	60.0±14.5	9.753	< 0.0001
II	60–120	91.0±13.9		

Table 3: Mean Onset Time for Intubation (Student's t Test)

Group	Range	Mean±SD	t–value	p-value
I	2 - 3	2.9±0.3	1.249	0.215
II	2 - 3	2.8±0.4		

Table 4: Mean Score for Jaw Relaxation (Student's t Test)

Group	Range	Mean±SD	t–value	p-value
I	2-3	2.9±0.2	0.739	0.462
II	2-3	2.8±0.3		

Table 5: Mean Score for Vocal Cord Position (Student's t Test)

Group	Range	Mean±SD	t–value	p-value
I	2-3	2.9±0.1	0.000	1.000
II	2-3	2.9±0.1		

Table 6: Mean Score for Intubation Response (Student's t Test)

Group	Range	Mean±SD	t–value	p-value
I	7–9	8.8±0.5	1.056	0.294
II	6–9	8.6±0.7		

Table 7: Mean Intubation Score (Student's t Test)

Group	Excellent	Good	Fair	Poor	Chi square	p–value
I	38 (95%)	2 (5%)	0	0	0.721	0.396
II	36 (90%)	4 (10%)	0	0		

Table 8: Intubation Grade (Chi Square Test)

Time	Group	Range	Mean±SD	t–value	p-value
Baseline	I	72–106	84.0±8.1	1.714	0.091
	II	72–89	81.5±4.4		
Intubation	I	76–110	85.5±6.4	1.586	0.117
	II	76–92	83.5±4.6		
1 minute	I	77-99	84.5±5.6	0.447	0.656
	II	76–92	85.0±4.3		
5 minutes	I	74–93	81.0±4.4	1.377	0.172
	II	72-96	82.5±5.2		

Table 9: Mean Heart Rate Response (Student's t Test)

Time	Group	Range	Mean±SD	t–value	p-value
Baseline	I	118–138	128.5±5.5	1.836	0.070
	II	118–132	126.5±4.1		
Intubation	I	120–146	129.7±6.3	0.139	0.890
	II	118–140	129.5±6.5		
1 minute	I	120–132	127.0±4.1	0.448	0.655
	II	114–140	126.5±5.7		
5 minutes	I	118–134	124.5±5.2	0.883	0.380
	II	110-140	125.7±7.2		

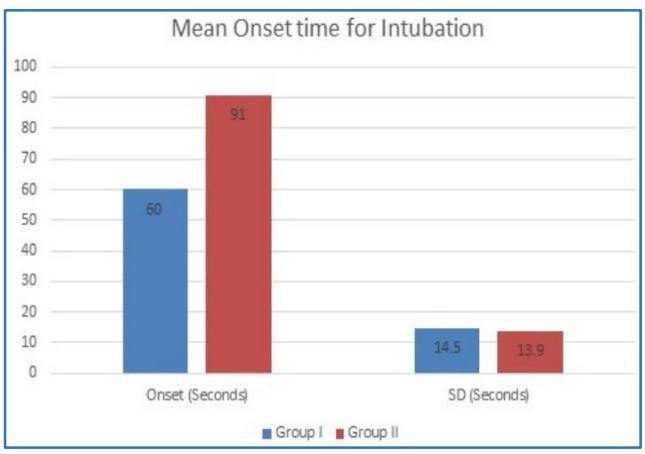
Table 10: Mean Systolic Blood Pressure Response (Student's t Test)

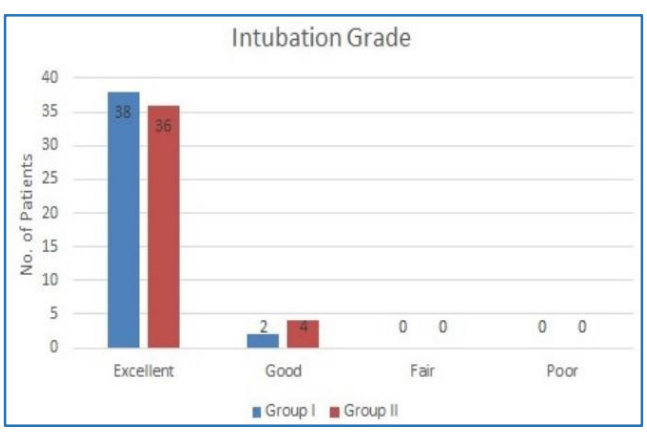
Time	Group	Range	Mean±SD	t–value	p-value
Baseline	I	70–88	81.0±4.2	0.000	1.000
	II	76–88	81.0±3.5		
Intubation	I	74–88	80.6±3.9	0.877	0.383
	II	70–90	81.5±4.7		
1 minute	I	70–94	81.1±5.4	0.851	0.397
	II	76–90	82.0±3.8		
5 minutes	I	64–90	78.1±5.0	1.454	0.150
	II	74-88	79.5±3.4		

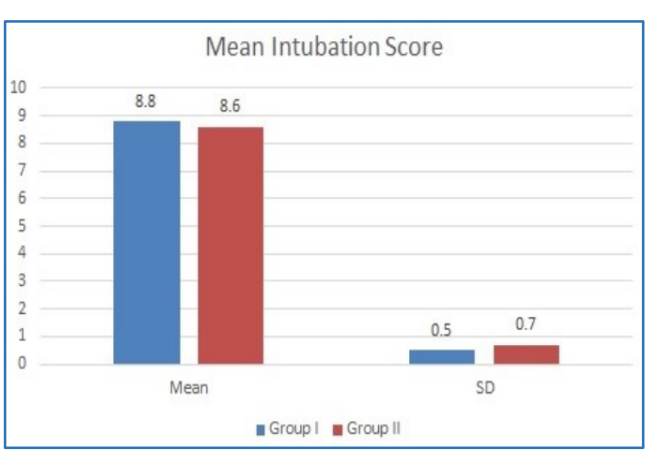
Table 11: Mean Diastolic Blood Pressure Response (Student's t Test)

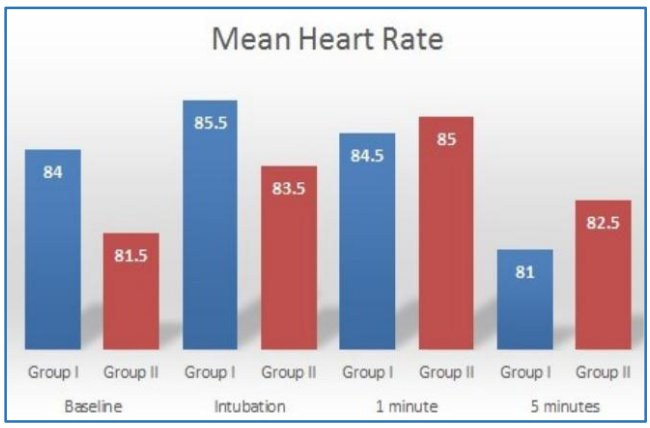
Time	Group	Range	Mean±SD	t–value	p-value
Baseline	I	90 – 104	96.5 ± 3.5	0.994	0.323
	II	90 – 102	95.8 ± 2.7		
Intubation	I	92 – 107	96.6 ± 3.4	0.634	0.528
	II	89 – 106	97.2 ± 4.2		
1 minute	I	89 – 107	96.3 ± 4.1	0.145	0.885
	II	90 – 105	96.5 ± 3.5		
5 minutes	I	83 – 101	93.5 ± 3.9	1.561	0.123
	II	87 - 104	94.8 ± 3.8		

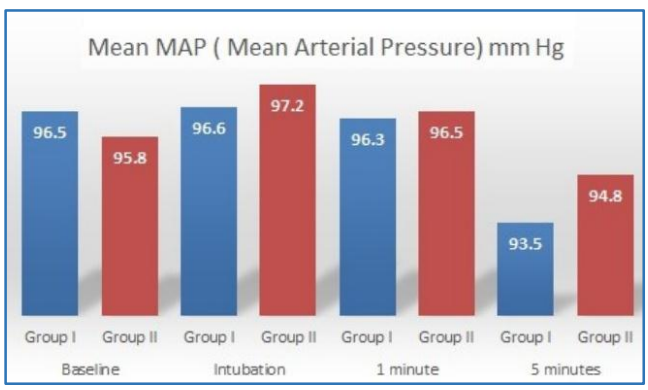
Table 12: Mean MAP (Mean Arterial Pressure) Response (Student's t Test)











DISCUSSION

Conventionally, Succinylcholine is used for rapid sequence intubation, but it is associated with several undesirable side effects. Among the non-depolarizing muscle relaxants Rocuronium bromide has the fastest onset of action, but when compared to succinylcholine the onset of action is slower at the standard 2xED95 dose. When used in doses more than 2xED95, even though the onset time is reduced it resulted in undue prolongation of the duration of action. Priming is a technique which is used to shorten the onset time for intubation with a non-depolarizing muscle relaxant.

In the present study, 80 patients were randomly divided into two groups. Group I receiving priming dose (10% of the intubating dose) and Group II receiving normal saline 3 minutes prior to the intubating dose (2xED95) of Rocuronium bromide. The intubating conditions between the two groups were studied.

This study has shown that the onset time for intubation was significantly reduced in patients receiving priming dose (Group I) prior to the intubating dose ($p<0.0001$). The onset time in group I was 60±14.5 seconds and in group II was 91±13.9 seconds.

This Result was Concurrent with the following Studies

1. Rao et al[13] concluded that the onset time of intubation was reduced in priming group (50.67±7.39 sec) compared to the control group (94±11.62 sec).
2. Griffith et al[14] revealed that the onset time with priming rocuronium (36±6 s) was significantly shorter than those without priming (59±14 s).
3. Naguib et al[15] reported that administration of rocuronium 0.06 mg/kg or mivacurium 0.015 mg/kg three minutes before the intubating dose of 0.54 mg/kg rocuronium resulted in onset time (73 and 58 sec respectively) that

resembles the onset of succinylcholine 1.0 mg/kg (54 sec); the onset time with rocuronium 0.6 mg/kg bolus group was significantly longer (90 sec) than the priming groups.

4. Soo Kyung Lee et al[16] concluded that the onset time even though reduced in priming group, it was not statistically significant.
5. In contrary, Md. Liaquatunnoor et al[17] concluded that the difference between the priming and the single dose rocuronium group was not statistically significant in terms of timing of intubation (p=0.329).

The reason for these disparities was attributed to the difference in the anaesthesia protocols. In the study conducted by Md. Liaquatunnoor et al. Inj. Thiopentone sodium 5.0 mg/kg was used as induction agent. The intubation was attempted at 30, 60 and 90 seconds after the intubating dose. Intubating conditions depend not only on the neuromuscular blockade, but also on the depth of anaesthesia. In our study propofol–fentanyl–midazolam induction was used which may influence the depth of anaesthesia.[18,19] Griffith et al also used propofol and fentanyl in his study. In Naguib et al study, anaesthesia was induced with midazolam 0.03 mg/kg followed three minutes later by Thiopentone 5-7 mg/kg and was maintained with N2O and O2 at a ratio of 70:30 and incremental doses of fentanyl. Additional thiopentone was injected before the administration of intubating dose of rocuronium.

In terms of intubating conditions, no significant difference was observed between the priming group (Group I) and the single dose rocuronium group (Group II) in jaw relaxation (p=0.215), vocal cord movement (p=0.462) and response to intubation (p=1.000). This result agreed with Griffith et al and Md. Liaquatunnoor et al[17] studies where they concluded that priming rocuronium before intubation produced no significant difference in jaw relaxation, vocal cord position and response to intubation when compared to patients receiving rocuronium bolus dose alone.

In our study, the mean intubation score of the two groups was not significantly different (p=0.294). Based on intubation score as described by Cooper et al, 95% of Group I and 90% of Group II were categorized as having excellent outcome. The rest of the respective groups had good outcome (Table 8). This result was concurrent with the study result of Rao et al[13] where the intubation score in both the priming and non-priming groups ranges from 8-9, which came under excellent grade of Cooper's scoring system. This result also agreed with the study of Soo Kyung Lee et al,[16] which concluded that the intubating condition was good-to-excellent in patients receiving priming dose of rocuronium bromide 0.06 mg/kg or pancuronium 0.015 mg/kg before the intubating dose of rocuronium bromide 0.54 mg/kg and in patients receiving rocuronium bromide bolus dose 0.60 mg/kg alone. Naugib et al also concluded that there was no significant difference in the intubating conditions between priming and non-priming groups, but he administered additional dose of thiopentone 2 mg/kg before the intubating dose to improve the intubating condition.

In the present study, there was significant reduction in the onset time for rocuronium bromide in the priming group. There was no significant difference in the intubating conditions and there was no significant change in the heart rate, systolic diastolic and mean arterial blood pressure in both groups measured at baseline, at intubation, 1 minute and 5 minutes after intubation. This was concurrent with the study of Md. Liaquatunnoor et al,[17] in which the haemodynamic variables were within normal physiological range and no significant difference were observed between the priming and non-priming groups before intubation immediately and 3 minutes after intubation.

SUMMARY

This double blinded prospective randomized controlled study was done to evaluate the onset of time and the intubating conditions with and without the priming of rocuronium bromide. The following observations were made.

- Priming rocuronium bromide with 10% of the intubating dose prior to the intubating dose significantly reduced the onset time for intubation.
- Excellent intubating conditions were obtained in both priming and non-priming groups.

CONCLUSION

Priming technique with rocuronium bromide has beneficial effect in reducing the onset time for intubation compared to non-priming dose; at the same time intubating conditions were comparable to the single bolus intubating dose of rocuronium bromide.

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