Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 03, 2023

Original research article

Efficacy and safety of rocuronium as intubating agent at different fixed doses in adults

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Abstract

Introduction: Neuromuscular-blocking drugs prevent neuromuscular transmission at the neuromuscular junction, resulting in skeletal muscle paralysis. It is accomplished by their activity on the post-synaptic acetylcholine (Nm) receptors. The neuromuscular block is clinically used adjunctively to anesthesia to produce paralysis, paralyze the vocal cords, permit intubation of the trachea, and optimize the surgical field by inhibiting spontaneous ventilation and causing relaxation of skeletal muscles. Rocuronium bromide is the new steroidal non-depolarizing neuromuscular blocking agent shown to have rapid onset of action. It has the fastest onset as compared to all other available non depolarizing neuromuscular blockers, with an onset time similar to succinylcholine.

Materials and Methods: This is a Prospective randomized study was conducted in the Department of Anesthesiology at Yashoda Hospital from February 2022 to January 2023. Over a period of 6 months among 90 patients were divided into three groups of 30 each. After 3 minutes of preoxygenation, the patient was induced with Inj. Propofol 2 to 2.5 mg / kg over 15 seconds. The H.R. and B.P. were measured. Depending on the Group, a bolus i.v. dosage of Inj. Rocuronium 0.6mg/kg (2 ED95), Inj. Rocuronium 0.9mg/kg (3 ED95), or Inj. Rocuronium 1.2mg/kg (4 ED95) was administered in 5 seconds. peripheral nerve stimulator was used to stimulate the ulnar nerve in the wrist. The current strength was gradually raised, and a single twitch was evoked. When the maximum amount of thumb adduction was accomplished, the current strength was recorded, and one and a half times the strength was utilized to elicit the Train of Four Stimulus.

Results: In our study, there is a significant difference among the three groups on mean onset time (p<0.05), but there is no significant difference between the Group 2 (0.9 mg/kg) and group 3 (1.2mg/kg). There is no significant difference among the three groups on duration of blockade, and there is a significant difference between group 2 (0.9 mg/kg) and group 3 (1.2 mg/kg) with p-value (p<0.05). There is significant difference among the groups (0.6 mg/kg, 0.9 mg/kg, 1.2 mg/kg) on systolic blood pressure after intubation, at 1 minute and 3 minutes. There is no significance among the groups at 5 minutes. There is no significance between group 2(0.9 mg/kg) and group 3 (1.2 mg/kg).

Conclusion: This study showed a significant difference of onset of action of rocuronium across various intubating conditions (73.6 seconds with 0.6mg/kg, 66.6 secpnds with 0.9mg/kg and 45 seconds with 1.2mg/kg). There is no statistical significant in change in duration of action of rocuronium across the various dosage observed. There is significant difference of intubating scores observed between group 1(0.6mg/kg) and group 2 (0.9mg/kg), group 1 (0.6mg/kg) and group 3 (1.2mg/kg) with no difference between group 2 and group 3. There is significant difference of blood pressure (systolic, dialstolic and mean) change observed across three groups but no change in heart rate.

Keywords: Neuromuscular-blocking drugs, neuromuscular transmission, acetylcholine, rocuronium bromide

Introduction

Neuromuscular-blocking drugs prevent neuromuscular transmission at the neuromuscular junction, resulting in skeletal muscle paralysis. It is accomplished by their activity on the post-synaptic acetylcholine (Nm) receptors [1].

The neuromuscular block is clinically used adjunctively to anesthesia to produce paralysis, paralyze the vocal cords, permit intubation of the trachea, and optimize the surgical field by inhibiting spontaneous ventilation and causing relaxation of skeletal muscles [2]. Mechanical ventilation should be available to ensure proper respiration since the right amount of the neuromuscular-blocking agent may paralyze muscles essential for breathing (i.e., the diaphragm) [3].

An ideal muscle relaxant should have a quick onset, deep muscular relaxation, and brief duration of action so that the patient's breathing function can be restored[1]. Even after a complete conduction block,

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 03, 2023

patients are conscious of pain; thus, general anesthetics and analgesics must be administered to avoid anesthetic awareness [4].

Rocuronium bromide is the new steroidal non-depolarizing neuromuscular blocking agent shown to have rapid onset of action [5]. It has the fastest onset as compared to all other available non depolarizing neuromuscular blockers, with an onset time similar to succinylcholine [6]. Rocuronium produces muscle paralysis by competitive antagonism to nicotine cholinergic receptors of skeletal muscles. It is about 15-20 percent potent to that of Vecuronium. With equipotent doses, the onset action of rocuronium at the adductor pollicis muscle is much faster than that of atracurium and vecuronium [7].

It has an intermediate duration of action, a swift recovery and minimal cumulation. Paralysis occurs first in the well perfused muscles and last in the diaphragm [8]. Onset of blockade is faster, but less intense at the diaphragm and adductor muscles of the larynx than at the adductor pollicis muscle [9]. The diaphragm is the last affected but recovers earlier than the adductor pollicis. The blockade produced by rocuronium is antagonized by anticholinesterases [10].

The onset time, duration of action and the intubating conditions are influenced by the dose of rocuronium. Our present study is to compare intubating conditions by using different doses of rocuronium in adults [11].

The muscle relaxant available for rapid tracheal intubation is succinylcholine. Its usage has been linked to several side effects, including bradycardia, hyperkalemia, asystole, increased intraocular pressure, and malignant hyperthermia [12].

Materials and Methods

This is a Prospective randomized study was conducted in the Department of Anesthesiology at Yashoda Hospital from February 2022 to January 2023 among 90 patients were divided into three groups of 30 each.

Inclusion criteria

1. Patient of A.S.A. grade I, II of either sex.
2. Age group 25-50 years.
3. Elective surgeries posted under G.A.
4. MPG I, II.

Exclusion criteria

1. Anticipated difficult airway.
2. Neuromuscular diseases.
3. Cardiac, renal, and hepatic disorders.
4. Known allergy to drugs.
5. Pregnant or breast feeding patients.
6. Patient refusal.

Study groups

Ninty patients who fulfilled the eligibility criteria were enrolled for the study. Preoperatively informed, written consent was obtained from these patients. These patients were systematically randomized into three groups of twenty each.

Group A: Rocuronium 0.6mg/kg
Group B: Rocuronium 0.9mg/kg
Group C: Rocuronium 1.2mg/kg

After 3 minutes of preoxygenation, the patient was induced with Inj. Thiopentone 5mg/kg 2.5 percent solution over 15 seconds. The H.R. and B.P. were measured. Depending on the Group, a bolus i.v. dosage of Inj. Rocuronium 0.6mg/kg (2 ED95), Inj. Rocuronium 0.9mg/kg (3 ED95), or Inj. Rocuronium 1.2mg/kg (4 ED95) was administered in 5 seconds. Peripheral nerve stimulator was used to stimulate the ulnar nerve in the wrist. The current strength was gradually raised, and a single twitch was evoked. When the maximum amount of thumb adduction was accomplished, the current strength was recorded, and one and a half times the strength was utilized to elicit the Train of Four Stimulus. T.O.F. was evoked every 10 seconds, and the trachea was intubated with an adequate size endotracheal tube after 90 seconds following a proper laryngoscopy.

Results

Table 1: Demographic profile

	Group 1	Group 2	Group 3	P
Gender (m/f)	10/20	13/17	151/5	
Age(years)	25.5±6.6	31.9±7.1	29.2±6.7	<0.05

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 03, 2023

Mean ± SD				
Weight (kg) Mean ± SD	51.2±10.8	51.8±14.1	52.95±8	>0.05

Group-1 has more female patients, whereas Group-3 has more male patients. Group 1 has a higher proportion of younger patients. The observed age difference between the groups is statistically significant (p<0.05). However, there is no substantial variation in the patient's weight across the three groups.

Table 2: Onset and duration

Mean			
Parameter	**Group 1 N=30**	**Group 2 N=30**	**Group 3 N=30**
Onset(Seconds)	73.6	66.6	45
Duration(minutes)	25.2	40.4	50.1

There is a significant difference among the three groups on mean onset time (p<0.05), but there is no significant difference between the Group 2 (0.9mg/kg) and group 3 (1.2mg/kg). There is no significant difference among the three groups on duration of blockade, and there is a significant difference between group 2 (0.9mg/kg) and group 3 (1.2mg/kg) with p-value (p<0.05).

Table 3: Jaw relaxation

Groups	**Impossible to open Score (0)**	**Open with Difficulty score (1)**	**Moderate Opening score (2)**	**Easy opening Score (3)**	**Mean ± SD**
Group1	2	10	14	4	1.7±0.7
Group2	0	0	12	18	2.7±0.5
Group3	0	0	10	20	2.9±0.4

There is significant difference between group 1 (0.6mg/kg) and group 2 (0.9mg/kg) on jaw relaxation (p<0.05). There is significant difference between group 1 (0.6mg/kg) and group 3 (1.2mg/kg) on jaw relaxation (p<0.05). There is no significant difference among the groups.

Table 4: Vocal cord position

	Close D (0)	**Closin G (1)**	**Moving Movement (2)**	**Open Relaxed (3)**	**Mean ± SD**
Group 1	3	7	14	6	1.7±0.8
Group 2	0	2	17	11	2.3±0.5
Group 3	0	2	5	23	2.7±0.3

There is a significant difference among the three groups on vocal cord position (p<0.05) along with a significant difference among group 2 (0.9mg/kg) and group 3 (1.2mg/kg)

Table 5: Response to intubation

	Severe Coughing (0)	**Mild Coughing (1)**	**Slight Diaphragm Movement (2)**	**No Movement (3)**	**Mean ± SD**
Group 1	2	10	11	7	1.7±0.8
Group 2	0	0	10	20	2.6±0.4
Group 3	0	0	5	25	2.8±0.3

There is significant difference on response to intubation among group 1 (0.6mg/kg) with group 2 (0.9mg/kg) and group 3 (1.2mg/kg). There is no significant difference among group (0.9mg/kg) and group 3 (1.2mg/kg).

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 03, 2023

Table 6: Systolic blood pressure

Time	Group 1	Group 2	Group 3	P-value
Baseline	108.2±7.52	121.95±14.5	122.8±14.2	0.00003
Intubation	110.1±14.3	131.3±13.3	135.9±19.02	<0.05
1 min	113.0±8.6	126.0±16.4	110.3±10.8	<0.05
3 min	120.1±14.2	123.95±7.0	109.2±10.9	<0.05
5 min	117.4±10.9	119.45±11	110.1±11.4	>0.05

There is significant difference among the groups(0.6mg/kg,0.9mg/kg,1.2mg/kg) on systolic blood pressure after intubation, at 1 minute and 3 minutes. There is no significance among the groups at 5 minutes. There is no significance between group 2(0.9mg/kg) and group 3 (1.2mg/kg).

Table 7: Diastolic blood pressure

Variable	Group 1	Group 2	Group 3	P-value
Baseline	72.5±5.9	82.1±7.7	81.12±12.5	0.001
Intubation	74.6±6.7	87.1±10.6	90.4±14.8	<0.05
1 min	79.2±12.5	86.0±9.3	72.0±5.2	<0.05
3 min	78.9±10.4	83.5±7.0	70.8±10.2	<0.05
5 min	77.0±11.9	82.7±8.8	70.1±4.4	<0.05

There is a significant difference among the groups on diastolic blood pressure at after intubation, 1 minute,3 minutes and 5 minutes. There is no difference among group 2 and group 3

Table 8: Mean arterial pressure

Variable	Group 1	Group 2	Group 3	P-value
Baseline	78.3±8.9	91.3±13.3	87.9±6.5	0.001
Intubation	79.4±8.9	97.9±9.8	92.7±17.2	<0.05
1 min	82.0±12.0	92.05±4.9	80.55±6.8	<0.05
3 min	85.25±12.0	89.55±7.8	81.25±4.9	>0.05
5 min	78.5±10.3	88.9±4.7	87.35±3.5	>0.05

It is significant among the groups on mean arterial pressure after intubation and at 1 minute.
There is no significance among group 2 and group 3

Table 9: Heart rate

Variable	Group 1	Group 2	Group 3	P-value
Baseline	78.2±17.7	86.6±13.8	100±18.9	0.00001
Intubation	90.0±13.3	96.9±11.6	107.3±16.2	<0.05
1 min	87.4±10.5	86.05±11.9	93.55±19.1	>0.05
3 min	86.25±11.0	91.55±7.8	81.25±4.9	<0.05
5 min	84.5±13.1	83.9±9.2	86.5±16.1	<0.05

There is a significant difference among the groups after intubation and at 3 minutes and
5 minutes. There is a significant difference after intubation between group 2 and group 3.

Discussion

In our study there was a significant difference with the fastest onset of action in group 3 with 45.5±9.2 seconds compared with group 1 (73.6±5.69 seconds) and group 2 (66.6±5.8 seconds). The onset of action was significant among the three groups with a p-value <0.05. The duration of action in group 1(0.6mg/kg) was 25.2 minutes, group2 (0.9mg/kg) was 40.4 minutes and in group3 (1.2mg/kg) it was 50.1 minutes.

Manoharan *et al*, [13] in 2010 compared the intubating conditions in patients receiving three different doses of rocuronium. He showed that the onset of the blockade is inversely proportional to the dose of rocuronium. The onset time for the intubating dose was significantly lower in Group 3 and between Group 1 & 2, the onset time was significantly lower in Group 2 (102.25±29.93sec in Group1, 70±20.13 sec in Group 2 and 61.2±12.95 sec in Group 3 Stoddart *et al* reported the onset time with succinylcholine 1mg/kg and rocuronium 0.6mg/kg 42 seconds and 92 seconds, respectively [14].

Our study showed a significant difference with the fastest onset of action in group 3 with 45.5±9.2 seconds compared with group 1 (73.6±5.69 seconds) and group 2 (66.6±5.8 seconds). The onset of action was significant among the three groups with a p-value <0.05

Mazurek A J *et al*, and Hann S, *et al*, [15] compared succinylcholine 1.5mg/kg with rocuronium 1.2mg/kg during rapid sequence induction. They found out that there was no significant difference in onset time of apnea for succinylcholine (22±13) versus rocuronium (16±8). They concluded that rocuronium is a

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 03, 2023

reasonable substitute for succinylcholine in children for rapid sequence induction when a rapid return to spontaneous respiration is not desired.

These observations are similar to our study. There were no significant differences among males and females in all three groups. Stoddart *et al*, [14] compared intubating conditions with succinylcholine 1mg/kg with rocuronium 0.6mg/kg and obtained 83% excellent intubating conditions with succinylcholine and 90% of people with rocuronium bromide.

In our study, we found similar results with rocuronium 1.2mg/kg Ali *et al*, [16] compared rocuronium1mg/kg with succinylcholine 1.5mg/kg for rapid sequence induction in elective cesarean sections. He found that the intubating conditions were similar in both the groups.

Cooper *et al*, [17], the intubating circumstances with rocuronium 0.6mg/kg and succinylcholine 1mg/kg were compared at 60 seconds with rocuronium. In the rocuronium group, 14/20 patients had exceptional intubating conditions, 4/20 had acceptable circumstances, and 2/20 had fair to bad conditions. In the suxamethonium group, the intubating circumstances were exceptional in 19/20 cases and satisfactory in 1/20, according to the study results.

In our study, we found that the intubating conditions were excellent in 25/30 patients with a higher dose of rocuronium, Bunburaphong *et al*, [18] evaluated the intubating conditions at 1 minute after 0.3mg/g, 0.6mg/kg, 0.9mg/kg of rocuronium in elective, elderly patients. They obtained excellent or good conditions in 50% at 0.3mg/kg, compared with 95% at 0.6mg/kg and 85% at 0.9mg/kg of rocuronium respectively. Their conclusion was rocuronium 0.6mg/kg or 0.9mg/kg is adequate for intubation at 1 minute.

In our study on comparing three different groups (0.6mg/kg, 0.9mg/kg, 1.2mg/kg) we found that intubating conditions were excellent in 50% at 0.6mg/kg, 67% with 0.9mg/kg and 85% with 1.2mg/kg and good intiating conditions in 33% with 0.6mg/kg, 33% with 0.9mg/kg and 17% with 1.2mg/kg which were similar to the above study.

Manoharan *et al*, [13] compared intubation response with three different doses of rocuronium (0.6mg/kg,0.9mg/kg, 1.2mg/kg). They obtained good intubating conditions with groups 2 and 3. When comparing Groups 2 and 3, the mean score for reaction to intubation was considerably greater than when comparing Group 1. Those in Groups 1, 2, and 3 had values of 1.55±0.82, 2.75±0.44, 2.8±0.41 correspondingly. They concluded that greater dosages result in a statistically significant improvement in the ease with which intubation can be performed. The mean total intubating score in Groups 2 and 3 was identical, which was considerably higher than the mean total intubating score in Group 1.

In our study on comparing the haemodynamic response between the Group, we found that the mean systolic blood pressure, mean diastolic pressure, and mean arterial pressure was higher in group 1(0.6mg/kg) compared to group 3 (1.2mg/kg), and statistical significance was seen among the groups. The mean heart rate did not show much difference among the groups.

Manoharan *et al*, [13] compared the haemodynamic response in three difference groups (0.6mg/kg, 0.9mg/kg and 1.2mg/kg). Statistical analysis in their study revealed that mean Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure during intubation in Group 1 was significantly higher than in Group 2 and Group 3. (108±11, 135.1±8.7, 85.45±8.9, 98.45±12.1 in Group1, 96.4±12.9,123.4±4.8, 79.05±6.5, 92.4±6.9 in Group 2 & 99.15±10.3, 126.05±7, 77.9±5.6, 92.45±6.0 in Group 3 respectively. 8. Mean Heart Rate at the end of 5 minutes was higher in Group 1 than in Group 2 and Group 3. (99.9±11.2, 86.4±10.3, 85.65±6.4 in Group 2 and 3, respectively), which was similar to our study.

Our study found no difference in heart rate among the three groups. This observation also correlates with the study of Nitschman P *et al*, [19], rocuronium dose of 0.9mg/kg produced no change in heart rate. Schramm *et al*, [20] studied the heart rate changes with rocuronium 0.6mg/kg and found no significant change in heart rate.

Conclusion

This study showed a significant difference of onset of action of rocuronium across various intubating conditions (73.6 seconds with 0.6mg/kg, 66.6 secpnds with 0.9mg/kg and 45 seconds with 1.2mg/kg). There is no statistical significant in change in duration of action of rocuronium across the various dosage observed. There is significant difference of intubating scores observed between group1 (0.6mg/kg) and group 2 (0.9mg/kg), group 1 (0.6mg/kg) and group 3 (1.2mg/kg) with no difference between group 2 and group 3. There is significant difference of blood pressure (systolic, dialstolic and mean) change observed across three groups but no change in heart rate.

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