

A Comparison on the Effects of Rocuronium and Vecuronium on Tracheal Intubation and Maintenance of Anaesthesia among Patients Undergoing Elective Surgery

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Abstract

Background: In this study we wanted to compare rocuronium and vecuronium with regard to change in hemodynamic parameters, the start time, tracheal intubation conditions, duration of action, and maintenance of anaesthesia with vecuronium and rocuronium using the TOF (Train of Four) guard monitor.

Methods: Over the course of 18 months, from November 2012 to April 2014, 60 patients who were admitted for elective surgeries to the Department of Anaesthesiology at Sree Gokulam Medical College and Research Foundation, Trivandrum, participated in this hospital-based experimental study. The study was approved by the institutional ethics committee, and written informed consent was obtained from the participants.

Results: In the rocuronium group, the mean time to the beginning of action was 122 seconds, while in the vecuronium group, it was 238 seconds. It was discovered that rocuronium has a quick start to action. The first dose's duration of effect was 31.7 minutes for the rocuronium group and 26.0 minutes for the vecuronium group. Rocuronium had an initial dose whose duration of action was noticeably longer. It was observed that, compared to vecuronium (26.2 minutes, 24.6 minutes), rocuronium had a longer mean duration of action (29.8 minutes, 29.6 minutes) during which the top-up dosages were administered. The two medications had steady hemodynamics with no discernible variations. Group A's heart rate ranged from 81.8 +/- 7.4 to 66 beats per minute, while group B's heart rate ranged from 80 +/- 6.8 to 67 +/- 6.2 beats per minute. The mean diastolic blood pressure for group A varied from 75.6 +/- 7.6 to 56, and for group B it varied from 76.56 +/- 1.7 to 63 +/- 5.0 (all values in mm of Hg). Group A saw variations in mean systolic blood pressure between 126 and 101, while group B experienced fluctuations between 126.5 +/- 4.2 and 105 +/- 3.2 (all values in mm of Hg).

Conclusion: Rocuronium appears to be a safe medication for rapid sequence intubation when there is no expectation of trouble with intubation and also for procedures of longer duration without any negative cardiovascular consequences, despite its high cost and restricted availability.

Keywords: Rocuronium, Vecuronium, Tracheal Intubation, Maintenance of Anaesthesia, Train of Four.

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Introduction

The introduction of neuromuscular blockers, or NMBs, transformed anesthesiology as a specialty and conceptually altered its practice. Both safety and the outcomes of numerous more recent and well-established surgical techniques have improved. In order to engage with the cholinergic receptor, neuromuscular blocking drugs either depolarize the endplate or compete with acetylcholine for binding sites. Depolarizing

medications tend to use the first mechanism, while non-depolarizing treatments use the second. Succinylcholine remains the only depolarizing agent in use. [1] Inhalational and intravenous anaesthetic agent dosages are reduced, mechanical breathing is facilitated, and surgical exposure is enhanced by muscle relaxants. After the discovery of neuromuscular agents, which are medications that cause narcosis, analgesia, and muscle relaxation, the term "anaesthesia" was

reinterpreted. Until the development of neuromuscular blocking medications, abdominal procedures required the use of inhalational medicines, or deep levels of ether anaesthesia, to produce sufficient muscle relaxation. [2]

In 1942, Griffith and Johnson introduced small dosages of intocostin and d-tubocurarine, which were found to enhance muscular relaxation during ether anaesthesia while simultaneously decreasing the latter's concentration. [3] With the advent of halogenated inhalational drugs, neuromuscular blockers became even more crucial because these agents required toxically large concentrations to achieve the necessary muscle relaxation, particularly for abdominal procedures. [3] What was required was a neuromuscular blocking agent with a quicker onset, a sufficient duration of action, low cardiovascular adverse effects, histamine release, residual paralysis, and allergy. Cardiovascular instability, residual paralysis, and recurrence incidence were side effects of long-acting neuromuscular blockers, pancuronium and pipercuronium, which were later used in anaesthesia practices.

The 1980s saw the introduction of vecuronium bromide and atracurium besylate for clinical use. These were non-depolarizing amino-steroid neuromuscular blocking drugs with moderate action potencies. Better hemodynamic stability, a quicker start to action, and demonstrable recovery were all present in these. Rocuronium was created in the 1990s as a result of the quest for a non-depolarizing neuromuscular blocking agent with a similar onset of action to succinyl choline, which was still the medicine with the fastest start of action. Although its structure was similar to that of vecuronium, what set it apart was its quick start of action and unmodified excretion in urine (meaning the metabolites had no side effects). In order to minimise undesired movements, protracted paralysis, and delayed recovery, neuromuscular monitoring aids in the provision of appropriate surgical conditions with the best doses of neuromuscular blocking drugs. Research has contrasted rocuronium to vecuronium, although primarily on the basis of dosage variations and adverse effects in particular clinical scenarios. Using a neuromuscular monitoring device as an adjunct, the effects of equivalent dosages of both medications on intubation and anaesthesia maintenance in patients undergoing elective procedures are studied in light of these data.

Aims and Objectives

- Using a TOF guard monitor, assess the onset time, circumstances for tracheal intubation, duration of action, and maintenance of anaesthesia with vecuronium and rocuronium.

- To compare the parameters of the hemodynamics when administering these two medications for anaesthesia.

Methods

Over the course of 18 months, from November 2012 to April 2014, 60 patients who were admitted for elective surgeries to the Department of Anaesthesiology at Sree Gokulam Medical College and Research Foundation, Trivandrum, participated in this hospital-based experimental study. The study was approved by the institutional ethics committee and written informed consent was obtained from the participants.

Inclusion Criteria

- Age: 18-50 years.
- ASA Grade: 1 or 2.
- Mallampati class: 1 or 2.
- Patients who underwent elective major surgeries.

Exclusion Criteria

- Allergic to study medication.
- Mallampati 3 and 4.
- Refusal.
- Requiring rapid sequence induction, GERD.
- With a history of cardiovascular or renal pathologies.
- With a history of neuromuscular disorders or on drugs influencing neuromuscular function.
- Pregnant patients.

Statistical Methods

The data were analysed using SPSS® software version 17.0 after they were gathered, tabulated, and coded. While frequency and percentage were used to represent categorical data, mean and SD (Standard Deviation) were used to represent numerical variables. When comparing groups based on numerical data, the unpaired student t-test was employed when suitable, while the chi-square test was utilised for categorical variables. Kruskal Wallis or Mann-Whitney U test If the data had a non-normal distribution, the U test was applied appropriately. A statistically significant difference was defined as one with a significant level (<0.05). A difference was deemed statistically very significant if it had a statistical threshold of less than 0.01.

Results

Comparison of Onset Variables

Table 1: Comparison of Group A and Group B Based on Cooper Scoring System

Copper	Group A			Group B			Z [#]	p
	Mean	SD	Median	Mean	SD	Median		
0s	0.00	0.00	0	0.00	0.00	0	0.00	1.000
30 s	2.83	1.12	3	1.53	0.63	2	4.7	0.001
60s	5.07	1.14	5	3.17	1.09	3	5.1	0.001
90s	7.07	1.36	7	4.50	1.17	5	5.89	0.001
120s	8.61	0.78	9	6.23	1.04	6	5.76	0.001
180s	9.00	0.00	9	7.57	1.19	7	2.18	0.029
240s	0.00	0.00	0	8.16	0.96	9	-	-
300s	0.00	0.00	0	9.00	0.00	9	-	-

Mann-Whitney U, p<0.05 – significant, p<0.01 – very significant

The p-value was consistently less than 0.05 following the drug's administration. According to the Cooper scoring system, there was therefore a statistically significant difference between the two groups' intubating conditions. Group A's mean Cooper score at 120 seconds was 8.61 +/- 0.78, suggesting a sufficient neuromuscular blockade for intubation, whereas group B's score was just 6.23 +/- 1.04. This demonstrates that, compared to

group B, group A received a medication that started working more quickly.

The statistical diagram pertaining to Cooper's scoring system for intubation adequacy indicates that, in the current study, group A acquired a sufficient score by the 120th second, but group B's score was not adequate at the same moment. This demonstrates group A's early dominance over group B.

Table 2: Comparison of Group A and Group B Based on TOF Response

Group	Mean (seconds)	Median (seconds)	N	Z [#]	p
Group A	122	120	30	6.56	0.001
Group B	238	240	30		

Mann-Whitney U, P value < 0.01, very significant

The time interval between the study drug's last injection and the elimination of three responses to a four-stimulation training set was used to determine the start of the effect. Group A's mean onset time was 122 seconds, whereas group B's was 238 seconds.

There was a highly significant difference between Group A and B regarding the commencement of action, as indicated by the p-value being 0.001 less than 0.01. This demonstrates that, compared to group B, group A received a medication that started working more quickly.

Table 3: Comparison of Groups A and B Based on Primary Durations

Group	Mean (minutes)	Median (minutes)	N	Z [#]	p
Group A	31.7	30	30	5	0.001
Group B	26.0	25	30		

Mann-Whitney U, p<0.01 – Very significant

The primary duration measures the amount of time that passes between the drug's intravenous injection and the onset of the first twitch in response to the TOF stimulus.

The mean primary durations of groups A and B are shown to be 31.7 and 26.0 minutes, respectively.

The statistical significance of the difference in the primary duration of action is indicated by the p-value, which was less than 0.05.

After the intubating dose, the medication in group A therefore had a longer duration of action than that of group B.

Table 4: Comparison of Groups A and B Based on Duration of Top-Up Doses

	Group A			Group B			Z [#]	P
	Mean (in minutes)	Median (in minutes)	N	Mean (in minutes)	Median (in minutes)	N		
Top-up 1	29.8	30	24	26.2	25	30	2.43*	0.015
Top-up 2	29.6	30	14	24.8	25	26	3.25**	0.001
Top-up 3	25.6	25	8	24.7	25	15	0.59	0.553
Top-up 4	25.0	25	1	22.9	25	7	-	-
Top-up 5	0.0	0.0	0	22.5	22.5	2	-	-

Mann-Whitney U, p<0.05 is significant p<0.01 is very significant

With a p-value less than 0.05, the first supplemental top-up dosages in groups A and B took an average of 29.8 and 26.2 minutes, respectively.

With a p-value less than 0.05, the mean duration of the second supplemental top-up doses in groups A and B was 24.8 minutes and 29.6 minutes, respectively.

The third supplemental top-up dosage took an average of 25.6 minutes for group A and 24.7 minutes for group B.

For groups A and B, the fourth supplemental top-up dose took an average of 25 minutes and 22.9 minutes, respectively.

The mean duration of action between the two medications after the first and second additional dosages differs statistically significantly. Group A also saw longer top-up periods on the third and fourth occasions.

Following group A's first and second supplemental medication dosages, group A experienced a longer mean duration of effect than group B.

Table 5: Comparison of Overall Duration of Groups A and B Based on Subgroups of Gender

		Mean (minutes)	Median (minutes)	N	Z [#]	p
Group A	Male	31.1	30.0	14	0.34	0.759
	Female	30.3	30.0	16		
Group B	Male	24.4	23.8	12	2.11*	0.035
	Female	26.3	26.7	18		

Mann-Whitney Up<0.05 is significant p<0.01 is very significant

Within each group, the gender-based means of the two groups' overall average durations of action are compared.

For the male and female gender groups in group A, the mean durations were 31.1 and 30.3 minutes, respectively.

There was no statistically significant difference in the overall average duration of action by gender, as indicated by the fact that the p-value for group A within the various sex groups was more than 0.05.

For the male and female gender groups in group B, the mean durations were 26.4 and 24.4 minutes, respectively.

There was a statistically significant difference in the total average length of action with gender, as indicated by the p-value for group B within the various gender groups being less than 0.05.

For both genders, the mean total length of action was 26.3 and 24.4 minutes, respectively. As a result, group B's average duration is longer in females than in males.

Discussion

The field of anaesthesia and its practice have evolved as a result of neuro-muscular blocking medications. "The first use of muscle relaxants not only ushered in the modern era of surgery and enabled the rapid advancement of neurology, cardiothoracic, and organ transplant surgery, but it also revolutionised the practice of anaesthesia." – Foldes and others. "The perfect" neuromuscular inhibitor, as described by Booij and Crul in 1983.^[4]

1. The action mechanism is non-depolarizing
2. Quick start of action.
3. Brief action duration.

4. Quick recuperation.
5. High strength.
6. No release of histamine.
7. No adverse effects on the heart.
8. Not cumulative.
9. Reversible using inhibitors of cholinesterase.
10. Metabolites that lack pharmacological activity.

The sixty/six patients in this study were admitted for elective procedures and were classified as class I and class II by the American Society of Anaesthesiologists (ASA). Depending on the kind of non-depolarizing muscle relaxant employed, they were randomly divided into two equal groups of thirty each.

- a) Group A: Thirty randomly chosen patients were given maintenance doses of 0.15 mg/kg in addition to 0.6 mg/kg of rocuronium at first.
- b) Group B: Thirty randomly chosen patients were prescribed an initial dose of 0.08 mg/kg of vecuronium and a maintenance dose of 0.025 mg/kg.

Ali H. H. invented TOF in the 1970s. [5] Without evoking an evoked response, it can be used to gauge the dosage of a non-depolarizing relaxant to a specific degree of blockage. Data was acquired and the thumb's movement in response to an application of stimulus to the ulnar nerve was seen. The fourth response in the train is removed at roughly 75% depression of the first twitch when neuromuscular block occurs. At 80% suppression of the first twitch, the third and fourth twitches disappear, and at 90% block of the first twitch, the second twitch is no longer visible.

By measuring the number of twitches in the train-of-four response, the degree of block and the dosage of non-depolarizing relaxant needed to reach a particular level of muscular relaxation can be determined. [5] It is generally agreed upon that a reasonable level of clinical relaxation is defined as neuromuscular block ranging from 95% to 75% twitch inhibition. In this study, the ulnar nerve at the wrist was used to count the adductor pollicis muscle's responses to four different types of stimulation. This method was used to monitor and evaluate neuromuscular function.

The following variables were tracked in order to evaluate the neuromuscular medications:

1. When the action starts?
2. How long does the first dose take to take effect?
3. The time that top-up doses take to start working.
4. The total length of both medications in relation to demographic factors.
5. Both medications' hemodynamic stability.

Demographic or Background Characteristics

Age, gender, and weight were equivalent between the rocuronium and vecuronium groups in the current study.

Comparison of Variables of Onset

The time interval between the study drug's injection and the elimination of three responses to a training set of four stimuli (a 90% block) was used to determine the research's beginning of action.

Based on the TOF stimuli, the mean time of onset for rocuronium was 122 seconds and for vecuronium it was 238 seconds in this investigation. There was a statistically significant difference in the onset times of both medications ($p = 0.001$).

The rocuronium group had a mean score of 8.61 ± 0.78 , while the vecuronium group had a mean score of 6.23 ± 1.04 at 120 seconds, according to the Cooper scoring method. This difference was statistically significant ($p = 0.01$) and showed that the vecuronium group had not attained the same level of blockage when the rocuronium group's degree of muscular relaxation was sufficient for intubation.

Therefore, based on the results of this investigation, it can be said that rocuronium acts more quickly than vecuronium.

Rocuronium's start of action in this study is similar to that of Alvarez – Gomez JA. [6] Additionally comparable are the findings of Mirakhur [7] and Foldes. [8]

The present study's period of action onset is consistent with the research conducted by Wierda JMKH[9] and Krieg N [10] Although it wasn't exactly the same, the dose range in Gramstad's [11] study is comparable to the current one.

The current investigation supports the findings of Booth MG, et al. [12] and Bartkowski RR et al. [13] who examined the equipotent dosages of rocuronium and vecuronium and discovered that rocuronium had a faster start time with very high statistical significance. Similar findings were reached by Carroll MT, Wierda JMKH, and Lin PL et al. [14]

Comparison of Variables Duration of Action

The Primary Duration of Action

The time interval between the start of the medication and the first twitch in the Train of Four was the primary duration of action in this investigation. Top-up doses were added after the first twitch in the TOF had recovered.

The mean main durations of rocuronium and vecuronium were found to be 31.7 and 26.0 minutes, respectively. The statistical significance of the difference in the primary duration of action is demonstrated by the p-value of 0.001, which is less than 0.01. Therefore, it may be concluded that, following the intubation or initial dose, rocuronium had a longer duration of action than vecuronium.

Depending on the amount used, the initial rocuronium dose's duration of action varied among studies, lasting anywhere from 11 to 40 minutes.

Various studies have determined that the duration of action of the first dose of vecuronium varied depending on the dose used, ranging from 22 to 43 minutes. The current study and the research by Carroll MT and Foldes FF support the finding that rocuronium requires a longer initial dosage duration than vecuronium. The research of Foldes FF, however, was not consistent with this.

The Duration of Action of Top-Up Doses

Following the return of at least one discernible response to TOF stimulation, a top-up dosage of the non-depolarizing relaxant was administered to maintain sufficient clinical relaxation for surgery by achieving >90% block. Group A received maintenance doses of injections of rocuronium (0.15 mg/kg) or vecuronium (0.025 mg/kg) as top-ups each time the TOF stimulus elicited a single response.

A statistically significant difference was seen between the mean duration of effect of the top-up dosages for rocuronium (29.8 minutes, 29.6 minutes) and vecuronium (26.2 minutes, 24.6 minutes).

Therefore, assuming that rocuronium and vecuronium were taken into consideration separately, it was concluded that the duration of the effect of future top-up dosages was comparable.

The Overall Duration of Action with respect to Demographic Variables Gender

Within each group, the gender-based means of the two groups' overall average durations of action are compared.

The mean durations for rocuronium in the male and female gender groups were 31.1 minutes and 30.3 minutes, respectively. The overall average time of action does not change statistically significantly based on gender; $p > 0.05$ (0.759).

The mean durations for vecuronium in the male and female gender groups were 24.4 and 26.3 minutes, respectively. A statistically significant difference ($p < 0.05$, 0.035) has been observed between gender and the total average duration of action.

In the instance of vecuronium in the current investigation, the total average duration is thus longer in females than in males; however, there was no such difference in the case of rocuronium.

Comparison of Intra Operative Haemodynamic Variables

When rocuronium and vecuronium were compared based on variations in heart rate during the procedure, it was observed that it ranged between 81.8 \pm 7.4 and 66 beats per minute for group A and between 80 \pm 6.8 and 67 \pm 6.2 for group B. These heart rate measurements did not deviate significantly from the pre-drug values, and the p-value was consistently greater than 0.05. Therefore, it can be said that there are no appreciable differences between the two groups in terms of intraoperative heart rate changes. During the surgery, rocuronium and vecuronium were compared based on changes in systolic blood pressure. For group A, the mean systolic blood pressure varied between 126 and 101, while for group B, it fluctuated between 126.5 \pm 4.2 and 105 \pm 3.2 (all values in mm of Hg). The p-value was consistently over 0.05, and these values did not significantly differ from the pre-drug systolic blood pressure reading. Thus, it can be said that there are no appreciable variations in intraoperative changes in systolic blood pressure between the two groups.

Rocuronium and vecuronium were compared based on changes in diastolic blood pressure that occurred during the surgery. For group A, the mean diastolic blood pressure varied between 75.6 \pm 7.6 and 56, and for group B, it varied between 76.56 \pm 1.7 and 63 \pm 5.0 (all values in mm of Hg). The p-value was consistently over 0.05, and these results did not significantly differ from the diastolic blood pressure levels before the medication. Thus, it may

be said that there are no appreciable variations in intraoperative changes in diastolic blood pressure between the two groups.

Therefore, it can be said that this study shows that, at the corresponding doses utilised, both rocuronium and vecuronium have no statistically significant effects on hemodynamic parameters and are hemodynamically stable. The numerous studies mentioned above all corroborate this conclusion.

Patients received reversal injections of neostigmine (0.05 mg/kg) and glycopylorate (8 mcg/kg) only after all four responses to the Train of Four were restored following the delivery of TOF stimuli. Extubation was performed following the proper suctioning, and three minutes later, a second train of four stimuli was performed and the muscular contraction was evaluated. The patients recovered fully and without incident.

Conclusion

We conclude that, despite its high cost and restricted availability, rocuronium seems to be a safe medication for rapid sequence intubation where no difficulties with intubation are expected, as well as for long-term procedures without any negative cardiovascular consequences.

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