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Rocuronium Versus Vecuronium in Endotracheal Intubation and Maintenance in General Anaesthesia

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Abstract

Introduction: Adequate maintenance of airways in patients undergoing surgeries under general anaesthesia was through proper intubation. Succinylcholine was the most opted neuromuscular drug in the past 50 years administered for tracheal intubation. A number of adverse reactions with its use. *Aim:* To evaluate onset time, tracheal intubation conditions, duration of action and maintenance of anaesthesia using two none depolarizing muscle relaxants vecuronium and rocuronium. *Materials and methods:* The study population consisted of 50 patients of ASA physical status I and II in the age group 18 to 50 years.The present studies was undertaken to evaluate the neuromuscular and haemodynamic properties of Rocuronium bromide and to compare it with Vecuronium bromide. Of the 50 patients studies, 25 patients received 0.6 mg/kg of Rocuronium bromide for the maintenance of anaesthesia and the other 25 patients received 0.1 mg/kg of Vecuronium bromide. The top-up doses administered were 0.15 mg/kg of Rocuronium and 0.025 mg/kg of Vecuronium. In both the groups, the efficacy of nondepolarizing muscle relaxant was assessed. *Results:* The onset time was significantly shorter in the Rocuronium group (108.8 seconds /mean±SD was ±28.875) compared to Vecuronium group (188.76 seconds/ mean SD±43.78). The duration of action of first dose was significantly longer in Rocuronium group (31.5 minutes) compared to Vecuronium group (24.5 minutes). The duration of action of top-updoses was similar in both the groups (p>0.05). There was no significant difference in any of the haemodynamic variables (Heart rate, Systolic blood pressure, Diastolic blood pressure and meanarterial pressure) between the two groups. All the patients in both the groups were easily reversible with Neostigmine (0.05 mg/kg) and no adverse reactions were found in any patient. *Conclusion:* Rocuronium has a significantly rapid onset of action and intermediate duration of action. It is easily reversible and produces no significant cardiovascular changes. It also has a good safety profile. Therefore, inspite of its high cost. Rocuronium appears to be the safest drug, near toideal NMBA for rapid sequence intubation and routine intubation when there is no anticipated difficulty in intubation.

Keywords: Rocuronium; Vecuronium; Endotracheal Intubation.

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Introduction

The introduction of neuromuscular blocking drugs into clinical practice representsone of the most significant advances in the development of anesthesiology and has revolutionized the practice of anesthesia. The use of neuromuscular blocking drugs has increased the safety and improved the results of many established surgical procedures aswell as many new ones. Abdominal surgeries require muscle relaxation for efficacious operating conditions. Before the advent of neuromuscular blocking drugs, surgical relaxation was achieved with the use of inhalation anesthetics. At deep levels of ether anesthesia relaxation of abdominal musculature is sufficient

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to permit exploratory laparotomy. Following the introduction of d-Tubocurarine, small doses of the same were seen to amplify muscle relaxation during either anesthesia and allow reduction of inhalational anesthetic concentration The advent of neuromuscular blocking drugs in the 1940's facilitated many advances in abdominal and thoracic surgeries. Muscle relaxants not only enhance surgical exposure but also facilitate mechanical ventilation and minimize the doses of general anesthesia. As halogenated anesthetics replaced ether in common practice, a greater need torely on curare-type drugs to block neuromuscular transmission developed, since the muscle relaxing properties of the halogenated anesthetics was not adequate for abdominal surgery unless high and toxic concentrations were used.

In Nearly simultaneous introduction of the two muscle relaxants, Atracuriumbesylate and Vecuronium Bromide, both intermediate acting, non-depolarizing aminosteroid neuromuscular blocking drugs, provided a break through by a faster onset, rapid and measurable recovery with little dependence on the kidneys for elimination and great haemodynamic stability. However, there was a need for a non-depolarizing neuromuscular blocking drug, which has a rapid onset of action. Continuous search for a non-depolarizing muscle relaxant with rapid onset of action led to the synthesis of Rocuronium. Rocuronium, anewer non-depolarizing muscle relaxant was introduced in 1990s. Its similar in structure and properties to Vecuronium but had an added advantage of rapid onset of action and unchanged excretion in urine thereby eliminating the side effects of the metabolites. Its introduction is considered an added advantage over Vecuronium. Neuromuscular monitoring helps to balance adequate surgical relaxation with safe restoration of neuromuscular function at the end of the procedure. It provide ideal operating conditions with optimal doses of muscle relaxant and helps to minimize side effects like unwanted movements, prolonged paralysis and delayed recovery. In the light of the above observations Rocuronium is compared with Vecuroniumas relaxants for abdominal surgeries using peripheral nerve stimulator as an adjunct in the study.

Materials and Methods

This was a randomized, prospective clinical double blinded trial studied over a period of 2 years from November 2012 to March 2014 in the Department of Anaesthesiology, Hyderabad.

Inclusion Criteria

1. Patients in age group of 18 to 50 years.
2. ASA Gr 1 or 2
3. Mallampatti class 1 or 2.
4. Patient who underwent elective general surgeries, orthopedic surgeries, gynaecological Surgeries, urological surgeries and ear, nose and throat surgeries

Exclusion Criteria

1. Patients with difficult airway [mallampati Gr 3 or 4].
2. Gastro esophageal reflux disease.
3. Known allergy to any of these drugs or its constituents.
4. BMI >25%.
5. Heavy smokers.
6. Patients with history of cardiovascular or renal disorders.
7. Patients with neuromuscular disorders or medications known to influence neuromuscular functions.
8. Hypertensive patients.
9. Pregnant patients

Patients were randomized into one of the two groups. Group V {Vecuronium} and Group R (Rocuronium) of 25 each for induction and maintenance of anaesthesia [sample size was taken in accordance with similar type of studies done in the past]. Pre-anaesthetic assessment was done the evening prior to the day of surgery. A detailed history was taken examination and investigation were reviewed. Informed consent was obtained after explaining the procedure to the patients. Tab. Diazepam 5 mg and Tab. Ranitidine 150 mg was given night before the surgery and morning of the day of surgery 1½ hours prior to the time of surgery. All the patients were fasting for at least 6 hours before surgery. Non-invasive monitors like Electrocardiogram (ECG), Non-invasive BP, and pulseoximetry were connected to the patient. Intravenous access was established and slow infusion of crystalloids commenced.

Prior to the induction of anaesthesia, patients in both groups were premedicated with midazolam 0.025 mg/kg, inj glycopylorate 5 mcg/kg and fentanyl 1 mcg/kg. Patient were preoxygenated with oxygen 100% for a period of three minutes followed by which patient were induced with inj Thiopentone 4 mg/kg intravenously. Patients in group V received vecuronium 0.1 mk/kg [9] and those in group R received rocuronium 0.6mg/kg

[7].

After the administration of the drug the clinical efficacy of the drug will be monitored by the adequacy of relaxed jaw movements a free mouth opening followed by viewing of a relaxed vocal cord using a laryngoscope. Intubating condition were scored as excellent [8-9], good [6-7], fair [3-5], and poor [0-2] according to a system described by Cooper.

Cooper Scoring System

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Impossible to open	Closed/ bucking	severe coughing
1	Opens with difficulty	Closing	Mild coughing
2	Moderate opening	Moving movement	Slight diaphragmatic
3	Easy opening	Open [relaxed]	No movement

Haemodynamic parameters like systolic, diastolic blood pressure and Heart Rate were recorded at base line during pre-oxygenation and 1st, 3, 5th and 10 minutes after induction. Trachea was intubated using a suitable size portex endotracheal tube. Anaesthesia was than maintained with 40% O_2 and 60% N_2O. After an effective tracheal intubation after 10 minutes maintenance dose of inj vecuronium 0.025 mg/kg and injrocuronium 0.15 mg/kg was anaesthesia was continued with O_2, N_2O, and halothane. During the conduct of anaesthesia patients vital were monitored regularly. Patients were administered reversal with inj neostigmine 0.05 mg/kg and injglycopylorate 5 mcg/kg. After appropriate suctioning extubation was done and readings measured.

Statistical Methods

Chi square test of significance has been used to find the significance of sex distribution between the two groups. Student t test has been used to find the significance of Haemodynamic parameters and duration of action in minutes between the two groups and to find the homogeneity of samples for age and weight between two groups.

Statistical software

The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, Tables etc. The inferences based on 'p' value were made as follows:

p>0.05 – Not significant: p<0.05 – Significant

Results

In the present study, 50 patients aged between 18 and 50 years belonging to ASA grade I and II were randomly divided into two groups, each group consisting of 25 patients.

Group V: Patients received Inj. Vecuronium as the non-depolarizing muscle relaxant for Intubation and maintenance of anaesthesia.

Group R: Patients received Inj. Rocuronium as the non-depolarizing muscle relaxant for Intubation and maintenance of anaesthesia.

Table 1: Demographic Data

	Group V		Group R	
	No	%	No	%
<20	1	4.0	0	0
21-30	8	32.0	8	32.0
31-40	10	40.0	7	28.0
41-50	6	24.0	10	40.0
Total	25	100	25	100
Mean±SD	34.64/ SD±9.26		37.2/SD±9.2	
Interference	Samples are age matched with p=0.332			
40-50	5	20	4	16
50-60	6	24	6	24
>60	14	56	15	60
Interference	samples are weighed matched with p =0.628			
Male	15	60	10	40
Female	10	40	15	60
Interference	Samples are sex matched with p=0.258			

The mean age in Group V was 34.64 years whereas in Group R it was 37.20 years. The difference in the mean age of the patients between the two groups was not statistically significant (p=0.332). The maximum number of patients in both the groups were above 60 kgs (56% in Group V and 60% in Group R). The mean weight in Group V was 60.68 kgs and in Group R was 59.12 kgs. The difference was statistically not significant (p=0.628).

The study comprised of 25 males and 25 females. Group V comprised of 60% (15) males and 40% (10) females whereas Group II comprised of 40% (10) males and 60% (15) females. The result of sex distribution was not statistically significant (p=0.258).

Table 2: Cooper score in relation to onset of Action

Seconds	Rocuronium	SD	Vecuronium	SD
0	0		0	
30	1.12	0.44	0.72	0.46
60	1.88	0.53	1.04	0.20

90	2.46	0.59	1.6	0.50
120	2.83	0.50	1.88	0.33
180	3	0.00	2.6	0.58
240			3	0.66
300			2.67	
360				

In relation to onset of action and cooper scoring for adequacy for intubation it was found that in the present study in Group R a score of more than 2.5 was achieved by the 120th second whereas in Group V only 1.8 was achieved in 120th second. This shows the rapid onset of group R over Group V.

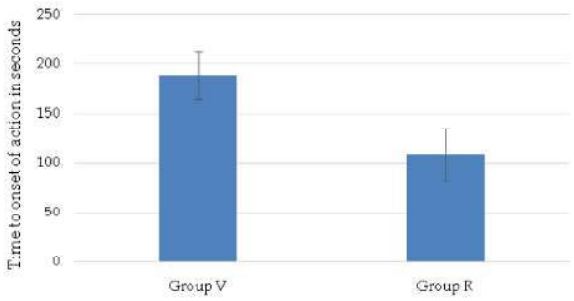

Fig. 1: Time to onset of action in both groups

Onset of action was taken as the time from the end of injection of the study drug to abolition of three responses to train of four stimulation. The maximum time to onset of action in Group V was 324 seconds and in Group R was 160 seconds. The minimum time to onset of action in Group V was 135 seconds and in Group R was 55 seconds.

The duration of action between the two groups, Group R had a longer duration of action when compared to vecuronium and also had a significant p value of 0.01. the top up doses also indicated that rocuronium seem to have a prolonged action than rocuronium.

Hemodynamic variables

In comparison between the two drugs there does not seem to be drastic variation in the heart rate systolic, diastolic blood pressure and the respiratory rate. There was only one patient who had a high systolic blood pressure before induction of anaesthesia and which later got optimized after induction of anaesthesia without any anti hypertensives.

Discussion

The introduction of neuromuscular blocking drugs into clinical practice represents one of the most significant advances in the development of anesthesiology and has revolutionized the practice of anesthesia. The use of neuromuscular blocking drugs has increased the safety and improved the results of many established surgical procedures as well as many new ones. As stated by Foldes and co-authors [1] "the first use of muscle relaxants not only revolutionized the practice of anesthesia but also started the modernera of surgery and made possible the explosive development of cardiothoracic, neurological and organ transplant surgery".

Abdominal surgeries require muscle relaxation for efficacious operating conditions. Before the advent of neuromuscular blocking drugs, surgical relaxation was achieved with the use of inhalation anesthetics. At deep levels of ether anesthesia relaxation of abdominal musculature is sufficient to permit exploratory laparotomy. Following the introduction of d-Tubocurarine, small doses of the same were seen to amplify muscle relaxation during either anesthesia and allow reduction of anesthetic depth.

As halogenated anesthetics replaced ether in common practice, a greater need to rely on curare-type drugs to block neuromuscular transmission developed, since the muscle relaxing properties of the halogenated anesthetics was not adequate for abdominal surgery unless high and toxic concentrations were used.

Booij and Crul [2] spelled out the requirements for the ideal neuromuscular blocking agent. Rocuronium has been shown to possess most of these properties of an "ideal" muscle relaxant except the high potency. Since, it has been shown

Table 3: Duration of action of intial and top up doses

Doses	Group V Mean [minutes]	Group Mean [minutes]	Group V SD	Group R SD
Intial dose	24.5	31.5	7.54	8.9
1 st top up	24.73	28.48	5.5	4.8
2 top up	24.44	28.14	6.6	5.27
3 top up	23.50	28.25	7.36	6.8
4 top up	20.50	31.50	6.65	2.12
5 top up	25			

by studies that a rapid onset of action, with a non-depolarizing muscle relaxant, is almost only produced by compounds of relatively low potency, Rocuronium which has a rapid onset has a very low potency.

The present study was undertaken to study the neuromuscular properties and cardiovascular effects of Rocuronium, the 'near-ideal' muscle relaxant and to compare it with Vecuronium, an already established drug. It is generally acknowledged that the response to neuromuscular blocking drugs is unpredictable in the population at large. This is more so in several physiologic andpathologic conditions directly or indirectly involving the neuromuscular junction. The monitoring of neuromuscular function provides valuable information to the anaesthesiologist and contributes to a more predictable and rational approach to the use of muscle relaxants, and hence to better patient care.

The study comprised of 50 patients of ASA grade I and II and patients with neuromuscular or systemic disease of significance were excluded. 25 patients each were randomly allocated to two groups for administration of the two study drugs, Group V (patients who received Vecuronium as the muscle relaxant for intubation and maintenance of anaesthesia) and Group R (patients who received Rocuronium as the muscle relaxant for intubation and maintenance of anaesthesia).

Foldes FF and colleagues [1] have studied the neuromuscular effects of Rocuronium in patients receiving balanced anesthesia with thiopental and nitrous oxide – oxygen. Both M G and colleagues while comparing the pharmacodynamics of Rocuronium and Vecuronium used halothane during maintenance of anesthesia. Maddineni VR et al [3] studied the duration of action and haemodynamic effects of Rocuronium bromide under balanced and volatile anaesthesia.

In the present study, patients were administered thiopental for induction and nitrous oxide-oxygen with halothane for maintenance of anaesthesia. The two groups are similar in terms of age, weight and sex distribution. Kreig N [4] performed a clinical study of pharmacodynamics of Vecuronium in doses of 0.06 mg/kg and 0.07 mg/kg and concluded that onset time was between 3 and 4 minutes.

In group R (Rocuronium group) the mean onset time of action was 108.8 seconds (mean±SD was ± 28.875). The present study concurs with the findings of the studies of Alvares Gomes, Mirakhur RK5 and Foldes FF [1] who have also reported the onset time similar to the present study. In relation to onset of action and cooper score for adequacy of intubation, it was found that in group R a score of 2.5 and above was achieved by 100-110 seconds whereas for group V a score of 1.7 was only achieved at at time interval of 100-110 seconds which shows the rapid onset of group R. A maximum score of 3 was obtained in group R by 120 to 150 seconds, whereas to achieve the maximum score in group V it took about 180-240 sewconds. Onset of action in Group R (Rocuronium) was rapid compared to Group V (Vecuronium) with very high statistical significance ($p<0.001$). The present study is in agreement with the study of Booth MG et al and Bartkowski RR et al. [6] who compared the onset of action of equipotent doses of Rocuronium and Vecuronium. Rocuronium onset time was found to be faster with very high statistical significance. Similar Observations were made by Bartkowski RR [6]**.** The faster onset of action of Rocuronium has been attributed to its low potency.

This necessitates a higher dose, which ensures the presence of more relaxant molecules in the bloodstream and thus due to a higher concentration gradient, the transport towards thebio phase is faster.

The duration of action of the initial dose of Vecuronium observed by various authors ranged from 22 minutes to 43 minutes depending on the dose employed. The various authors who have studied the duration of action of different initial doses of Vecuronium and the reported duration of action as follows:

In Group V (Vecuronium group) the duration of action of initial dose was 17-32 minutes (mean 24.5 minutes). The duration of action of the initial dose of Rocuronium observed by various authors ranged from 11 minutes to 40 minutes depending on the dose employed. The various authors who have studied the duration of action of different initialdoses of Rocuronium and the reported.

In Group R (Rocuronium group) the duration of action of initial dose was 13-50 minutes (mean 31.5 minutes). The duration of action of initial dose of Rocuronium in the study correlates with the findings of Mirakhur RK and Carroll MT who have found similar duration of action with a dose of 0.6mg/kg of Rocuronium. In group V (Vecuronium) the mean duration of action was 24.5 min and in group R (Rocuronium) it was 31.5 min. This difference was found to be statistically significant ($p<0.01$). In the studies of Levy JH et al., Lambalk LM et al. [7], Foldes FF et al. [1], the top-up dose of Rocuronium administered was 0.15mg/kg. In the

present study, the top-up dose administered was 0.025 mg/kg of Vecuronium and 0.15 mg/kg of Rocuronium.

There was no prolongation of duration with subsequent doses of Vecuronium inthe studies by Crul JF et al. [2] The duration of action of the maintenance doses of Vecuronium in the present study ranged from 21.8 minutes for first maintenance to 25 min for 6th maintenance and there was no prolongation of duration with subsequent doses. There was no prolongation of duration with subsequent doses of Rocuronium inthe studies by Lambalk LM et al. [7] who found no increase in the duration of the maintenance doses even after 4 to 5 doses and the duration ranged from 15.1 to 18.7 minutes. The duration of action of the maintenance doses of study ranged from 25.3 minutes for first maintenance to 27 minutes for fourth maintenance and there was no prolongation of duration with subsequent doses.

This finding of the present study is in agreement with the study of Maddineni VR et al. [3] who studied the haemodynamic effects of Rocuronium in the doses of 0.6 mg/kg and 0.9 mg/kg under balanced and volatile anaesthesia. They concluded that no significant change in heart rate occurred with both doses and both techniques.

This observation also correlates with the study by Hudson ME et al. [8] with Rocuronium in a dose of 0.6 mg/kg wherein they concluded that no changes in heart rate occurred with the given dose of Rocuronium.

Levy JH [9] studied the heart rate changes with Rocuronium in doses ranging from 0.6 mg/kg to 1.2 mg/kg and found no significant changes in heart rate even in high doses.

The heart rate differences between the two groups were compared at every 2 minute interval for the first ten minutes after onset of action of the non-depolarizing muscle relaxant and followed by every 5-minute interval for next twenty minutes and than every fifteen minutes till the end of surgery. The difference in mean heart rate between the two groups was not significant at any timeinterval ($p>0.05$).

In Group V (Vecuronium group), the systolic blood pressure at pre-induction level Was 128.16 mm of Hg? At onset of action of Vecuronium the systolic blood pressure was 130.52 mm of Hg. Throughout the study period the systolic blood pressure remained between 124.24 mm of Hg to130.88 mm of Hg, which was comparable to the pre-drug level, and there was clinically no significance in p value Ease of reversibility in the present study was assessed by clinical criteria for neuromuscular recovery.

Mirakhur R et al. [5] compared the antagonism of Vecuronium induced neuromuscular blockade by either edrophonium or neo stigmine and found adequate antagonism in all patients given neostigmine. Wicks TC [10] and Lambalk LM et al. [7] have found in their studies that neuromuscular block induced by Rocuronium is promptly reversed with conventional doses of cholinesterase inhibiting drugs.

In the present study, in both the groups, Inj. Neostigmine 0.05 mg/kg with Inj. Atropine 0.02 mg/kg was employed for reversal. There was complete and rapid recovery of neuromuscular blockade in all the patients in both the groups. No adverse effects like bronchospasm, hypotension or rashes were noted in any patient during the study.

Conclusion

Rocuronium has a significantly rapid onset of action with a mean of 108.8 seconds and intermediate duration of action. It is easily reversible and produces no significant cardiovascular changes. It also has a good safety profile. Therefore in spite of its high cost, rocuronium appears to be the safest drug for rapid sequence intubation and routine intubation and it is near to ideal NMBA when there is no anticipated difficulty in intubation and also in surgeries of prolonged duration. It provides excellent intubating conditions with completely relaxed vocal cords, and good heamodynamic stability during intubation.

It has no significant adverse cardiovascular effects and no adverse reactions on reversal with Neostigmine. The synthesis of this drug has proven to be potentially very useful for anaesthetists all over the world because of its rapid onset of action and easy reversibility.

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