



EVALUATION OF INTUBATING CONDITIONS WITH VECURONIUM AND ROCURONIUM

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ABSTRACT AIM:

Evaluation Of Intubating Conditions With Rocuronium And Vecuronium

OBJECTIVES : 1) To search for a suitable alternative for succinylcholine for intubation. 2) To study and compare the intubating conditions. 3) To study and compare the haemodynamic changes.

METHODS AND MATERIALS:

This prospective, randomized, double blinded, comparative study was carried out in 60 patients, aged 18-60 years, of ASA 1-2 of either sex, who were scheduled to undergo various surgeries under general anaesthesia. Patients were divided into two groups. Group-R30 received rocuronium 0.6mg/kg intravenously and Group-V30 received vecuronium 0.08 mg/kg intravenously after induction with thiopentone sodium. Intubation was attempted on fading of all four twitches of orbicularis oculi muscle stimulation on train of four stimulation given to temporal branch of facial nerve at every 15 seconds after the injection of muscle relaxant. Intubating conditions were assessed by the cooper scoring system.

RESULTS:

The mean onset time was significantly rapid in Gr. R30 80 ± 15.42 seconds as compared to Gr. V30 135 ± 36.74 seconds. The mean duration of action was longer in Gr. R30 that is 34.3 ± 6.20 compared to Gr. V30 30.16 ± 10.54 . Overall intubating conditions were excellent in 90% patients in Gr. R30 as compared to 73.3 % patients in Gr. V30.

CONCLUSION:

Both rocuronium and vecuronium have intermediate duration of action, however rocuronium provides clinically acceptable intubating conditions much earlier than vecuronium.

KEYWORDS : Rocuronium, Vecuronium, Endotracheal intubation**INTRODUCTION:**

Now-a-days Endotracheal intubation is an integral part of administration of anaesthesia during surgical procedures¹. In the present day practice, muscle relaxation is used to serve two prime purposes².

- 1) To facilitate endotracheal intubation
- 2) To provide surgical relaxation.

The ideal neuromuscular blocking agent for intubation should have a fast onset, brief duration of action, provide profound relaxation & be free from haemodynamic changes³ and unwanted side effects.

Succinylcholine is the gold standard muscle relaxant for rapid sequence intubation. However, due to its side effects, the search has always been made to find out an alternative to suxamethonium with the same onset time, excellent intubating conditions & without the side effects of suxamethonium⁴. Vecuronium bromide and Atracurium besylate are attractive choices. However neither of these agents have been demonstrated to have significantly shorter onset time as needed for rapid tracheal intubation.

The work carried out by various authors⁵ have confirmed the long held belief, that a rapid onset of action can be produced by the compounds of relatively low potency. This concept was in part the basis for the development of Rocuronium. Rocuronium Bromide, intermediate acting aminosteroid, non depolarizing muscle relaxant, chemically 2-morphine, 3-diacetyl, 16-Nallylpyrrolidone derivative of Vecuronium is five to seven times less potent than Vecuronium. Several clinical studies conducted in the past have confirmed shorter onset time of Rocuronium.

The purpose of this study is to compare the onset time as well as intubating conditions of rocuronium and vecuronium in equipotent (2ED95) doses for tracheal intubation.

Materials and Methods:

The present study was a prospective double blinded randomized clinical study carried out in the department of Anaesthesiology, Medical College and Government General Hospital Kurnool during the period of 2013 to 2015.

(A) STUDY MATERIALS

After approval from ethical committee the present study was carried out on 60 patients posted for elective surgery under general anaesthesia. All patients underwent a thorough Pre Anaesthetic Check (PAC) which included history of present complaints, past illness, general and systemic examination and routine and specific investigations depending on the age, complaints and examination findings of the patient. The selection criterion for the inclusion of a particular patient in our study was as follows:

SELECTION CRITERIA:

- Age 18-60 years
- Sex Male/Female
- ASA Grade I & II
- Mallampati grade I & II
- Weight Average (not obese or underweight)
- Planned surgery
- Under general anaesthesia
- Patients willing to participate in the study.

EXCLUSION CRITERIA:

- Age younger than 18 years
- Obese and cachexic patients
- Expected difficult intubation
- Pre-existing hepatic, renal or neuromuscular disease
- Allergic disorders
- Pregnancy or lactating mothers
- Patients on medications known to interact with neuromuscular blocking drugs like Ca^{++} channel blocker, aminoglycosides, anticonvulsants, diuretics, Magnesium etc.

(B) STUDY DESIGN:

Once the patients were selected for inclusion in the study, they were informed about the motto, methodology and likely complications. If they expressed willingness to participate in the study then a written informed consent was taken from them. They were kept nil by mouth for eight hours. On the day of surgery patients were randomly divided into two groups using sealed envelopes.

Group V30 - receive vecuronium bromide
Group R30 - receive rocuronium bromide

After taking them on the operation table, a vital signs monitor (schiller truscope elite-A3) was attached and then baseline pulse rate, systolic and diastolic blood pressure were recorded. An intravenous line was secured with 18G IV cannula and iv fluid DNS was started slowly. The site of temporal branch of facial nerve stimulation at preauricular area was chosen and local preperation of the part was done.

(C) PREMEDICATION

Patients were pre-medicated with
 Inj. Glycopyrrolate 0.2mg I.V
 Inj. Tramadol 1mg/kg I.V
 Inj. Ranitidine 1mg/kg I.V
 Inj. Ondansetron 4 mg I.V

D) INDUCTION AND GROUPING OF PATIENTS:

All the patients were pre oxygenated with 100% oxygen for three minutes. Induction was done with inj. thiopentone sodium (2.5%) 5-7mg/kg intravenous till loss of eyelash reflex. Just after the induction of the patient four successive stimuli of train of four were delivered at 2 Hz by placing gel electrodes over the temporal branch of facial nerve. The resultant four twitches of orbicularis oculi muscle were observed visually. The time was noted. A Muscle relaxant was now given to the patient depending on the group for which he/she was selected randomly as follows.

Group R₃₀(n=30) - Inj. Rocuronium 0.6 mg/kg given I.V
 Group V₃₀(n=30)- Inj. Vecuronium 0.08 mg/kg given I.V

The train of four stimulation was then delivered at every 15 seconds after the injection of muscle relaxant till the fading of all four twitches. Time from injection of muscle relaxant to the fading of all four twitches was taken as time of onset of action of muscle relaxant.

Intubation was done with PVC cuffed endotracheal tube of appropriate size . Intubation was done by same person in all the cases and he was unaware of the muscle relaxant used. After checking for the bilateral air entry, the tube was fixed and attached to closed circuit. The patients were maintained on oxygen and nitrous oxide in 33%:66% ratio and sevoflurane. Time taken for appearance of one twitch response to Train of four stimulation was taken as the duration of action of muscle relaxant and inj. vecuronium bromide was given in both the groups.

(E) MONITORING:

All the patients were observed for onset time of muscle relaxant under study, its duration of action, intubating conditions at the time of intubation, hemodynamic variables and side effects/ complications.

- (i) For onset time and duration of action of drug, peripheral nerve stimulator (mindray) was used. It has got 2 electrodes. All four modes of stimulation i.e. Single twitch, Train of four, Tetanic stimulation and Double burst stimulation are present on this.
- (ii) The intubating conditions were judged clinically after the injection of study drug with the help of four point scale given by Cooper R, Mirakhr RK 1992, which is as follows.

Scoring of intubating conditions			
Score	Jaw relaxation	Vocal cords	Response to intubation
0	Poor (impossible)	Closed	Severe coughing or bucking
1	Minimal (difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None
Total score	Excellent (8-9), Good (6-7), Fair (3-5), Poor (0-2)		

(iii) The vital parameters like pulse rate, systolic and diastolic blood pressure were recorded at fixed time intervals i.e. pre induction, after induction, immediately after intubation, then at 1,5,10,15 minutes and then every 15 minutes till the end of surgery and in immediate post operative period with the help of vital sign monitor.

(iv) All the patients were observed for various side effects of vecuronium and Rocuronium like bradycardia(values less than 30% of baseline), tachycardia (values more than 30% of baseline), hypotension (values less than 30% of baseline), hypertension (values more than 30% of baseline), anaphylactic reaction, rash, exanthema, urticaria and bronchospasm.

(F) REVERSAL AND EXTUBATION:

At the end of surgery the neuromuscular block was reversed by using Inj. Glycopyrrolate 0.01mg/kg and Inj. Neostigmine 0.05mg/kg. Patients were extubated after return of reflexes, consciousness and after fulfilling the criteria for extubation.

(G) STATISTICAL CALCULATIONS:

The observed results were compiled and analyzed statistically by using chi-square test for qualitative data and students "t" test for quantitative data, the analyzing system being that of GRAPH PAD. Difference between the groups were considered significant when p value was <0.05 and highly significant when <0.001.

Statistical analysis was done using Graph pad prism version 6.05, Graph pad Inc, USA.

OBSERVATIONS AND RESULTS:

Table: DEMOGRAPHIC DATA

MEAN	GROUP V ₃₀	GROUP R ₃₀	p value
AGE(YRS)	40.26±15.56	37.73±13.37	p > 0.05 (NS)
SEX (M/F)	16/14	16/14	p > 0.05 (NS)
WEIGHT (Kg)	57.96±6.54	58.53±10.41	p > 0.05 (NS)
ASA GRADING	-	-	-
ASA I	25	25	p > 0.05 (NS)
ASA II	5	5	p > 0.05 (NS)

***NS- NOT SIGNIFICANT**

Demographic data of this study correlate well with each other. The mean time to achieve maximum block i.e. onset time of action of Rocuronium was 80±15.42 seconds and of Vecuronium was 135±36.74 seconds

Table: ONSET & DURATION OF ACTION

GROUPS	GROUP V ₃₀	GROUP R ₃₀	P VALUE
			V ₃₀ /V S R ₃₀
ONSET OF ACTION	135±36.74	80±15.42	<0.01,(S)
DURATION OF ACTION	30.16±10.54	34.3±6.20	P>0.05,(NS)

*** NS- NOT SIGNIFICANT, S-SIGNIFICANT**

The mean duration of action in group V₃₀ was 30.16±10.54 min while 34.3±6.20 min in group R₃₀. Thus duration of rocuronium was longer as compared to vecuronium. The difference was statistically not significant (p>0.05).

Table: OVERALL INTUBATING CONDITIONS

INTUBATING CONDITION	GROUP V ₃₀	GROUP R ₃₀	P VALUE		
	N	%	n	%	V ₃₀ Vs. R ₃₀
EXCELLENT (8-9)	22	73.3	27	90	<0.001(HS)
GOOD (6-7)	8	26.6	3	10	
FAIR (3-5)	-	-	-	-	
POOR (0-2)	-	-	-	-	

*** NS- NOT SIGNIFICANT, S-SIGNIFICANT, HS-HIGHLY SIGNIFICANT**

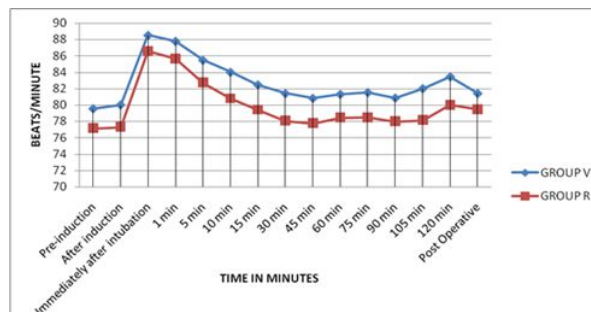
This table shows the intubating conditions. Tracheal intubation was done after four twitches in the train of four were disappeared visually. Intubating conditions were assessed using scoring system given by Cooper R, Mirakhr RK 1992 which takes into account the vocal cord movements, jaw relaxation and the response to intubation.

In our study, intubating conditions were excellent (score 8-9) in 22 patients (73.3%) in Group V₃₀, in 27 patients (90%) of Group R₃₀. The intubating conditions were good in the remaining number of patients in both the groups. Fair or poor intubating conditions were not seen in any of the patients of any group. Furthermore in cases rated as good in V₃₀ and R₃₀ Group, we observed only a slight movement of diaphragm on intubation.

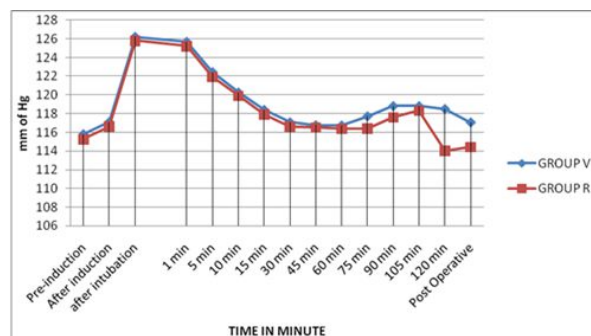
The changes in Pulse rate, mean systolic blood pressure, mean diastolic

blood pressure, compared with basal value in individual group was showing statistically significant difference immediately after intubation and at 5 minutes after intubation ($p < 0.05$). This could be due to stress of intubation. But there was no significant difference.

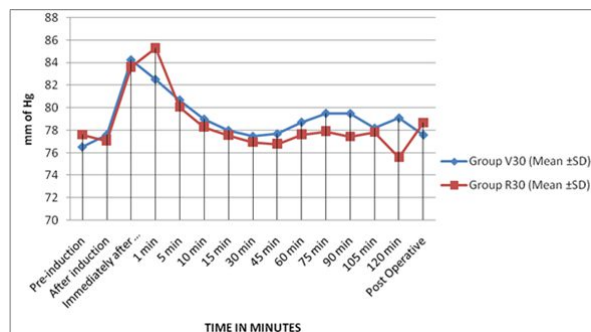
PERIOPERATIVE CHANGES IN MEAN PULSE RATE



PERIOPERATIVE CHANGES IN MEAN SYSTOLIC BLOOD PRESSURE



PERIOPERATIVE CHANGES IN MEAN DIASTOLIC BLOOD PRESSURE



DISCUSSION:

We have found that onset of action of rocuronium is much faster than vecuronium. The main reason for this rapid onset of neuromuscular block has been suggested to be the low potency of rocuronium, entailing the presence of more relaxant molecules in the blood stream which results in a large concentration gradient towards the biophase. 7,8 Rocuronium Bromide is a derivative of Vecuronium Bromide and is 5-7 times less potent than Vecuronium. The mean onset time in our study was 80 ± 15.42 seconds in GR. R30 and 135 ± 36.74 seconds in GR. V30, the difference in onset time being very highly significant. In comparison to our study, the study done by various workers, found the onset time in their study to be 82 ± 25 seconds in rocuronium group and 151 ± 39 seconds in vecuronium group. Though their results are comparable with our study with regard to faster onset of action in rocuronium group, in our study onset of action of rocuronium as well as vecuronium was much faster as compared to their study. This could be due to orbicularis oculi muscle stimulation in our study as compared to adductor pollicis muscle stimulation in their study.

According to a study done by Meistelman C et al orbicularis oculi exhibits similar features i.e. time course of neuromuscular blockade and sensitivity to muscle relaxants to that of laryngeal adductors and the diaphragm which are blocked more rapidly than the peripheral adductor muscles of thumb. So we have selected Train of four response

to orbicularis oculi muscle stimulation in our study. The faster onset of neuromuscular blockade at Orbicularis oculi compared to Adductor Pollicis might be due to differences in circulation time and muscle blood flow. Muscles which are closer to the central circulation like the orbicularis oculi or the diaphragm have relatively greater perfusion and tend to be paralysed more rapidly than the more peripheral muscles like adductor pollicis. Orbicularis oculi is made up of small, round and 89% fast twitch type II fibres. Adductor pollicis is made up of slow oxidative type of fibres.

Bharati Neerja et al (2001),¹¹ also reported significantly faster intubation time of 60-90 seconds in rocuronium group as compared to 120-180 seconds with vecuronium group. The intubating conditions were assessed by Cooper et al scoring system. In our study in GR. R30 excellent intubating conditions were achieved in 27(90%) patients which was consistent with a study done by Zhou et al^{11,12} Wierda et al. Intubating conditions were good (due to some diaphragmatic movement or mild coughing during intubation) in 3(10%) patients in Group-R30 and 8(26.6%) patients in Group-V30.

Bharti Neeraja used a standardized intubation technique (according to Copenhagen consensus conference rules) in which the intubation was attempted at every 30 seconds intervals starting at 60 seconds after administration of muscle relaxant and completed only when the intubating conditions were judged clinically acceptable by using CCC Rating scale. They observed that in rocuronium group 10/20 patients had excellent intubating conditions as compared to only 3/20 in vecuronium group. Rocuronium was used in the dose of 0.6 mg/kg which is twice its ED95 dose and for intubation purpose usually twice the ED95 dose of a non-depolariser is required. We selected twice ED95 dose of rocuronium (0.6 mg/kg) for intubation in our study.

Many other workers like Diefenbach et al and Shukla et al have also used 2ED95 dose of Rocuronium in their study. Study by S.A. Feldman et al, using dose of Rocuronium higher than 2ED95 was associated with a longer duration of action which may be inappropriate in many clinical situations.

In our study we used neuromuscular monitoring by Train of four as it is said to be more sensitive index of receptor blockade compared to single twitch stimuli. We, in our study assessed the neuromuscular blockade visually because it is non invasive and more relevant in clinical practice. Lecorre et al also assessed the Neuromuscular Blockade visually and stated that intubation can be safely performed when no visual responses at orbicularis oculi can be detected after Train of four stimulation. Mechanomyography has been considered as gold standard and used in most of the studies conducted in the past (Bartowski et al) but it lacks accuracy due to subjective interpretation of responses. Electromyography provides accurate and objective information (as used by M. Mayer) but the equipment is bulky and difficult to operate. So we assessed neuromuscular blockade by giving Train of four stimulation to temporal branch of facial nerve and seeing the response visually.

In the present study there was significant but less than 30% from baseline rise in pulse rate and systolic blood pressure and that might be due to the stress response of intubation which became insignificant by 10 minutes of intubation. In contrast to our study, Robertson EN et al (1994) when compared cardiovascular effects with 3ED95 dose of rocuronium and vecuronium, he found that there was statistically significant increase from baseline in one or more haemodynamic parameters in rocuronium group compared to vecuronium group. He attributed these cardiovascular changes to vagolytic action of rocuronium and although statistically significant, they were not likely to be clinically important. It was concluded from this study that Rocuronium bromide and Vecuronium bromide are potent, competitive neuromuscular blocking agents with intermediate duration of action. The onset of action is shorter for Rocuronium compared to Vecuronium. Both drugs provided excellent to good intubating conditions but Rocuronium has better intubating conditions as compared Vecuronium and both the drugs are cardio-stable. Thus we can say that Rocuronium being less potent than Vecuronium, provides excellent intubating condition within 90 seconds of drug administration. Hence it can serve as a good alternative to Vecuronium for tracheal intubation in conditions where Suxamethonium is contraindicated or where its use is hazardous and in clinical situations where rapid sequence induction technique is needed.

CONCLUSION:

Thus from the observations of the present study it can be concluded that Rocuronium bromide and Vecuronium bromide are potent, competitive neuromuscular blocking agents with intermediate duration of action. The onset of action is shorter for Rocuronium compared to Vecuronium. Both drugs provide excellent to good intubating conditions but Rocuronium has better intubating conditions as compared to Vecuronium and both the drugs are cardio stable.

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