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Evaluation of intubating conditions following administration of different doses of Rocuronium bromide: A comparative study

Dr. Arunima Saikia[1], Dr. Arnav Das[2*], Dr. Raju Tayung[3]

[1] Associate Professor, Department of Anaesthesiology, Assam Medical College & Hospital, Dibrugarh, Assam, India
[2] Senior Resident, Department of Anaesthesiology, Assam Medical College & Hospital, Dibrugarh, Assam, India
[3] Assistant Professor, Department of Anaesthesiology, Assam Medical College & Hospital, Dibrugarh, Assam, India

Abstract
Background: Rocuronium Bromide is the first nondepolarizing drug to become an acceptable substitute for succinylcholine to perform rapid sequence intubation during emergency. So, the aim was to study the intubating conditions with three different doses of rocuronium, viz: 0.6 mg / kg, 0.9mg / kg and 1.2 mg / kg after 60 sec.
Material and Methods: The study included 90 cases divided randomly according to intubating doses into three groups (each=30): Gr I = 0.6 mg/kg, Gr II = 0.9 mg/kg, Gr Ill = 1.2 mg/kg
Results: In the study it was found that intubating condition at 60 secs were much better with 0.9 mg/kg and 1.2mg/kg than 0.6 mg/kg. ($p< 0.05$), without much side effects. Although higher dose such as 1.2 mg/kg' of the drug is associated with prolonged duration of action delaying recovery for moderate duration of' surgery.
Conclusion: From our study conducted on patients undergoing elective surgery, it can be concluded that Rocuronium 0.9 mg/kg can be used as suitable substitute forsuxamethonium 1.0 mg/kg for rapid sequence induction after 60 secs for both elective and emergency surgery.

Keywords: rocuronium, intubating conditions

Introduction
It is generally accepted that the time interval between the suppression of' protective reflexes by the induction of anaesthesia and the development of satisfactory intubating condition is a potentially dangerous phase of anaesthesia. Regurgitation, tracheobronchial aspiration of stomach contents occur most frequently during this period. It is therefore most desirable to shorten the time interval between the onset and intubation as much as possible.
Succinylcholine is unique for rapid sequence intubation with rapid onset of relaxation, ultrashort duration and rapid recovery. But as it is a depolarizing drug, it has many side effects which restricts its use in all types of patient or surgery.
Rocuronium Bromide is the first nondepolarizing drug to become an acceptable substitute for succinylcholine to perform fast tract intubation during emergency. The onset time ofrocuronium is reported to be faster than all other non-depolarizing drugs currently available. It is also observed by various workers that the intubation time of rocuronium is directly proportional to the dose. So, it was considered to be most relevent to study the intubating conditions with three different doses of rocuronium, viz. 0.6 mg / kg,0.9mg / kg and 1.2 mg / kg.

Aim of Study
Here a modest endeavour has been tried to study the intubating conditions following Rocuronium Bromide in different doses. The aim of the present study is:
1. to compare the intubating condition after 60 sec(1min) of administration of three different doses of Rocuronium bromide i.e.0.6 mg/kg, 0.9 mg/kg and 1.2 mg/kg in patients undergoing elective surgery.
2. Also to study the haemodynamic effect ofrocuronium following intubation.

Materials and Method
The present clinical comparative study was undertaken with the aim to evaluate the intubating conditions following administration of different doses ofrocuronium bromide in 90 healthy patients, selected for different elective surgical procedures under general anaesthesia.

Place and Period of Study
The present study was conducted in different operation theatres of Gauhati Medical College and Hospital, Guwahati, within a period of one year from July 2002 to June 2003.

Selection Criteria
The study included patients of ASA -1 and ASA -2 physical status of either sex in the age group of 18-50 years. Airway assessment done with different scoring system like Malampati's classification, Patil's scoring, only Malampati grade I and II patients were taken for the study.
The exclusion of cases were done on the basis of the following criteria:
1. Potential airway problems
2. Cardiovascular disease
3. Pregnancy
4. Muscle weakness or skeletal abnormality
5. Known to be on drug interacting with neuromuscular blocking agent.
6. Renal or hepatic dysfunction

7. Metabolic disease
8. Pulmonary disease

Tile plan of Study

The study was carried out in 90 adult patients both male and female of different ages (18-50 yrs). They were allocated randomly into three different groups, consisting of 30 patients in each group. The groups were composed according to the three different intubating doses to each group.

Gr I = 0.6 mg/kg
Gr II = 0.9 mg/kg
Gr Ill = 1.2 mg/kg

Equipments

Before the patient arrived into the operation theatre, the following drugs and equipments were kept ready -

1. Boyles anaesthesia machine with two full cylinders of oxygen and nitrous oxide each and fresh soda lime.
2. Suction apparatus
3. The set of required Magills cuffed endotracheal tubes along with stylet.
4. Laryngoscope (Macintosh)
5. Airway (Guedels)
6. Syringes 2m1, 5m1, l0ml along with sterile IM or IV needles
7. A tray of emergency drugs - Atropine, Hydrocortisone, Dexamethasone, deriphylline, adrenaline, dopamine etc.
8. Specific drugs required in the study.
    a. Inj. Glycopyrrolate
    b. Inj. Tramadol
    c. Inj. Midazolam.
    d. Inj. Thiopentone Sodium (500 mg vial) with distilled water ampoules.
    e. Inj. Rocuronium bromide - 5 ml vial (50 mg).
    f. Inj. Neostigmine Methyl sulphate
    g. IV fluids crystalloids.

Preparation of the Patient

A pre anaesthetic visit to the ward for the assessment of the patient was undertaken. It consisted of taking a detailed history, clinical examination, specially the airway assessment for difficult intubation, and checking of' all the routine investigations and special investigation if any. All the information were recorded in the proforma. The patients were advised to have a light diet on the night before surgery and table *et al.* prazolam 0.5 mg and tablet Ranitidine 300 mg orally and to stay nil by mouth following morning on the day of surgery. This visit was also attempted at developing a cordial and friendly relationship with the patient to allay the anxiety and fear related to the surgery and anaesthesia. Written informed consent for surgery and anaesthesia was taken.

Premedications

All patients received Tramadol hydrochloride 1.5 mg/kg, midazolarn 0.03 mg/kg, glycopyrrolate 0.2 mg IV about 10 - 15 minutes prior to surgery.

Anaesthetic Procedure

After positioning the patient on the OT table, pulse rate and blood pressure was monitored, then ECG machine and pulse oximetry were attached to the patient and monitored. An iv line with an 18 G cannula was started. The preinduction pulse and B.P. re-corded. Patients were pre-oxygenated for three minutes with 100% oxygen using the Magil's circuit. All patients were induced with thiopentone sodium 2.5%, 5-6mg/kg body weight, the IV line flushed and then a bolus dose of either of the three doses of Rocuronium bromide injected according to the body weight (0.6mg/kg, 0.9mg/kg and I.2mg/kg). Patients were ventilated with 50% nitrous oxide and 50% Oxygen. Laryngoscopy done at 60 secs. After administration of the relaxant and the intubating condition was assessed. If intubation was possible, then adequate size tube passed and cuff inflated to place the tube properly. Anaesthesia was maintained in the semiclosed absorption circuit by IPPV delivering 66% nitrous oxide in 33% oxygen with a flow of 4.5- 5 litres/minute. The subsequent maintanence dose of' relaxant was I/4th the initial dose of' Rocuronium. Assessment of the intubating conditions was done on first attempt of intubation. Pulse and blood pressure was recorded at regular intervals. Antagonism of the residual neuromuscular block at the end of operation was done with neostigmine 0.05 mg/kg (2.5 mg average) and glycopyrrolate 0.00lmg/kg body weight injected by titration, intravenously.

Monitoring

Monitoring of the patient during the period of surgery com-prised of blood pressure, pulse rate, oxygen saturation by pulse oximetry and ECG monitoring.

Parameters Recorded during the Study

1. Assessment of intubating conditions at 60 seconds based on.
    a. Ease of laryngoscopy.
    b. Effect of the relaxant on the vocal cords.
    c. Response to tracheal intubation.
2. Effect of muscle relaxant on the cardiovascular system - blood pressure and pulse were recorded in 1 minute after intubation and then five minutes and fifteen minutes and after that at regular intervals during the surgery.

Side Effect

During the perioperative period any side effect like hypertension, hypotension, tachycardia, bradycardia, any abnormal movement of the body and limbs, rash etc. were observed.

Statistical Evaluation of Data

Statistical analysis and comparison of various data were done using fisher's t test, paired samples test, Levene's test for equality of variances for comparison of pulse and mean arterial pressure in different groups and chi-square test for comparison of intubating condition, setting $p<0.05$ significant and $p<0.01$ as highly significant, and $p>0.05$ was considered as not significant.

Observation Tables

1. **Rating of intubating conditions - by Magorianetal (1993). Excellent** -Jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement.

Good - Jaw relaxed, vocal cords apart and immobile, some diaphragmatic movement.

Poor - Jaw relaxed, vocal cord moving, bucking.

Inadequate - Jaw not relaxed, vocal cords closed.

2. Scoring of intubating conditions: Mirakhuretat (1992)

Table

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Poor	Closed	Severe coughing or bucking
1	Minimal	closing	Mild coughing
2	Moderate	Moving	Slight diaphragmatic Movement
3	Good	Open	None

Total score of 8 – 9 = Excellent
6-7 = Good
3-5 = Fair
0-2 = Poor

Results and Observation

Table 1: Types of operations

Type of surgery performed	Gr-I	Gr-II	Gr-III
Appendicectomy	8		1
Cholecystectomy	16	23	20
Herniorrhaphy	1	1	6
Mastectomy	4	4	3
Fracture Humerus	1	1	
Orthopaedic Surgery			
Total	30	30	30

Table 2: Intubating Condition in percentage

Drugs Dose kg-1	Excellent		Good		Poor	
	Intubation condition at 60 sec					
	No. of pt's	%	No. of pt's	%	No. of pt's	%
Roc. 0.6mg	12	40	14	46.6	4	13.3
Roc. 0.9mg	24	80	3	10	3	10
Roc. 1.2mg	26	86.6	4	13.3		

Table 3: Intubating score

Group	Dose in mg/kg	Time of intubation (s)	Intubation scores		Number
			excellent	good	
Gr-1	0.6	60	12	18	30
Gr-2	0.9	60	24	6	30
Gr-3	1.2	60	26	4	30

Table 4: Jaw relaxation

Drug	Good	Moderate	Minimal	Poor
Dose in mg		No of patient		
0.6	30	0	0	0
0.9	30	0	0	0
1.2	30	0	0	0

Table 5: Condition of the vocal cord

Group	Open no of patient	Moving no of patient	Closing no of patient	closed
Group-I	16	10	4	0
Group-II	22	5	3	0
Group-III	24	6	0	0

Table 6: Response to intubation

Drugs	None	Slight diaphragmatic movement	Mild coughing	Severe coughing or bucking
Roc. 0.6mg	10	10	10	0
Roc. 0.9mg	25	3	2	0
Roc. 1.2mg	24	6	0	0

Table 7: Mean pulse rates

Time	Mean pulse rate + S.D (per min)		
	Grade-I	Grade-II	Grade-III
Before relaxant	80.7±8.75	82.2±7.44	80.6±7.48
After initial dose of relaxant			
1 min	82.8±9.71	88.5±7.1	88.9±7.72
5 min	89.5±9.36	89.9±7.0	89.2±7.68
15 min	89.9±8.9	90.5±6.7	90.1±8.6

Table 8: Mean Arterial Pressure

Time	Mean pulse rate + S.D (per min)		
	Grade-I	Grade-II	Grade-III
Before relaxant	81.7 ± 2.65	83.3 ± 6.68	82.4 ± 7.36
After initial dose of relaxant			
1 min	89.1 ± 9.36	89.1 ± 6.71	89.3 ± 7.58
5 min	89.9 ± 9.1	90.4 ± 6.73	89.9 ± 7.48
15 min	90.1 ± 8.6	90.7 ±6.77	90.3 ± 7.76

Discussion

An excellent intubating condition is the 'standard goal' for intubation in all patients who are undergoing general anaesthesia especially in emergency cases. A good intubating condition will minimize the risk ofserious complications of intubation which may be due to failure of intubation or due to haemodynamic effect. Hypoxia, hypercarbia, arrythmia, aspiration, cardiac arrest are the hazardous effect of had intubating condition. Since long, suxamethonium remains the `gold standard' for rapid tracheal intubation during emergency and also elective surgery despite its many side effects and possible serious consequences. After the introduction of RocuroniumBromide, the newer non depolarizingneuromusclular blocking agent, the anaesthesiologists are releived to get a competitor of suxamethonium for rapid tracheal intubation without its side effects. Rocuronium, due to its rapid onset of action (within 60 sec.) helps to minimize the crucial induction to intuhation time.

The present study has been conducted to compare the intubation conditions between three different doses of Rocuronium Bromide i.e. 0.6 mg/kg, 0.9mg/kg and 1.2mg/kg body wt., within 1 minute (60 sec.) of their administration in 90 ASA 1 & II patients undergoing elective surgical procedures in the department of surgery and orthopaedics, Gauhati Medical College and Hospital. The results of our study are being tried to be compared with those ofother similar studies.

The patients of three groups in our study were comparable in age, weight, and sex. Most of the patients underwent cholecystectomy for cholelithiasis (65.5%), being more prevalent in females and their number was more (70%) in our study to that of males (30%). The maximum cases \ ere in the age group of 2 1 -30 yrs. (43.3%) (Table-111).

The doses used for intubation in this study were - 0.6 mg/kg, 0.9mg/kg and 1.2mg/kg body weight respectively. Our study was to compare the better acceptable intuhatingcondition between these three doses within 60 secs. After administration of the drug.

The intubating doses of Rocuronium Bromide in the present study are similar to that used by Tony Magorian *et al.* (1993) [1] and P. Schultz *et al.* (2001) [2]. In the first study,

Tony Magorian *et al.* (1993) [1] did the comparative study with the three doses (above mentioned) of Rocuronium bromide for RSI within 60secs along with succinylcholine 1 mg/kg and vecuronium O. l mg/kg. They used as premedication Midazolam 0.02 - 0.05mg/kg IV and then 100% 02 and fentanyl and induced by 2-7 mg/kg thiopentone and intubated after 60 secs of giving the muscle relaxant drug. They got the result that onset time for patients receiving 0.9mg/kg and 1.2mg/kg Recuronium was same with that of succinylcholine 1mg/kg.

Our study was almost same with the author except that they used fentanyl before induction instead of Tramadol that we used. The results we got were also similar with the author.

In the present study we found that 26 patients out of30 (86.6%) developed "acceptable" intubating conditions at 60 secs after administration of Rocuronium 0.6mg/kg, being "excellent" in 12 patients (40%) and good in 14 patients (46.6%). 4 patients had bucking and movement of both limbs following attempt to intubation and graded as poor.

In the 0.9 mg group, we found that 27 patients (90%) shows acceptable intubating conditions, among which 24 (80%) shows "excellent" and 3 (10%) shows good intubating conditions and 3 (10%) shows poor intubating conditions with movement of vocal cord, active movement and bucking.

In the 1.2 group 100% patients showed acceptable intubating conditions, out of them 26 (86.6%) showed excellent and 4 (13.3%) showed good intubating conditions.

The skill of the anaesthetist, and the depth of anaesthesia, background anaesthetics, the duration between the time of' giving the induction agent and the neuromuscular blocking drug, the state of the patients circulation and cardiac output, the respiratory drive produced by $PaCO_2$ relative to threshold resulting from opiates drugs and risk of observer bias may all influence the interpretation of the result (Feldman SA *et al.* 1994) [3].

The present study was also similar with the study by P. Schultz *et al.* (2001) [2]. They found that 100% neuromuscular block was significantly shorter with the two higher doses of Rocuronium than 0.6mg dose of the drug: (1 min versus 1.3 min). At the time of laryngoscopy (was easy in all patients) and intubation, the median depression of "T_1 was 94% (38-100) in 0.6mg/kg, 100% (58-100) in 0.9 nag/kg and 100% (83-100) in 1.2mg/kg respectively. They also found that no further improvement in intubating conditions at 60 secs was evident by increasing the Rocuronium dose from 0.9mg/kg to 1.2mg/kg.

Intubation condition with different doses of Rocuronium was studied by different authors.

We also compared the different doses of Rocuronium by scoring the intubating conditions which were similar to different authors like Cooper *et al.* [4], Mirakhur *et al.* [5].

Table 9: Scoring of Intubating Conditionsby Different Authors.

References	Time of Intubation	No. Of pt.	Doses in mg (%)								
			0.6			0.9			1.2		
			Excellent	Good	Poor	Excellent	Good	Poor	Excellent	Good	Poor
Tom Magonan ct al (1993)[1]	60 secs.	10	10	0	0	8	2	-	7	3	-
J C DE MAY ct al (1994)[6]	60 secs.	10	6	4	0	8	2	-	-	-	-
Present Study(2003)	60 secs.	30	12	18	-	24	6	-	26	4	-

Dubois MY *et al.* (1992) [7] studied the pharmacodynaemic effect with three doses (2, 2.5 & 3 X ED 95 doses) of Rocuronium in 36 patients of 18-65 yrs age and found adequate intubating condition with the higher groups with no significant changes in heart rate and blood pressure between these groups.

We also observed the same in the present study.

Light hall GK *et al.* (1995) [8] studied the onset an intubating dose of Rocuronium with 0.9mg and I.2mg/kg with cisatracurium using balanced anaesthesia with opioid / isoflurane. They found faster onset time with the two higher doses of Rocuronium compared to that of cisatracurium.

Mc Court KC *et al.* (1998) [9] also compared tracheal intubating conditions during RSI using Rocuronium 0.6 (n=61) or 1 mg/kg (n-130) withsuxamethonium 1.0mg (n=I27) as the NMB drug. They used fentanyl and thiopentone as the inducing agent. They found that Rocuronium high dose was significantly superior for RSI (P<0.01) then Rocuronium 0.6 mg/kg group and found no significant difference between suxamethonium and rocuronium high dose group.

Our study also correlates with the results of the doses of Rocuronium.

Richard MPino *et al.* (1998) [10] also compared the intubating condition between three doses of RocuroniumBromide like the present study (0.6mg/kg, 0.9mg/kg, 1.2mg/kg) along with mivacurium. They found that Rocuronium was faster in onset at the higher doses (0.9mg/kg and 1.2mg/kg). They found the result that Rocuronium 0.6mg group, 27% had excellent intubating conditions, whereas in 0.9mg group 93% and in 1.2 mg group 100% patients shows excellent intubating conditions in 60 secs. They also found that there were no statistically significant changes in MAP and heart rate between these three groups.

Our observations were similar to the author. We found excellent intubating condition in 40% cases in 0.6 mg Rocuronium group, 80% in 0.9 mg group and 100% in 1.2 mg group and also no statisstically significant changes in MAP and heart rate.

Hanskirkegaard-Nielsen and co-workers (1999) [11] also found in their study that Rocuronium high dose 0.8mg to 1.2mg/kg shows 95% probability of successful intubation at 60 secs. They used fentanyl and propolol as the induction agent.

In our study we used thiopentone, tramadol and midazolam and found similar results with the author.

Cheng Cay *et al.* (2002) [12] also found in their study that Rocuronium 0.9 mg/kg was as effective for RSI as suxamethonium.

It has been observed that propofol causes greater suppression of laryngeal reflexes and the addition of fentanyl, alfentanyl and or lignocaine makes intubation more acceptable than propofol alone. Thiopentone does not have any effect on laryngeal or pharyngeal reflexes. In our study, due to nonavailability of fentanyl or alfentanyl and for proper assessment of the dose response to the intubating condition of the drug, we used tramadol hydrochloride, a synthetic opioid of lower potency and low dose midafolam

along with thiopentone 6mg/kg body weight. M. Trybae*t al.* (1994) [13] and T. Magorian *et al.* (1993) [1] also used thiopentone 6 mg/kg in their study similar to us. We also did not used any inhalational agent like halothane, isoflurane etc. as a supplementary anaesthetics which are used with many clinical studies by different authors.

Our study was solely dependent on the intravenous inducing agent with the dose of the specific drug.

Though our results of different parameters varies with the others, yet the conclusive results that we get from the study correlates well with them.

In our study attempt was also made to assess the cardiovascular stability with monitoring of pulse and blood pressure with the three different groups before and after the injection of' the drug at regular intervals, I min, 5 min and 15 mins and thereafter regularly upto the end of the surgery.

We used in our study glycopyrrolate 0.2 mg IV dose irrespective of' age and weight to all patients before I 0 - 15 miss of the induction. As glycopyrrolate increases the pulse rate minimally it was used here only as an antisecretory agent as a routine premedication. We did not used IM injection due to the inconvenience of the operation time. So, we took the preinduction pulse and blood pressure to compare with that of' the post induction. We found that pulse rate and MAP increases in the 2nd and more in the 3rd group of our study compared to the first group. But when we analysed it statistically, we found that both pulse and MAP increases was insignificant ($P > 0.05$).

Our findings were similar to L.H. Hanwell *et al.* [8], Tony Magorian *et al.* [1], Dubois MY *et al.* [7], Mc Coy *et al.* [15].

The induction of anaesthesia in the above studies were however different from ours as none of them used glycopyrrolate or Tramadol and low dose midazolam as premedication. Instead, in majority of the study, they used fentanyl / alfentanyl / midazolam and propofol with inhalation anaesthetics as isoflurane, enflurane or savoflurane. We used thiopentone solely as induction agent. Magorian *et al.* (1993) [1] found that high dose thiopentone (6mg/kg) were only feasible for good to excellent incubating condition with Rocuronium. They found longer onset times with lower doses of thiopentone. In our study we donot have any neuromuscular monitoring devices like TOF, electromyogram etc., and the monitoring is completely based on clinical findings, so our neuromuscular blockade could not be appropriately compared with that of others.

In our study, we observed a few reactions of the patients inthe all three groups like instant movement of the hand on starting the injection of the drug (< 5 sec), involuntary movement of single limb on the same side or opposite side of the injecting hand. These findings are supported by Chiarella AB, Jolly DT, Huston CM, Clanachan AS *et al.* [14]. They described these observations are due to pain on injection of Rocuronium and they also evaluated the remedies to relief this complication with various drugs like NaHco, 8.4%, fentanyl, lidocaine, normal saline etc.

In our study as we do not have any facility to evaluate the pain caused by the drug after intravenous induction and as these events did not effect on the course of the onset and intubating conditions, we just observed and did not take all measure to prevent it

Conclusion

From the present clinical study to evaluate the effective dose of, Rocuronium bromide for intubation after 60 sec. of injecting the drug, we arrived at the following conclusion. Rocuronium definitely offers satisfactory intubating conditions at 60 secs.

1. In the study it was found that intubating condition at 60 secs was much better with 0.9 mg/kg dose than 0.6 mg/kg ($p < 0.05$).
2. Acceptable intubating condition at 60 secs between 0.9 mg/kg and 1.2 mg/kg is statistically insignificant ($p > 0.05$).
3. Higher dose more than 0.9 mg/kg of the drug is associated with prolonged duration of action delaying recovery for moderate duration of' surgery.
4. It was also observed that Rocuronium has favourable cardiovascular profile. Though pulse rate and MAP increases with higher dose group, it was found statistically insignificant ($p > 0.05$).

Mild effects like transient movement of limbs on injection does not effect the onset of action of the drug.

So, from our study conducted on patients undergoing elective surgery, it could be concluded that Rocuronium 0.9 mg/kg body weight dose may be a suitable substitute of suxamethonium 1.0 mg/kg body weight for rapid sequence induction within 60 secs for both elective and emergency surgery, provided there is no unanticipated difficulty in mask ventilation.

"The **s**earch for truth is more precious than its possession"

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