http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i8.33

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Research Article

A Comparative Study of Onset Time and Intubating Conditions with Suxamethonium and Rocuronium Bromide– An Evaluation by Neuromuscular Monitoring

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Abstract
Objective: *To evaluate the onset of action of different doses of rocuronium bromide and suxamethonium and to observe the ideal intubating conditions of the drugs belonging to different groups.*
Methods: *Ninety adult patients were randomly allocated to one of the three groups, to receive either inj.suxamethonium 1.5mg/kg (group-I) or inj.rocuronium bromide 0.6mg/kg (group-II) or inj.rocuronium bromide 0.9mg/kg (group-III).*
Results: *The results showed that the onset time for suxamethonium group was 66secs compared to 86.5secs of the rocuronium 0.6mg/kg group and 59secs with the rocuronium 0.9mg/kg group. The intubating condition scores were 8.53 each for suxamethonium group and rocuronium 0.6mg/kg group respectively and 8.70 for rocuronium 0.9mg/kg group.*
Conclusion: *There was apparent difference in the onset time of the drugs among the three groups but all the three groups have similar intubating conditions. Suxamethonium 1.5mg/kg has faster onset of action than rocuronium at a dose of 0.6mg/kg. Rocuronium at a dose of 0.9mg/kg is the most suitable dose of rocuronium for endotracheal intubation and this is the dose to be recommended for rapid sequence intubation, an alternative to suxamethonium in conditions where the latter is contraindicated or hazardous.*
Keywords: *Rocuronium bromide, Suxamethonium, intubation.*

Introduction

In the present day practice endotracheal intubation is an integral part of administration of general anaesthesia during surgical procedures. The time interval between the suppression of the protective reflexes by induction of anaesthesia and the development of satisfactory intubating conditions is a critical period.

From a pharmacodynamic standpoint, succinylcholine, a depolarizing muscle relaxant with its extremely rapid onset of action and its short duration of action make it the ideal neuromuscular blocking agent to facilitate tracheal intubation.

Unfortunately, succinylcholine can cause such adverse effects as fasciculation, increased

intracranial pressure and increased intraocular pressure, intracellular release of potassium from myocytes, resulting in a transient state of hyperkalemia which precipitate severe dysrrhythmias and cardiac arrest.

Rocuronium is a 2-morpholino,3-deacetyl,16-N-allyl pyrrolidino derivative of vecuronium. It is less liposoluble than vecuronium being mainly excreted by the liver and the kidneys. Its neuromuscular blocking potency is six times lower than that of vecuronium. The ED_{95} is 0.3mg/kg during anaesthesia with opioids and is reduced in the presence of inhalation agents.[1]

Intubating conditions at 60 seconds after administration of rocuronium 0.6mg/kg have been reported to be similar to those after succinylcholine. This similarity in intubating conditions is surprising, because the onset of action of rocuronium at the laryngeal adductor muscles is slower than that after succinylcholine and the degree of block at these muscles is less intense.[2]

Because of its absolute contraindication as allergy it is not advisable to use in those cases like myasthenia gravis or myasthenic syndrome, hepatic disease, neuromuscular disease, carcinomatosis and severe cachexia, as the duration of action in these conditions may be profoundly increased.[3]

The appropriate timing of tracheal intubation has been determined by clinical judgement, predetermined time and neuromuscular monitoring either by single twitch suppression or train-of-four (TOF) ratio. Both modes of monitoring have been used to determine potency, speed of onset, duration of action, recovery and adequate antagonism of neuromuscular blockade. The technique using judgement alone is relatively insensitive and more accurate by TOF stimulation than single twitch stimulation.[4]

In our study, we compared the onset time and intubating conditions of different doses of rocuronium and suxamathonium with the help of TOF stimulation.

Materials and Methods

After institutional ethical board approval, ninety (90) adult patients of age group 20 to 60 years, ASA physical status grade I and II of both sexes scheduled for various elective surgical procedures under general anaesthesia were taken up for the study. The study was carried out during March 2007 to May 2008 in the Department of Anaesthesiology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

All the patients were randomly distributed into three groups of 30 each. Patients having disorders of neuromuscular, renal, hepatic and anticipated difficult airway were excluded from the present study.

Patients in all the groups were premedicated with injection glycopyrrolate 0.04mg/kg/body weight intramuscularly (i.m) and injection midazolam 0.07mg/kg/body weight i.m one hour prior to induction of anaesthesia.

Group-I received injection succinylcholine chloride 1.5mg/kg body weight

Group-II received injection rocuronium bromide 0.6mg/kg body weight

Group-III received injection rocuronium bromide 0.9mg/kg body weight.

After preoxygenation for 3 minutes, anaesthesia was induced with injection Propofol (1%), 3mg/kg/body weight till the eyelash reflex disappears.

For neuromuscular monitoring, a peripheral nerve stimulator, TOF watch, Organon (Infar), Netherland, was used.

Results and Observations

In order to achieve the aims and objects of the proposed study, 90 patients within the age range of 20 – 60 years who underwent surgical procedures were taken up for the study.

The primary sample of 90 individuals were classified into 3 groups comprising of 30 individuals each with matching of sex, age and weight. The group - I consists of those who received suxamethonium 1.5mg/kg body weight whilst group – II and group – III received

rocuronium bromide 0.6mg/kg body weight and the same drug with 0.9mg/kg body weight respectively.

The data were processed through SPSS version 13 and for statistical analysis x^2 - test and t – test were advocated wherever found suitable and necessary, and accordingly interpretation was made.

Table – I deals with distribution of cases with respect to sex and group. It was further observed that the number of female (74.4%) was more than that of male (25.6%) in the study sample. This was true in all the groups too. However insignificant x^2 - value (x^2=0.818, p=0.664) suggested that male – female ratio for the group was almost alike to other group. Thus one can say that sex was matched to group, in the sense that the extraneous effect of sex on the main findings was controlled.

The average age of those individuals who were in the group-III was 40.23 years which was followed by the age of those in the group-I i.e., 37.16 years and the lowest age i.e., 36.23 years belongs to the group-II. The variation of average age among the groups is very least. In order to decide whether the variation is significant or not, t-test was advocated for each pair of groups (shown in Table-II(A)). All the t-value were found to be insignificant even at 5% probability level and therefore it may be concluded that the extraneous effect of age on the study was controlled as age structure for all the groups was almost same.

Table – I Sex – wise distribution of cases over the groups

Sex	Group-I	Group-II	Group-III	x^2-value	d.f	p-value	Remark
Male	9 (30.0)	6 (20.0)	8 (26.7)				
Female	21(70.0)	24(80.0)	22(73.3)	0.818	2	0.664	IS
Total	30(100)	30(100)	30(100)				

Figures within parenthesis indicate percentage
d.f: degree of freedom
IS: insignificant
S: significant
HS: highly significant
VHS: very highly significant

Table – II Comparison of mean±SD of age and weight over the groups

Parameter	Group-I(30) Mean±SD	Group-II(30) Mean±SD	Group-III(30) Mean±SD
Age (years)	37.16±15.54	36.23±11.64	40.23±12.30
Weight (kg)	52.40±7.50	56.43±12.50	51.60±7.44

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Table – II (A) Statistical Test findings of Table-II

Test	t-value	d.f	p-value	Remark
Between groups (Age)				
Group-I & Group-II	0.658	58	0.513	IS
Group-I & Group-III	0.635	58	0.528	IS
Group-II & Group-III	1.498	58	0.140	IS
Between groups (Weight)				
Group-I & Group-II	1.514	58	0.135	IS
Group-I & Group-III	0.414	58	0.680	IS
Group-II & Group-III	1.819	58	0.074	IS

Table – III Comparison of mean±SD of onset time over the groups

Parameter	Group-I (30) (Mean±SD)	Group-II (30) (Mean±SD)	Group-III (30) (Mean±SD)
Onset time (sec)	66.00±14.82	86.50±29.94	59.00±19.97

Table – III (A) Statistical Test findings of Table-III

Intergroups	t-value	d.f.	p-value	Remark
Group-I & Group-II	3.360	58	0.001	VHS
Group-I & Group-III	1.542	58	0.129	IS
Group-II & Group-III	4.182	58	0.000	VHS

At the same time, the influence of weight of the individual on the results of the study is also control since there is no variation of average weights over the three groups under study which is evidenced by the insignificant values of p (shown in the Table-II (A)). However, group-II has little bit higher weight than that of other groups while group-III has the lowest.

In order to study the onset of action of different doses of Rocuronium bromide and Suxamethonium, the mean onset of time (in seconds) was calculated for each group (detailed is set forth on Table-III) and their variations were tested by t-test and results were shown in Table-III (A).

Those who received Rocuronium bromide 0.9mg/kg body weight had the shortest onset time (59 sec), next to it belonged to those who received Suxamethonium 1.5mg/kg body weight (66 sec), and the Group-II of Rocuronium bromide 0.6mg/kg body weight had witnessed the longest time, i.e., 86.50 sec.

These variations were tested and very highly significant values show that there was a great difference of mean onset time between Group-I and Group-II as well as between Group-II and Group-III. However, the difference between Group-I and Group-III was not significant enough statistically.

From this interpretation findings we can conclude that Group-III had the best in terms of short onset time and Group-I had also almost (little more) similar effect to Group-III.

Here, to evaluate the ideal intubating condition, the above three tables were introduced. The Table-IV dealt with the comparison of mean intubating score over the groups whilst Table-IV(A) consisted their test results. Finally Table-IV(B) showed the pattern of intubating condition level over the three groups.

Table – IV Comparison of mean ± SD of "intubating condition score" over the groups

Parameters	Group–I (30) (Mean ± SD)	Group–II (30) (Mean ± SD)	Group–III(30) (Mean ± SD)
Intubating condition score	8.53 ± 0.68	8.53 ± 0.93	8.70 ± 0.95

Table – IV (A) Statistical Tests findings of Table-IV

Intergroups	t-value	d.f.	p-value	Remark
Group-I & Group-II	0	58	1	IS
Group-I & Group-III	0.78	58	0.439	IS
Group-II & Group-III	0.683	58	0.497	IS

Table – IV (B) Intubating condition level-wise distribution of cases over the groups

Intubating condition	Group-I	Group-II	Group-III	x^2-value	d.f	p-value	Remark
Fair	-	-	1 (3.3)				
Good	3(10.0)	5(16.7)	-	2.963	2	0.227	IS
Excellent	27(90.0)	25(83.3)	29(96.7)				
Total	30(100)	30(100)	30(100)				

*Figures within parenthesis indicate percentage.

From the Table-IV it is witnessed that average intubating score for all groups were more or less same. Further this statement is supported by the insignificant values of t (for each pair of combination) shown on the Table-IV(A). Of course, the Group-III had highest score (8.70), followed by Group-I and Group-II, each had same score i.e., 8.53.

Table-IV(B) highlights that excellent intubating condition level had been observed highest percentage in comparison with other level like good and fair. This is true in all the groups. Nevertheless the pattern which is observed in Group-I is almost alike in both Group-II and Group-III as evidenced by the insignificant values of x^2.

Thus it may be concluded that the three types of drug/dose have similar intubating conditions.

Discussion

Traditionally, suxamethonium was the neuromuscular blocking drug of choice for rapid tracheal intubation and minimizing the chances of regurgitation and aspiration. The use of suxamethonium can however, be associated with many side effects.

Some of the commonly available non-depolarizing muscle relaxants have been tried to facilitate endotracheal intubation but on an average the time lapse before intubation is usually 2 to 3 minutes which is not ideal for rapid tracheal intubation especially in emergency situations because of the dangers of gastric aspiration, regurgitation, hypoxia and hypercarbia.

A less potent neuromuscular blocking agent is required in larger doses to produce blockade of neuromuscular transmission. Rocuronium is a less potent non-depolarizing neuromuscular blocking agent having ED_{95} of 0.3mg/kg as against 0.064mg/kg of pancuronium and 0.056mg/kg of vecuronium. Rocuronium does not produce histamine release manifestations, cardiovascular instability as it is evident from clinical studies. This clinical study was undertaken using rocuronium in doses of (2 – 3) x ED_{95} to see if rocuronium could provide intubating conditions as rapidly and satisfactorily as with suxamethonium.

Use of higher doses of rocuronium to improve intubating conditions during rapid sequence intubation and to cut short the onset time below 60 seconds has been advocated by Wierda JMKH et al, but dose larger than 0.6mg/kg would be associated with a longer duration of action which may be inappropriate in many situations.[5]

Puhringer FK et al had shown that intubating conditions at 60 seconds were generally excellent or good with a dose of 0.6mg/kg and were 95% clinically acceptable at 45 seconds.[6] Cooper et al found onset time for rocuronium 0.6mg/kg as 90 seconds by 0.1 Hz stimulation and 58 seconds using TOF stimulation.[4]

In our study, the intubating conditions were assessed by Cooper et al scoring system.[7] We had compared the individual parameters i.e., jaw relaxation, condition of vocal cords and response to intubation by quantitative score rated on a 0 – 3 scale but no significant difference has been observed between the quantitative value of each component of intubating score. Results of the intubating condition of the present study are summarized in Table IV (B), showing total intubating score achieved and the frequency distribution of excellent, good, fair and poor conditions achieved after the administration of suxamethonium 1.5mg/kg, rocuronium 0.6mg/kg and rocuronium 0.9mg/kg respectively following routine induction for elective operations.

Puhringer et al found the onset time as 72 seconds and 48 seconds for rocuronium 0.6mg/kg and suxamethonium 1mg/kg respectively.[6] The time to achieve maximum block was approximately 88 seconds with rocuronium 0.6mg/kg and 65 seconds with suxamethonium 1.5mg/kg in the study made by Singh A et al.[8]

No significant side effects were observed during laryngoscopy and intubation in all the groups. However, we had come across one case with rocuronium 0.9mg/kg (Group-III) where there was cough in response to intubation with the jaw and vocal cord moving during intubation. No intervention was required and there was no complication during and after the operation.

On the other hand, in some studies 0.9mg/kg rocuronium and 1mg/kg suxamethonium showed the same onset time for ideal tracheal intubation. This makes rocuronium an alternative to suxamethonium in the rapid sequence intubation

for emergency surgeries with the benefit of not having its side effects. Such conclusion is made by some authors, namely Cooper et al,[9,10] Huizinga et al,[11] Magorian et al[12] and Puhringer et al.[6] ED_{95} of rocuronium is 0.3mg/kg, however, the dose most frequently used to facilitate intubation is 0.6mg/kg ($2xED_{95}$). The inconvenience of increasing the dose from 2 to $3xED_{95}$ is expected and proportional increase in neuromuscular block duration from an approximate average of 35 minutes with rocuronium 0.6mg/kg to 55 minutes with rocuronium 0.9mg/kg. This had been observed by Magorian et al.[12] For this reason, suxamethonium is still irreplaceable for short surgical procedures.

In our study, we found excellent intubating conditions with suxamethonium 1.5mg/kg in 27 (90%) patients and 3(10%) patients showing clinically acceptable intubating conditions in Group-I. In Group-II, 25 (83.3%) of the patients showed excellent intubating conditions with rocuronium 0.6mg/kg and 5 (16.7%) showed clinically acceptable intubating conditions, while 29 (96.71%) patients in Group-III with rocuronium 0.9mg/kg showed excellent intubating conditions and 1 (3.3%) patient showed fair intubating condition. The mean onset time was 66±14.82 seconds, 86.5±29.94 seconds and 59±19.97 seconds in Group-I, Group-II and Group-III, rocuronium respectively. The mean onset time we observed with suxamethonium 1.5mg/kg and rocuronium 0.6mg/kg are supported by the observations made by Bharti et al,[13] Cooper et al,[10] Magorian et al[12] and Shukla et al.[14]

In conclusion, Suxamethonium at a dose of 1.5mg/kg and rocuronium in doses of 0.6mg/kg and 0.9mg/kg provides acceptable conditions for endotracheal intubation. Suxamethonium 1.5mg/kg has faster onset of action than rocuronium at a dose of 0.6mg/kg. Rocuronium at a dose of 0.9mg/kg is the most suitable dose of rocuronium for endotracheal intubation and this is the dose to be recommended for rapid sequence intubation, an alternative to suxamethonium in conditions where the latter is contraindicated or hazardous.

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