

Evaluation of Intubating Conditions and Cardiovascular Effects of Rocuronium, Suxamethonium and Vecuronium

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Abstract

Background: Provision of muscle relaxation for endotracheal intubation demands a relatively safer drug than suxamethonium, which can provide good intubating conditions as early as possible with minimal side effects and stable haemodynamic profile. **Objectives:** The present study aimed at evaluating the intubating condition and cardiovascular effects of rocuronium and compares it with suxamethonium and vecuronium. **Subjects and Methods:** The study was conducted on 120 patients divided randomly into three groups of forty each, on the basis of muscle relaxant used for tracheal intubation as Group A with rocuronium, 0.6 mg/kg, Group B with suxamethonium, 1.5 mg/kg and Group C with vecuronium, 0.08 mg/kg. All the patients were premedicated with 0.2 mg glycopyrrolate and anaesthesia was induced by thiopentone sodium 2.5%, 4-5 mg/kg given intravenously then maintained on N2O: O2 mixture (66.6% & 33.3%) and intermitted injection of vecuronium. Parameters were observed like onset of apnoea, jaw relaxation, vocal cord position, vocal cord movement, coughing, limb movement cardiovascular response and fasciculations. **Results:** Onset of action in Group A slightly longer than Group B but far shorter than Group C. Fasciculations was absent with both Group A and C but was present with Group C. Intubating conditions were better after Group C. None of the patients developed complication of any type during the procedure. **Conclusion:** It is thus concluded from the above study that rocuronium can very well substitute suxamethonium for tracheal intubation when a rapid return to spontaneous respiration is not desired. It thus fills the gap between suxamethonium and non-depolarizing neuromuscular blocking agents and is a step ahead in search for an ideal neuromuscular blocking drug.

Keywords: Anaesthesia, Endotracheal Intubation, Rocuronium, Suxamethonium, Vecuronium.

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Received: December 2019

Accepted: December 2019

Introduction

The state of anaesthesia 50 years ago was, by the standards of today, primitive. Some volatile agents, intravenous agents, local infiltration and some nerve blocks were used by the anesthetist of that time. A tracheal tube was not usually passed before the introduction of neuromuscular blocking drugs, and intubation was considered as an art to be learnt with considerable dedication and hardship. Following the introduction of neuromuscular blocking drugs, in anaesthetic practice, the role of tracheal intubation has undergone a complete metamorphosis. The incontrovertible advantage of intubation in the safe maintenance of airway has changed the indication of intubation from specific need to almost a routine use in general anaesthetic practice. Thus, the use of muscle relaxant has become an important aspect of modern anaesthesia.

Succinylcholine, introduced by Thesleff and Foldes et al in 1952, revolutionized anaesthetic practice by providing intense neuromuscular blockade of very rapid onset and ultra short duration, thereby greatly easing the maneuver of

tracheal intubation. The unwanted side-effects which may be encountered with suxamethonium includes: muscle fasciculations, post-operative myalgia, hyperkalemia, increased intraocular, intragastric as well as intracranial pressures, and cardiovascular effects which include varied forms of cardiac arrhythmias especially bradyarrhythmias and asystole. In addition to these potential problems, prolonged apnoea may be encountered in individuals with atypical pseudo-cholinesterase. It may also induce malignant hyperthermia and myoglobinuria, a grave situation in susceptible patients. Thus, it falls short of an ideal muscle relaxant due to its potentially hazardous side effects, although it has the advantage of rapid action and quick recovery. Thus, the need for a rapid acting non-depolarizing neuromuscular blocking agent to replace suxamethonium for rapid sequence induction of anaesthesia has therefore been obvious for many years.

The properties of an ideal neuromuscular blocking agent includes non-depolarizing mechanism of action, rapid onset and short duration of action, rapid recovery, non cumulative effect, no cardiovascular effect, no histamine release,

reversible by cholinesterase inhibitors, high potency and it should have pharmacologically inactive metabolites.

The search for better drugs to meet the properties of an ideal neuromuscular blocking agent, led to the development of new nondepolarizing neuromuscular blocking drugs. Recently, developed drugs of intermediate duration includes vecuronium and atracurium "Which are, to a major extent, free from various side effects encountered with suxamethonium. However, even after intubating doses, onset time is relatively slow as compared with that of suxamethonium for rapid tracheal intubation. The use' of high initial bolus dose of either atracurium or vecuronium shortens the onset time, but at the expense of a prolonged duration of action, which may be undesirable in certain situations.

The new addition in the list of neuromuscular blocking agents is rocuronium bromide, which fills the gap for an agent, with rapid onset while lacking the potentially adverse features associated with suxamethonium, retaining a medium duration of action and meeting most of the requirements of an ideal neuromuscular blocking agent.

Thus, rocuronium has narrowed the gap between the onset of action of suxamethonium and the non-depolarizing neuromuscular blocking drugs. Rocuronium, 0.6 mg/kg (2xED95) was found to have an onset of action of 60-90 seconds at the adductor pollicis muscle, comparable with that of suxamethonium. At appropriate dosage (0.6-1.2 mg/kg) rocuronium may provide favourable conditions for tracheal intubation. This new aminosteriod neuromuscular blocking drug is devoid of many side effects which is encountered with suxamethonium. It has practically no effect on autonomic ganglia, there is no evidence of histamine release after its use, possess a very stable cardiovascular profile and is stable in aqueous solution.

Preliminary studies with Org 9426, suggested that it may very well fit in the category of an ideal muscle relaxant. Subsequent extensive clinical trial showed that it has a rapid onset time with favourable condition for tracheal intubation, an intermediate duration of action, coupled with cardiovascular stability, virtually no histamine release and other side effects. These characters make rocuronium the muscle relaxant, which best approaches the requirements of an ideal neuromuscular blocking drug.

Weighing the pros and cons of every drug, if a rapid tracheal intubation is required in certain situations where suxamethonium is contraindicated or may prove harmful, it is suggested that rocuronium may very well take its place.

Considering the various attractive properties of rocuronium, the present study is undertaken to evaluate the intubating conditions and cardiovascular effects of rocuronium and compare it with suxamethonium and vecuronium.

Subjects and Methods

The present study was conducted in the department of Anaesthesiology, Sri Shankaracharya Medical College and hospital, Bhilai, Durg, Chhattisgarh, in the period of six months march 2019 to September 2019. MLB, on 120 patients from different surgical specialities, scheduled for various elective surgeries under general anaesthesia.

Patients of either sex, in the age group of 20-60 years, belonging to ASA grade I and II, were selected as subject for the present study.

Patients having paralysis, or any neuromuscular disorder, any history of drug intake, patients with cardiovascular disease or any other systemic disorders like impaired renal or liver function other than that for which they are to be scheduled for surgery were excluded from the study.

All the patients were subjected to a detailed pre-anaesthetic checkup in regard of history, a thorough general and systemic examination. After this, they were ordered routine and any specific investigation if required. An informed consent of the entire patient was also taken after the evaluation.

Patients were randomly divided into three groups:

Group A-All patients were given an intubating dose of rocuronium, 0.6 mg/kg

Group B-In this group all patients received an intubating dose of suxamethonium, 1.5 mg/kg Group C-All patients in this group, were given an intubating dose of vecuronium, 0.08 mg/kg

Pulse rate, blood pressure, and SpO₂ were monitored preoperatively and recorded in all the cases.

All the patients were premedicated with 0.2 mg glycopyrrolate. The patients were pre-oxygenated with 100% oxygen for 3 minutes before induction. Induction- of anaesthesia was performed with thiopentone sodium 2.5%, 4-5 mg/kg given intravenously. After the abolition of eye lash reflex, intubation dose of muscle relaxant was pushed intravenously according to the group.

Group A, received 0.6 mg/kg rocuronium, group B, 1.5 mg/kg suxamethonium and group C, 0.08 mg/kg vecuronium. The time of administration of the relaxant was noted.

The onset of apnoea was appreciated by the loss of respiratory effort felt in the reservoir bag. The time interval from the administration of the relaxant to the onset of apnoea was noted. After the onset of apnoea, direct laryngoscopy was performed and the intubating conditions were assessed according to 'Copenhagen consensus conference rating scale'. The patient was then intubated with adequate size cuffed endotracheal tube and intermittent positive pressure ventilation was started with N₂O and O₂ mixtures through Bain circuit. Just immediately after intubation, pulse rate and blood pressure were recorded. After an interval of 10 minutes these parameters were again recorded.

When the respiratory excursions were first felt in the reservoir bag, the time was noted. The time interval from the onset of apnoea to the return of first respiratory excursion was noted, which gave the clinical duration of action of the respective relaxant used.

All the patients were maintained on nitrous oxide and oxygen mixture (66.6% & 33.3%) and intermittent injection of vecuronium. Analgesics and halothane were given as per requirement. The patients were given IPPV by Bain circuit.

At the end of the operative procedure, reversal was done by neostigmine and glycopyrrolate. After the return of adequate respiratory effort and upper airway reflexes along with spontaneous eye opening, extubation was done. The patient was then shifted to the recovery room.

The following observations were made and recorded during

the perioperative period.

Onset of action was assessed by onset of apnoea, Intubating conditions like Laryngoscopy, Jaw relaxation, Vocal cord position, Vocal cord movement

Response to intubation - Coughing Limb Movement

Cardiovascular Response like pulse rate, blood pressure and oxygen saturation (SpO₂) were recorded immediately after intubation and 10 minutes later.

Fasciculations like duration of action, assessed by the interval from the onset of apnoea to the return of first respiratory effort.

Intubating conditions were assessed as excellent, good or poor using the 'Copenhagen Consensus Rating Scale'.

Copenhagen Consensus Conference Rating Scale

Laryngoscopy

- Easy: Jaw relaxed no resistance to blade in the course of laryngoscopy.
- Fair: Jaw relaxed, slight resistance to the blade.
- Difficult: Poor jaw relaxation, active resistance of the patient to laryngoscopy.

Intubating Conditions

- Excellent: All variable listed under 'excellent' must be present.
- Good: Only variable listed under 'excellent' or 'good' must be present.
- Poor: The presence of any variable listed under 'poor'.

Results

Table 1:

Age Group (Years)	Group A		Group B		Group C	
	No	%	No	%	No	%
20-30	22	55	25	62.5	18	45
31 -40	8	20	7	17.5	14	35
41 - 50	9	27.5	6	15	8	20
51 - 60	1	2.5	2	5	0	-
Total (n)	40		40		40	
Mean	32.5		32.4		32.9	

Discussion

The present study is an attempt to evaluate the intubating condition and cardiovascular profile of rocuronium and compare it with suxamethonium and vecuronium.

Despite the multiple adverse effects of suxamethonium, this drug is often preferred for intubation purpose, because it offers a brief onset time, reliable optimal intubating conditions and a brief duration of action. Provision of muscle relaxation for endotracheal intubation demands a relatively safer drug than suxamethonium, that can provide good intubating conditions as early as possible with minimal side effects and stable haemodynamic profile.

Rocuronium bromide, introduced into practice since early 1990s is the first non-depolarizing muscle relaxant having an onset time and intubating conditions comparable with suxamethonium with less adverse effects.

The studies conducted by J .M.K. H. Wierda et al (1990), R. Cooper et al (1992), Toni Magorian ' et al (1993) and J. Engback et al (1994) showed that rocuronium provide

clinically acceptable intubating conditions comparable with that of suxamethonium. Aleksandra J. Mazurek et al (1998) and J .I. Andrews et al (1992) concluded that rocuronium is a reasonable substitute for suxamethonium for rapid sequence intubation. The results of the above studies have encouraged us to undertake the present study.

Our study was 'conducted on 120 patients, between 20 - 60 years, of age and belonging to ASA grade I &II who were scheduled for various elective surgeries under general anaesthesia. These patients were randomly allocated into three groups of forty each. All were premedicated with glycopyrrolate and induced by thiopentone. After induction tracheal intubation was facilitated by giving rocuronium 0.6 mg/kg, suxamethonium 1.5 mg/kg and vecuronium 0.08 mg/kg to patients of group A, B & C respectively. Anaesthesia was then maintained on N₂O (66.6%) and O₂ (33.3%) mixture and vecuronium. Analgesics and halothane were given intermittently as required.

The demographic data in all the groups were comparable. (Table - Ia &b) Most of the patients in each group were between 20 to 40 years of age. The mean age was 32.2 years in group A, 32.4 in group B and 32.9 in group C .

The male-female ratio in all the three groups were comparable (Table - II) with a ratio (M/F) of 0.81 in group A, 1.1 in group B and 1 in group C. Mean weight (in kg) ranges from 40-50 kg in all the groups.

Patients undergoing ENT surgeries (MRM or Tonsillectomy) and Gynaecological surgery (Abdominal hysterectomy) constituted a major portion of the study (Table - III).

The mean pulse rate variation was observed just immediately after intubation and ten minutes later. There was a significant rise in the pulse rate immediately after intubation, but was not significant when compared with values 10 minutes after (Table IV a& b)pressure, which shot up immediately after intubation, only to return slowly to near its basal value within ten minutes in all the three groups (Table Va &b). Since these changes were common to all the three groups, it can be inferred that, presser response during laryngoscopy and intubation was responsible for this transient rise rather than the drugs used. The oxygen saturation (SpO₂) was maintained throughout the procedure. The results observed above coincide with the findings of W.M. Schramm, K. Strasser et al (1996) which concluded that there was no significant change in the heart rate and mean arterial pressure after treatment with rocuronium (0.6 mg/kg) and vecuronium (0.1 mg/kg). In doses upto 1.2 mg/kg rocuronium has minimal cardiovascular effects both in heal thy patients and those with cardiovascular disease (Levy et al 1994).

The mean onset of action, as assessed by the onset of apnoea was 55.15±8.5 1 seconds -in group A (0.6 mg/kg, rocuronium), 48.45±6.95 seconds in group B (1.5 mg/kg, suxamethonium) and 131.60±21.41 seconds in group C (0.08 mg/kg, vecuronium) [Table VIII] The onset of apnoea was earliest in group B followed by group A and then group C Group B <Group A <Group C

It was inferred statistically that, the onset of apnoea in group C was significantly longer than that of group A and B. Although, onset of apnoea was slightly longer in group A as compare to group B, it was obviously very much shorter than group C. The findings of J.M.K. Wierda et al (1990), R. Cooper et al (1992), Neeraja Bharti and Sunila Sharma, et al

(2001) support the above results. In their studies they demonstrated that the rate of development of neuromuscular block and hence the onset of action was faster with rocuronium than vecuronium or with any other currently available non-depolarizing neuromuscular blocking drugs. The explanation given by them was that rocuronium being six to eight times less potent than vecuronium, accounted for early development of neuromuscular blockade. The low potency of Org 9426, results in a higher molecular load being present at the neuromuscular junction, producing an initial high concentration gradient and transfer of molecules of the drug to the biophase. Although rocuronium appears to have a short onset time of less than minute, it was found to be significantly longer than suxamethonium which still has the shortest onset time amongst all available muscle relaxant, a finding similar with those of Toni Magorian et al (1993) & Dr. Madhavi Barve and Dr. Roopa Sharma (2002).

The time interval from the onset of apnoea to the return of the first respiratory excursion gave the clinical duration of action of the respective relaxant used.

The mean duration of action of group A was 21.30 ± 5.01 minutes, group B was 4.79 ± 1.05 minutes and that of group C was 22.65 ± 4.78 . (Table - IX) There was no statistical significance in the duration of action of group A and C i.e. they were comparable. But the duration of action in group B was significantly shorter than both groups A and C. In a study conducted by Susan Woelfel, (1992) clinical duration was found to be 26.7 ± 1.9 minutes with rocuronium (0.6 mg/kg). Fuchs-Buder (1996) observed it to be 21 ± 4.0 minutes whereas Stoddart (1998) observed a clinical duration of 24.2 ± 6.6 minutes with same dose.

Similar results were observed in our study, a clinical duration of 21.30 ± 5.01 minutes with 0.6 mg/kg rocuronium. Clinical duration of action of rocuronium (21.30 ± 5.01 minutes) and that of vecuronium (22.65 ± 4.78 minutes) was found to be comparable in our study. This is supported by the results of R. Cooper et al (1992), Toni Magorian et al (1993), and Neeraja Bharti et al (2001) who reported that the clinical duration of action of rocuronium did not differ appreciably from the equipotent doses of vecuronium or atracurium.

Although duration of action of rocuronium is similar to that of vecuronium, it has a significantly faster onset of action, which is due to its low potency.

The duration of action of suxamethonium (4.79 ± 1.05) minutes was significantly shorter than that of rocuronium (21.30 ± 5.01) minutes. This result is similar with that of Toni Magorian et al (1993), who showed that clinical duration was least in succinylcholine group, as compared to rocuronium and vecuronium groups.

Thus, despite its brief onset of action, rocuronium has a longer duration of action than suxamethonium, hence it must be left to the clinician to decide in each case whether duration of action is an important determinant in the choice of muscle relaxant.

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Fasciculations were present in all the patients in group B whereas it was absent in both group A and C. The

depolarizing nature of suxamethonium, induces fasciculations in those patient who received it and is more in young healthy muscular adults. Both rocuronium and vecuronium are non-depolarizing blockers so they are devoid of fasciculations.

Intubating conditions can be influenced by the choice of anaesthetic and the use of adjuvant drugs, such as narcotics, sedatives, lidocaine or inhalational agents. Because propofol depress pharyngeal and laryngeal reflexes, we avoided this agent and selected thiopental to minimize the enhancement of muscle relaxation. We did not administer any sedative or analgesic prior to induction and intubation since these agents may act as confounding factors in the evaluation. Although inhalational agents potentiate neuromuscular effects of non-depolarizing muscle relaxants these do not effect the onset time, but the intubating conditions and clinical duration of action maybe significantly affected by the depth and type of anaesthesia. Thus, these, agents were avoided during induction of anaesthesia for proper evaluation or correlation between onset times and intubating conditions.

In many previous studies a fixed intubation time was used to assess intubating conditions like 60 secs (Magorian, M.S., Chetty, AJ England) or 90 secs (JMKH Wierda). While in some other studies, the intubation was performed when the neuromuscular blockade at wrist exceeded 90% (M. Mayer). They have also used different scoring systems for evaluation of intubating conditions.

A standardized intubation score according to "Copenhagen consensus conference rating scale" has been used for the evaluation of intubating condition during this study. Intubation was attempted, just immediately after the onset of apnoea and certain parameters were assessed. The observer was unaware of the muscle relaxant used.

Conclusion

It is thus concluded from the above study that rocuronium can very well substitute suxamethonium for tracheal intubation when a rapid return to spontaneous respiration is not desired. It thus fills the gap between suxamethonium and non-depolarizing neuromuscular blocking agents and is a step ahead in search for an ideal neuromuscular blocking drug.

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How to cite this article: Ali RZ, Akhtar P, Rangari P. Evaluation of Intubating Conditions and Cardiovascular Effects of Rocuronium, Suxamethonium and Vecuronium. *Acad. Anesthesiol. Int.* 2019;4(2):299-303.

DOI: [dx.doi.org/10.21276/aan.2019.4.2.67](https://doi.org/10.21276/aan.2019.4.2.67)

Source of Support: Nil, **Conflict of Interest:** None declared.