

COMPARISON OF ROCURONIUM BROMIDE WITH SUXAMETHONIUM CHLORIDE FOR TRACHEAL INTUBATION

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ABSTRACT

Background: Endotracheal intubation is of paramount importance in general anaesthesia requires relaxation of laryngeal musculature leading to total inactivity of vocal cords. Suxamethonium chloride, a depolarizing muscle relaxant due to its quick onset of action and excellent intubating conditions has remained a muscle relaxant of choice. Rocuronium was proved to be safe alternative to suxamethonium for endotracheal intubation.

Aims & Objective: To find out the utility of Inj. Rocuronium Bromide a non-depolarizing muscle relaxant (NDMR) as an alternative to Suxamethonium chloride, a depolarizing muscle relaxant (DMR) for the purpose of intubation of trachea with emphasis on onset of time for muscle relaxation, duration of action, hemodynamic changes and complications if any.

Materials and Methods: This is a randomized clinical study carried out at tertiary care center. 90 patients were randomly divided into three groups. Group S₆₀ (n=30) - Inj. Suxamethonium 1.5 mg/kg IV given I.V, Group R₆₀ (n=30) - Inj. Rocuronium 0.6 mg/kg IV given I.V and Group R₉₀ (n=30) - Inj. Rocuronium 0.6 mg/kg IV given I.V. The intubating conditions were judged clinically at fixed time interval i.e. either at 60 seconds or 90 seconds as per the group of patient, after the injection of study drug with the help of four point scale. The observed results were compiled and analyzed statistically by using chi-square test for qualitative data and students "t" test for quantitative data, the analysing system being that of EPI INFO.

Results: The mean age was 29.2 ± 12.60, 28.83 ± 8.50 & 30.1 ± 10.47 years, respectively in S₆₀, R₆₀ and R₉₀ group. Intubating conditions were excellent (score 8-9) in all the 30 patients (100%) in Group S₆₀, in 23 patients (76.66%) of Group R₆₀ and in 28 patients (93.33%) of Group R₉₀. The mean onset time in our study were 46.66±5.46 seconds in Group S₆₀, 76.33 ± 10.33 seconds in Group R₆₀ and 78.33 ± 9.4 in R₉₀. The duration of action in our study was 5.93 ± 1.25 minutes in Group S₆₀ compared to 29.83±5.49minutes in Group R₆₀ and 27.83 ± 3.13 minutes in R₉₀.

Conclusion: Rocuronium can serve as a good alternative to Suxamethonium for tracheal intubation in conditions where Suxamethonium is contraindicated or where its use is hazardous.

Key Words: Rocuronium; Suxamethonium; Tracheal intubation

Introduction

Anaesthesiology is one of the most fascinating and challenging branch of medical science. Since its first public demonstration by WTG Morton in October 1846, it has undergone tremendous advancement and has made it unimaginable for people to think about surgery without anaesthesia.^[1] Today it not only meets all the requisites of any modern and sophisticated surgery but at the same time it assures a reasonable degree of safety to the life of patients. The period after 1846 witnessed the arrival of new inhalation agents, intravenous agents, local anaesthetics, equipment, newer techniques and ultra-modern injection devices for administering anaesthesia and a voluminous increased knowledge and understanding of body physiology, pharmacology of drugs, challenges of surgeries and strategies to decrease morbidity and mortality.

Endotracheal intubation is one of such development without which general anaesthesia cannot be considered

safe for any major surgery particularly head and neck, thoracic and abdominal surgeries. Before its advent the mortality rate was huge due to aspiration problems. Putting a tube in trachea not only avoid this complication but also helps to maintained breathing and respiration of patient and directly delivers anaesthetic gases into the lungs. Endotracheal intubation is of paramount importance in general anaesthesia requires relaxation of laryngeal musculature leading to total inactivity of vocal cords. Moreover the time interval between the injection of the drug and the occurrence of acceptable muscle relaxation for intubation should be as minimal as possible to avoid precipitation of silent regurgitation and aspiration.

Out of all the relaxants, Suxamethonium is the only which is depolarizing and the rest being non-depolarizing muscle relaxants. Besides the difference in mechanism of action, various muscle relaxant vary in their onset and duration, pharmacokinetics and pharmacodynamic and various side effects. Depending upon these differences, their use is made in clinical practice.

Suxamethonium chloride, a depolarizing muscle relaxant due to its quick onset of action and excellent intubating conditions has remained a muscle relaxant of choice for endotracheal intubation for years together not only in planned surgeries but also in emergency surgeries. However due to its side effects particularly like increased intra-abdominal pressure, increased intracranial pressure, hyperkalaemia and myalgia, the search has been always made to find out an alternative to Suxamethonium with the same onset time, excellent intubating conditions and without the side effects of Suxamethonium. Rocuronium has proven, its onset time and intubation condition are comparable with suxamethonium and without the side effects.^[2,3] Rocuronium was proved to be safe alternative to suxamethonium for endotracheal intubation.^[4]

The main aim of the present study was to find out the utility of Inj. Rocuronium Bromide a non-depolarizing muscle relaxant (NDMR) as an alternative to Suxamethonium chloride, a depolarizing muscle relaxant (DMR) for the purpose of intubation of trachea with emphasis on onset of time for muscle relaxation, duration of action, hemodynamic changes and complications if any.

Materials and Methods

This is a randomized clinical study carried out at tertiary care center in western India from 2006 to 2008. 90 patients were enrolled in study, for planned surgery under general anaesthesia. Patients from 18 to 60 years from both sex, with ASA grade I and II. Written informed consent was taken from patients. All patients underwent a thorough Pre Anesthetic 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. Patients who were less than 18 years, obese and cachexic, expected difficult intubation, who are pregnant or lactating, suffering from hepatic, renal, neuromuscular or allergic disorders were excluded from the study. Patients who were taking medication which might interact with neuromuscular blockers and patients who refused to participate in the study were also excluded from study.

Patients who were enrolled for the study were randomly divided into three groups. Group S₆₀ (n=30) - Inj. Suxamethonium 1.5 mg/kg IV given I.V, Group R₆₀ (n=30) - Inj. Rocuronium 0.6 mg/kg IV given I.V and Group R₉₀ (n=30) - Inj. Rocuronium 0.6 mg/kg IV given I.V. Patients were kept nil by mouth for twelve hours prior to surgery. After taking them on the operation table, a vital signs

monitor (Concept Integra) was attached and then baseline pulse rate, systolic and diastolic blood pressure was noted down. As intravenous line was secured with 18G IV cannula and inj. Dextrose 5% was started slowly. The other arm on which vein was not taken was fixed to armrest and site of ulnar nerve stimulation at medial side of wrist near proximal crease was chosen. It was shaved and cleansed with spirit.

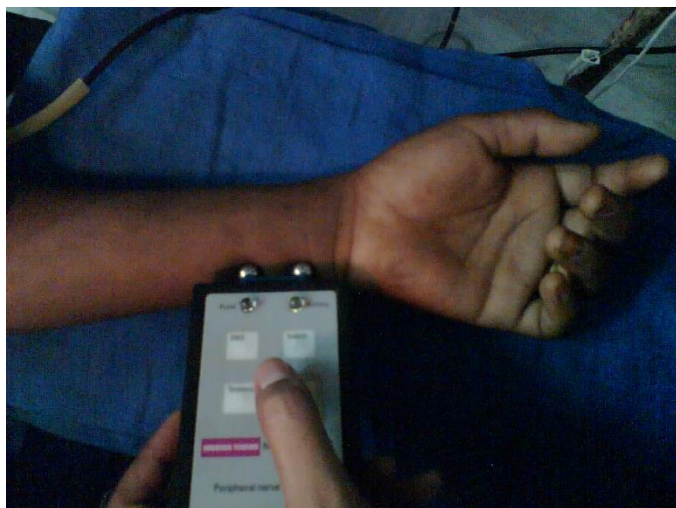


Patients were pre-medicated with inj. Atropine, inj. Tramadol, inj. Ranitidine and Inj. Ondansetron. All the patients were pre-oxygenated with 100% oxygen for 3 min through Bain's circuit. They were induced with Inj. Thiopentone Sodium 5-7 mg/kg till the loss of eyelash reflex. Muscle relaxant was now given to the patient depending on the group for which he/she was selected randomly.

The intubation was done with PVC cuffed endotracheal tube of appropriate size at a fixed time that is at 60 seconds in Group S₆₀ and R₆₀ and at 90 seconds in Group R₉₀. The intubation was done by one person only in all the cases and he was unaware of the muscle relaxant used and the time interval chosen. After checking for the bilateral air entry, the tube was fixed and attached to Bain's circuit. The patients were maintained on oxygen and nitrous oxide in 33%:66% ratio, Isoflurane 0.5-1% and muscle relaxant Vecuronium on arrival of one twitch response to Train of four stimulation. 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.

For onset time and duration of action of drug, peripheral nerve stimulator (MICROSTIM PLUS) was used. It has got rounded or ball shaped electrodes. All four modes of stimulation i.e. Single twitch, Train of four, Tetanic

stimulation and Double burst stimulation are present on this. Just after the induction of the patient, ball shaped electrodes were applied to the stimulation site and four successive stimuli of Train of four were delivered at 2 Hz i.e. one stimulus at 0.5 seconds. The resultant four twitches of the adductor pollicis muscle were observed visually. The train of four stimulation was then given at every 10 seconds after the injection of muscle relaxant to the loss of all four twitches. The train of four stimulation was then given every five minutes till the recovery of first twitch response. The time from the injection of muscle relaxant to the recovery of first twitch response was taken as the duration of action. This was followed by supplementation of muscle relaxant with Vecuronium.



The intubating conditions were judged clinically at fixed time interval i.e. either at 60 seconds or 90 seconds as per the group of patient, after the injection of study drug with the help of four point scale given by Cooper R, Mirakhur RK 1992.^[5] 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.

All the patients were observed for various side effects of Suxamethonium and Rocuronium like muscle fasciculation, bradycardia (values less 30% of baseline), tachycardia (values more 30% of baseline), hypotension (values less 30% of baseline), hypertension (values more 30% of baseline), anaphylactic reaction, rash, exanthema, urticaria and bronchospasm. At the end of surgery the neuromuscular block was reversed by using Inj. Atropine 0.02 mg/kg and Inj. Neostigmine 0.05 mg/kg. Oropharyngeal suction was done and patient was extubated when fully awake and fulfilled the criteria of extubation.

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

Results

The onset time and duration of action of drug was determined by peripheral nerve stimulator and intubating conditions were assessed using clinical criteria. Hemodynamic status was monitored by observing changes in pulse rate, systolic and diastolic blood pressure.

The mean age was 29.2 ± 12.60 , 28.83 ± 8.50 & 30.1 ± 10.47 years, respectively in S₆₀, R₆₀ and R₉₀ group. There was no statistical significant difference between three groups. In group S₆₀ and R₆₀ there were 16 males each while 13 in Group R₉₀. There were 14 females in Group S₆₀ & R₆₀ each, while 17 in group R₉₀. There was no statistical significance difference between the three groups in terms of gender distribution. The mean weight was 52.46 ± 7.02 , 52.86 ± 4.83 & 50.36 ± 8.04 in Group S₆₀, R₆₀, and R₉₀ respectively. There was no statistical significance difference between the three groups in terms of weight wise distribution.

In each group of S₆₀ & R₆₀ there were 25 patients of ASA grade I, while 24 patients in Group R₉₀. And rest was of ASA grade II in all three groups. Thus there was no statistical significance in the ASA grading.

In our study, intubating conditions were excellent (score 8-9) in all the 30 patients (100%) in Group S₆₀, in 23 patients (76.66%) of Group R₆₀ and in 28 patients (93.33%) of Group R₉₀. The intubating conditions were good in the remaining number of patients in all the three groups. Fair or poor intubating conditions were not seen in any of the patients of any group. Furthermore in cases rated as good in R₆₀ and R₉₀ Group, we observed only a slight movement of diaphragm on intubation, the rest of thing setting perfectly in the scoring of excellent. Only muscle fasciculations were seen in 83% of patients of suxamethonium group. No other side effects were noticed in any patients of either group.

Table-1: Time Course and Duration of Action

	Groups			P Value		
	S ₆₀	R ₆₀	R ₉₀	S ₆₀ Vs. R ₆₀	S ₆₀ Vs. R ₉₀	R ₆₀ Vs. R ₉₀
Onset of Action	46.66 ± 5.46	76.33 ± 10.33	78.33 ± 9.4	<0.01, S	<0.01, S	>0.05, NS
Duration of Action	5.93 ± 1.25	29.83 ± 5.49	27.83 ± 3.13	<0.001, HS	<0.001, HS	>0.05, NS

HS: Highly Significant; NS: Not Significant; S: Significant

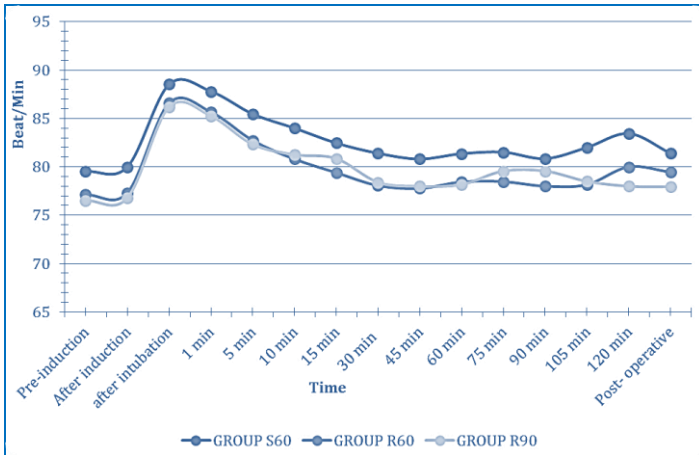


Figure-1: Perioperative changes in mean pulse rate

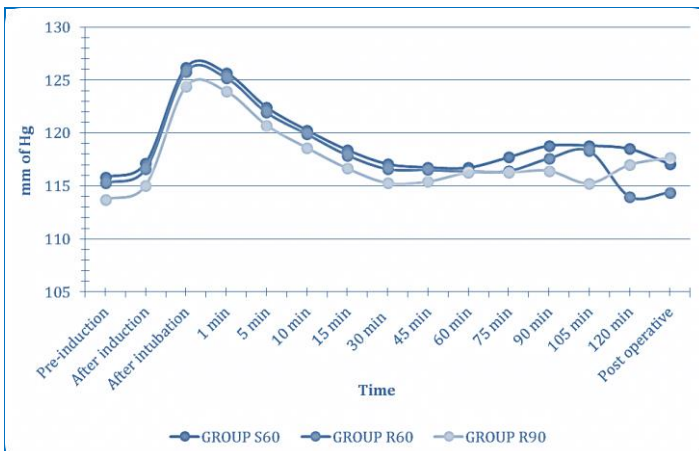


Figure-2: Perioperative changes in mean systolic blood pressure

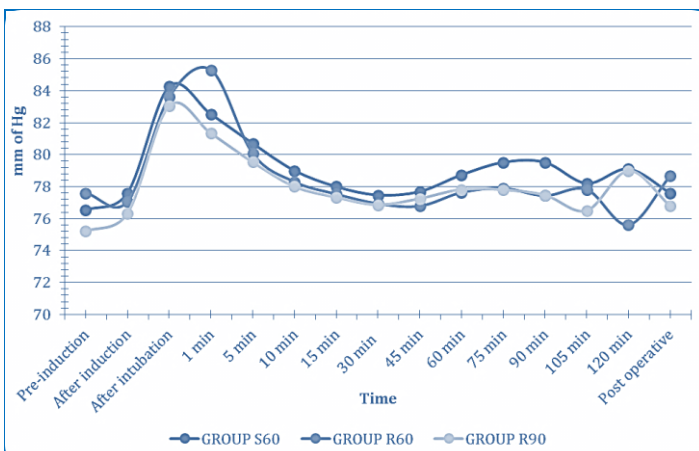


Figure-3: Perioperative changes in mean diastolic blood pressure

Discussion

The provision of muscle relaxation during endotracheal intubation demands a drug that can provide good to excellent intubating conditions, as early as possible, with minimal side effects and stable hemodynamic profile. Till date, Suxamethonium chloride is the drug of choice for this purpose as it provides excellent intubating conditions within 60 seconds when given in a dose of 1-1.5 mg/kg. However, its use is frequently associated with some

undesirable side effects like muscle fasciculations, postoperative muscle pain, hyperkalaemia, increased intra-ocular and intra-abdominal pressure and occasionally malignant hyperthermia. Hence, its use in certain conditions like burns, perforating eye injury, renal failure etc. is contraindicated.

Rocuronium bromide is a derivative of Vecuronium bromide and is 5-7 times less potent than Vecuronium. However it is reported to have shorter onset time compared to Vecuronium & Atracurium.^[6] Furthermore, when compared with Mivacurium and Suxamethonium both Rocuronium and Mivacurium were found to be good alternative for Suxamethonium.^[7-9] Among the Rocuronium and Mivacurium, Rocuronium was found to have shorter onset time but longer duration of action compared to Mivacurium.^[2,10] Hence in our study we used Rocuronium bromide to test its utility as an alternative to Suxamethonium chloride for the purpose of tracheal intubation.

The dose of Suxamethonium used in our study was 1.5 mg/kg which is in resemblance to the dose used in previous studies.^[4,5] while Suxamethonium was used in the dose of 1 mg/kg while comparing it with Rocuronium.^[11] Rocuronium was used in the dose of 0.6 mg/kg which is twice its ED 95 dose, the latter being 0.3 mg/kg. ED95 is the dose which is required to produce 95% depression of twitch response of the thumb on single twitch stimulation and for intubation purpose usually twice the ED95 dose of a non-depolarizer is required. Many other workers have also used 2 X ED95 i.e. 0.6 mg/kg dose of Rocuronium in their study.^[2,4,5,10]

By further increasing the dose of Rocuronium, can we still reduce the onset time is questionable. Significant reduction in the onset time of Rocuronium by giving it in 1.2mg/kg dose has been achieved in a study^[11] (the onset time almost equal to that of Suxamethonium), while another researcher had come to conclusion that there was no advantage of increasing the dose of Rocuronium above 2 X ED95 on its onset time.^[12]

In most of the studies workers have used either clinical criteria or neuromuscular monitoring or predetermined time interval for assessing utility of muscle relaxant for tracheal intubation. In our study we used all these three methods of assessment as in similar study.^[4] The intubation was done at fixed time interval i.e. at 60 and 90 seconds and the intubating conditions were judged at these times by clinical criteria. The intubation was done at 60 and 90 seconds because most of the studies done in

past have reported good clinically acceptable Intubating conditions within 60-90 seconds with 0.6mg/kg of Rocuronium. A fixed intubation time has been used to assess intubating conditions like 60 seconds in a similar study and 90 seconds in a study.^[2,11]

We selected patients of age 18-60 years, of either sex, ASA grade I and II, average weight (not obese, not cachexic) for our study. The three groups i.e. Group S 60, Group R60 and Group R90 were comparable to each other statistically with reference to mean age, mean weight, male to female ratio and number of patients in ASA grade I and II.

The onset time of muscle relaxant is defined as the time from the injection of drug to its peak effect.^[13] As we used peripheral nerve stimulator with TOF as mode of stimulation for the onset and duration of action. Hence, onset time was taken as the time from injection of drug to loss of all four twitches on TOF stimulation (i.e. 100 % block). The mean onset time in our study were 46.66 ± 5.46 seconds in Group S60, 76.33 ± 10.33 seconds in Group R60 and 78.33 ± 9.4 in R90, the difference in onset being significant. Our results in this regard are very much in resemblance with those of Shukla, Dubey, and Sharma 2004.^[4] In their study, the onset time with Suxamethonium was 46.05 ± 4.7 seconds and 80.1 ± 5.42 seconds with Rocuronium. Similar results have been reported in other studies (89 sec with Rocuronium) and (89 ± 33 sec with Rocuronium 0.6 mg/kg).^[5,11]

While using PNS for neuromuscular monitoring, duration of action was measured as the time taken from the injection of drug till the recovery of first twitch response on TOF stimulation. The duration of action, measured in this way in our study was 5.93 ± 1.25 minutes in Group S60 compared to 29.83 ± 5.49 minutes in Group R60 and 27.83 ± 3.13 minutes in R90, the difference being statistically highly significant. Our results in this regard are again in resemblance with those of Shukla, Dubey and Sharma 2004, who observed duration of 7.9 ± 0.95 minutes with Suxamethonium and 30.8 ± 17 minutes with Rocuronium.^[4] Similar results with Rocuronium 0.6 mg/kg have been reported by many other authors.^[5,6] Slightly higher duration has been seen in the study Wierda JMKH 1991(53 minutes).^[2]

Tracheal intubation was done at fixed time interval i.e. at 60 seconds in Group S60 & R60 and at 90 seconds in Group R90. Intubating conditions were excellent (score 8-9) in all the 30 patients (100%) in Group S60, in 23 patients (76.66%) of Group R60 and in 28 patients (93.33%) of Group R90. The intubating conditions were good in the

remaining number of patients in all the three groups. Fair or poor intubating conditions were not seen in any of the patients of any group. Furthermore in cases rated as good in R60 and R90 Group, only a slight movement of diaphragm on intubation was observed, the rest of thing setting perfectly in the scoring of excellent. Our results in this regard are slightly better than those of Shukla, Dubey, and Sharma 2004. They observed excellent conditions in 95% patients of Suxamethonium group, 50% of patients in Rocuronium group at 60 seconds and 85% of patients in Rocuronium group at 90 seconds.^[4] Good to excellent intubating conditions within 60-90 seconds of giving 0.6 mg/kg of Rocuronium have been reported in many other studies.^[2,5,10]

There was significant but less than 30%(from baseline)rise in pulse, systolic and diastolic blood pressure soon after intubation and the rise gradually became insignificant by 10 minutes of intubation. Similar results were obtained in other studies.^[4,5]

No adverse effects like bradycardia, tachycardia, hypo or hypertension, cutaneous flushing, urticaria, rash and anaphylactic reaction were seen in any of the groups. Only muscle fasciculations were seen in Suxamethonium group. Shukla, Dubey, and Sharma 2004 have also reported only muscle fasciculations in Suxamethonium group in 95% of patients. They did not find any other side effects in any of these groups.^[4]

Conclusion

There is no doubt that Suxamethonium has short onset time compared to Rocuronium and provides excellent intubating conditions within 60 seconds of drug administration but Rocuronium in dose of 0.6mg/kg also provides equally excellent intubating conditions at 90 seconds. Hence, it can serve as a good alternative to Suxamethonium for tracheal intubation in conditions where Suxamethonium is contraindicated or where its use is hazardous.

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