



RANDOMIZED DOUBLE BLIND STUDY ON ROCURONIUM BROMIDE AND SUCCINYLCHOLINE CHLORIDE DURING RAPID SEQUENCE INTUBATION.

Anesthesiology

Anil Kori

Ram Krishna Care Hospital Raipur (C.G) India

**Sankalp Sanjay
Diwan***

Ram Krishna Care Hospital Raipur (CG) india*Corresponding Author

ABSTRACT

The prospective randomized comparative study was done to compare succinyl choline and rocuronium bromide during rapid sequence induction, following various Surgeries under General Anaesthesia, study is randomized case control clinical trial with double blind method carried out in Ramkrishna CARE hospital Raipur (CG) India

KEYWORDS

Succinyl choline, Rocuronium, Rapid Sequence Induction, General Anaesthesia

INTRODUCTION:

The introduction of neuromuscular blocking drugs revolutionized the practice of anaesthesia. Before the advent of muscle relaxants, anaesthesia was induced and maintained by intravenous or inhalation agents. Tracheal intubation was uncommon, and muscle relaxation if needed was secured by deep inhalation anaesthesia with its attendant risks of respiratory or cardiac depression. After the introduction of muscle relaxants, anaesthesia underwent a conceptual change. Anaesthesia was redefined as a triad of narcosis, analgesia and muscle relaxation, specific drugs being used to produce each of these effects. Muscle relaxants are broadly divided into two groups, the depolarizers and the nondepolarizers. Depolarizers mimic the effect of acetylcholine at the neuromuscular junction, first causing muscle contractions (fasciculation) and then paralyzing. Suxamethonium, the only depolarizer in use, has the advantage of acting within 60 seconds. Muscle relaxation lasts for under 5 minutes. It is not reversed by anticholinesterases such as Neostigmine but plasma cholinesterase causes the effect to wear off quickly. Unwanted effects include malignant hyperpyrexia, increased intraocular pressure and life-threatening hyperkalaemia. Several deaths attributable to hyperkalaemic cardiac arrest have occurred following the use of Suxamethonium in children with undiagnosed muscular dystrophies. There is a clinical need for a safer drug that works equally quickly. Nondepolarizers have slower onset (2-3 minutes) and are therefore unsuitable for rapid control of the airway. They work by competitive blockade of neuromuscular junction and are reversed. The first skeletal muscle relaxant d-tubocurarine which was Non-depolarizing in nature was introduced in 1942 to fulfill the need for Jaw relaxation. Though this drug provided excellent muscle relaxation, it had additional ganglion blocking properties causing tachycardia, hypotension even in clinical doses. Further it had a delayed onset, making it unsuitable for use during rapid sequence intubation in emergency cases. Hence a search began for a relaxant which had a rapid onset and short duration of action.

In 1951, Burns and Paton ascribed the neuromuscular blocking effects of decamethonium to depolarization of the motor endplate. It was realized that bulky molecules, the pachycurares, caused nondepolarizing block and leptocurares, the slender molecules, caused depolarizing block. Three independent groups, from Italy, England and the United States, worked on simpler quaternary salts. Suxamethonium, two molecules of acetylcholine arranged back to back, was the result. Bovet, who had moved to Italy, published his work on Suxamethonium in 1949. For his contribution to pharmacology, he was awarded the Nobel Prize for Medicine in 1957. By the end of the 1950s, d-tubocurarine and Gallamine (the two nondepolarizers) and Suxamethonium (the depolarizer) were available. Succinylcholine Chloride, introduced in 1951, was a synthetic depolarizing muscle relaxant. It fulfilled both of the above requirements, and soon became the drug of choice for endotracheal intubation especially in rapid sequence intubation in emergency cases.

But all did not go well for Succinylcholine Chloride when its adverse effects started surfacing especially hyperkalemia, rise in intragastric, intraocular, intracranial pressures and cardiovascular effects. Thus the

quest began for a safer substitute for Succinylcholine Chloride.

The aim of research on neuromuscular drugs was to have non depolarizing muscle relaxant, which is like Succinylcholine Chloride without its side effects. Though many NDMR drugs like Atracurium besylate, Vecuronium bromide and Mivacurium chloride were introduced, none of them could challenge Succinylcholine Chloride in terms of its onset. The next major advance in the development of neuromuscular blockers came from the work of Bowman, who in 1988 established that with the aminosteroidals the speed of onset is related to the potency, with less potent drugs having a faster onset of action. Rocuronium is a desacetoxo analogue of Vecuronium. With Vecuronium as the framework, substitutions on the single quaternary group produced a much less potent but faster acting molecule. Rocuronium, in appropriate doses, has a speed of onset only marginally slower than that of Suxamethonium. It has an intermediate duration of action and depends on the kidney and liver for elimination. Rapacuronium, a later developed analogue of Vecuronium with a rapidity of onset that comes close to that of Suxamethonium. After its introduction into clinical practice several instances of severe bronchospasm were reported and the drug has now been withdrawn.

The new NDMR drug Rocuronium Bromide introduced in 1994 became the first competitor for Succinylcholine Chloride. Rocuronium Bromide when given in two to three times the ED95 dose is said to produce excellent to good intubating conditions in 60 seconds. Further Rocuronium Bromide is said to be devoid of the adverse effects that are seen with Succinylcholine Chloride.

Hence, the present study was undertaken to evaluate the intubating conditions with Rocuronium Bromide 0.6 mg/kg body weight and to compare the intubating conditions with that of Succinylcholine Chloride 1 mg/kg body weight, for use during rapid sequence intubation of anaesthesia in adult patients.

REVIEW OF LITERATURE:

Trann DTT, Newton EK, Mount VAH in 2015[1] conducted review controlled trials to compare the quality of intubation conditions (the ease with which anaesthetist can quickly and safely pass the endotracheal tube) between Rocuronium and Succinylcholine in all ages and varying clinical situations. They concluded that Rocuronium is slightly less effective than Succinylcholine for creating excellent and acceptable intubation conditions. Rocuronium should therefore only be used as an alternative to Succinylcholine when it is known that Succinylcholine should not be used and a more prolonged intubation is expected.

Lyon R, Perkins Z, Chatterjee D in 2015[2] performed a comparative cohort study of major trauma patients undergoing pre-hospital RSI to compare the safety and effectiveness of a traditional RSI protocol using Etomidate and Suxamethonium with a modified RSI protocol using Fentanyl, Ketamine and Rocuronium. They concluded that pre-hospital RSI using Fentanyl, Ketamine and Rocuronium produced superior intubating conditions and a more favourable haemodynamic response to laryngoscopy and tracheal

intubation.

Gowda V, Ranganath N, Asha N in 2015 [3] conducted a prospective clinical study to compare the intubating conditions of Rocuronium bromide with that of Succinylcholine and to evaluate the haemodynamic effects of these agents during laryngoscopy and intubation using Train of Four Watch as a neuromuscular monitor. They concluded that changes in heart rate and mean arterial pressure was a haemodynamic response to laryngoscopy and endotracheal intubation, which subsided to near pre induction, values 20 minutes after intubation. Trend in haemodynamic changes to laryngoscopy and intubation were more in Succinylcholine chloride than Rocuronium bromide. It is possible to achieve perfect intubating condition with Rocuronium bromide and can be used as an alternative to Succinylcholine particularly in patients who are at risk for adverse sequelae of Succinylcholine. Rocuronium bromide 0.9mg/kg may be considered an optimum dose for intubation. Rocuronium bromide is a hemodynamically stable drug.

Sabo D, Jahr J, Pavlin Jet al. in 2014 [4] conducted a randomized active-controlled study in adult patients undergoing short surgical procedures in an outpatient setting received either Rocuronium 0.6 mg/kg for intubation with Sugammadex 4.0 mg/kg for reversal (n = 70) or Succinylcholine 1.0 mg/kg with spontaneous recovery (n = 80). Blood potassium concentrations were assessed at baseline (before study drug administration) and at intervals up to 15 min after Rocuronium, Sugammadex, and Succinylcholine. They concluded that Succinylcholine was associated with a modest increase in potassium concentration; these changes were not seen after Rocuronium or Sugammadex.

Madhusudan M, Rao MH, Reddy AKS et al. in 2014 [5] conducted a randomised double blind control study to compare the intubating conditions and haemodynamic responses during rapid tracheal intubation using either Suxamethonium or Rocuronium with ephedrine pretreatment. They concluded that Suxamethonium still continues to be the "gold standard" for providing ideal tracheal intubation conditions. However, in conditions where Suxamethonium is contraindicated, Rocuronium-Ephedrine combination can be used as an alternative to intubate the trachea at 60 seconds.[28]

Khamankar S, Belekar V in 2013[6] conducted a randomised prospective study to compare the intubating conditions between inj. Rocuronium and inj. Succinylcholine during rapid sequence intubation in patients posted for emergency surgeries. They concluded that Rocuronium (0.6mg/kg) provided acceptable intubation conditions in most of the patients at 60 seconds but, unable to provide excellent intubating conditions in all of them during rapid sequence intubation. Suxamethonium is still the best muscle relaxant to accomplish intubation in emergent cases. If Suxamethonium is contraindicated, Rocuronium may be used as an alternative.

MATERIALS AND METHODS:

Patients posted for various elective surgeries under general anaesthesia at RAMKRISHNA CARE HOSPITAL. Between age group of 18-60 years, with total body weight between ranges of 50-90 kilograms, ASA grade 1& 2 were included in study. All patients with Diabetes mellitus, Ischemic heart disease, Bronchial asthma, Anticipated difficult airway & Other absolute contraindications of succinylcholine (known hypersensitivity to Succinylcholine, personal or familial history of malignant hyperthermia, burn injury > 24 hours and atleast till 18 months of injury, Raised intraocular pressure, Hyperkalemia) were excluded from study. After taking permission from ethics committee of our institution the study population was randomly divided into two groups with 30 patients in each group. Group I consisted of 30 patients to receive Succinylcholine Chloride 1 mg/kg body weight and intubation attempted at 60 seconds.

Group II consisted of 30 patients to receive Rocuronium Bromide 0.6 mg/kg body weight and intubation attempted at 60 seconds. The baseline heart rate, oxygen saturation and electrocardiogram, systolic, diastolic, mean arterial blood pressure was recorded. All patients were preoxygenated with 100% oxygen via a face mask for 5 minutes. inj. Ondansetron 4mg, injection Glycopyrrolate 0.004 mg/kg, inj. midazolam 0.02mg/kg, Injection Fentanyl 100mcg/kg were given to all patients 3 minutes prior to administering induction agent, patient induced with injection propofol 2mg/kg body weight intravenously. In group I, Succinylcholine Chloride 1 mg/kg body weight was given intravenously Similarly in group II, Rocuronium Bromide 0.6 mg/kg

was given intravenously,

In all the three groups of patients, oral endotracheal intubation was attempted at 60 seconds following the administration of muscle relaxant and intubating conditions were graded using the score adopted by Magorian T [7]

Excellent = Jaw relaxed, vocal cords apart and immobile, no diaphragmatic movements.

Good= Jaw relaxed, vocal cords apart and immobile, some diaphragmatic movements.

Poor= Jaw relaxed, vocal cords moving and bucking.

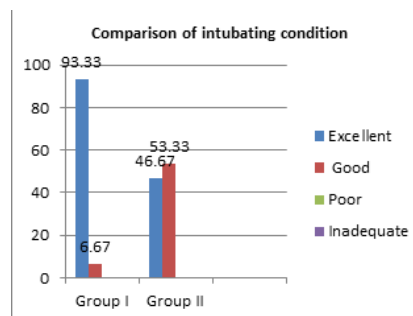
Inadequate= Jaw not relaxed, vocal cords closed.

All the patients were intubated with appropriate sized oral endotracheal tubes (cuffed), bilateral air entry was checked and the tube was firmly secured. Maintenance of anaesthesia was done with 50% oxygen and 50% nitrous oxide and isoflurane, on close circuit with anaesthesia workstation. Monitoring of vital parameters like heart rate, oxygen saturation, systolic, diastolic and mean arterial blood pressures, electrocardiogram were recorded 1, 3 and 5 minutes following intubation. The clinical duration of action that is the time from administration of relaxant to first attempt at respiration of initial bolus doses of Succinylcholine Chloride and Rocuronium Bromide were noted down. Subsequently, the muscle relaxation was maintained with Atracurium 0.1 mg/kg body weight till the end of surgery. At the end of surgery all the patients were reversed with injection Neostigmine 0.05 mg/kg body weight and injection Glycopyrrolate 0.008 mg/kg body weight. Other side effects like histamine releasing property associated with administration of Rocuronium Bromide and Succinylcholine Chloride were also noted. The haemodynamic parameters in the present study was compared statistically using p value. All vital parameters data taken as mean value, quantitative & qualitative analysis done by Chi Square test, randomisation done by computer software SPSS 16.0

OBSERVATION:

TABLE-1 INTUBATING CONDITIONS

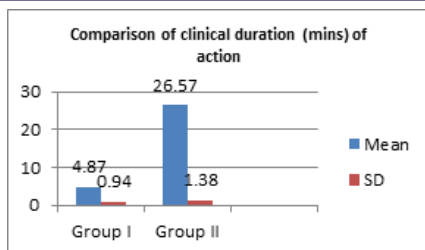
Intubating conditions	Group I Succinylcholine Chloride 1 mg/kg (n = 30)	Group II Rocuronium Bromide 0.6 mg/kg (n = 30)	P value (Chi sq test)
a. Excellent	28(93.33)	14(46.67)	0.0001 HS
b. Good	2(6.67)	16(53.33)	
c. Poor			
d. Inadequate			



Intubating conditions in group 1 were :28- excellent,2-good, Intubating conditions in group 2 were :14 excellent,16 –good, The p value is 0.0001 for intubating conditions therefore distribution of samples according to intubating condition in 2 groups are statistically highly significant.

TABLE- 2 CLINICAL DURATION OF ACTION

Clinical duration of action	Group I Succinylcholine Chloride 1 mg/kg (n = 30)	Group II Rocuronium Bromide 0.6 mg/kg (n = 30)	P value (chi square test)
(min) ± SD	4.87±0.94	26.57±1.38	0.00001 HS

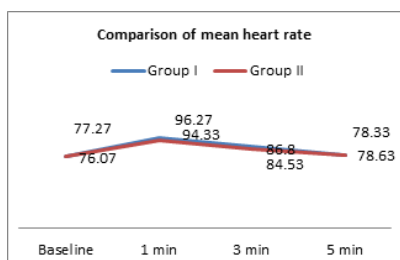


The mean duration of action for group 1 was 4.87 ± 0.94 mins, 26.5 ± 1.38 for group 2. The difference was found to be highly statistically significant (p Value=0.00001).

The mean duration of action for group 1 was 4.87 ± 0.94 mins, 26.5 ± 1.38 for group 2. The difference was found to be highly statistically significant (p Value=0.00001).

TABLE-3 MEAN HEART RATE (BEATS/MIN)

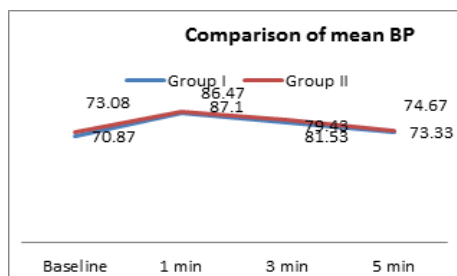
Mean heart rate $\pm$ SD (beats/min)	Group I Succinylcholine Chloride 1 mg/kg (n = 30)	Group II Rocuronium Bromide 0.6 mg/kg (n = 30)	P value (chi square test)
Base line (pre induction)	76.07 $\pm$ 5.52	77.27 $\pm$ 12.73	0.23 NS
1 min after intubation	96.27 $\pm$ 11.43	94.33 $\pm$ 11.62	0.78 HS
3 min after intubation	86.8 $\pm$ 8.1	84.53 $\pm$ 7.74	0.45 HS
5 min after intubation	78.63 $\pm$ 6.97	78.33 $\pm$ 5.41	0.61 NS



The p value for change in mean heart rate during pre induction period, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation are >0.05 , so they are highly insignificant.

TABLE-4 MEAN ARTERIAL PRESSURE

Mean BP $\pm$ SD (mm Hg) $\pm$ SD	Group I Succinylcholine Chloride 1 mg/kg (n = 30)	Group II Rocuronium Bromide 0.6 mg/kg (n = 30)	P value (chi square test)
Base line (pre induction)	70.87 $\pm$ 5.34	73.08 $\pm$ 2.48	0.17 NS
1 min after intubation	86.47 $\pm$ 13.69	87.1 $\pm$ 7.03	0.30 NS
3 min after intubation	79.43 $\pm$ 9.42	81.53 $\pm$ 5.32	0.33 NS
5 min after intubation	73.33 $\pm$ 6.2	74.67 $\pm$ 2.81	0.18 HS



The p values for change in mean arterial blood pressure during pre-induction phase (baseline), 1 minute after intubation, 3 minutes after intubation & 5 minutes after intubation are >0.05 , which is statistically insignificant.

RESULTS:

In the present study total 60 research participants has been recruited & mean age of group I 46.2 ± 10.44 years and group II 47.17 ± 5.16 respectively. As per their gender wise distributions in both of the groups were 1.5:1 & 1.73:1 respectively.

Comparison of Intubation Score of two groups it was found that Intubating conditions in group 1 were :28- excellent, 2-good, Intubating conditions in group 2 were :14 excellent, 16 -good, The p value is 0.0001 for intubating conditions therefore distribution of samples according to intubating condition in 2 groups was statistically highly significant (Table 1). When compare the duration of action among the Succinylcholine & Rocuronium Group it was for group 1 was 4.87 ± 0.94 mins, 26.5 ± 1.38 for group 2. The difference was found to be highly statistically significant (p value=0.00001). (Table-2)

In continuation the Comparison of Mean Heart rate (beats/min) at different time interval in both of the groups; The p value for change in mean heart rate during pre induction period, 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation are >0.05 . So it was highly insignificant. (Table-3)

Group -I & Group -II was compared for mean Blood Pressure at different time interval the p values for change in mean arterial blood pressure during pre-induction phase (baseline), 1 minute after intubation, 3 minutes after intubation & 5 minutes after intubation are >0.05 , which is statistically insignificant. (Table-4)

CONCLUSION :

1. Succinylcholine chloride 1 mg/kg body weight produces excellent intubating conditions in 93.3% of the patients at 60 seconds and good to excellent intubating conditions in 6.67% of the patients with an average clinical duration of action of 4.87 ± 0.94 minutes.

Rocuronium Bromide 0.6 mg/kg body weight produces excellent intubating conditions in 46.6% of the patients at 60 seconds and good to excellent intubating conditions in 53.4% of the patients with an average clinical duration of action of 26.57 ± 1.38 minutes.

1. Rocuronium Bromide is a safe alternative to Succinylcholine Chloride for rapid sequence induction in adult patients in situations where Succinylcholine Chloride is contraindicated. Discussion - Succinylcholine Chloride introduced in 1951 was unparalleled in terms of its onset and duration of action. The type of relaxation obtained with this drug was so good that even today it is used as a gold standard and other drugs are compared with it. But with time, adverse effects of Succinylcholine Chloride like bradycardia, nodal and junctional rhythms, rise in intraocular, intracranial pressure started surfacing; quest began for better relaxants devoid of these adverse effects. Many drugs like Vecuronium, Atracurium and Mivacurium were introduced into clinical practice, but none could challenge Succinylcholine Chloride in terms of onset time. Further they were associated with side effects like Histamine releasing property of Mivacurium.

DISCUSSION:

Rocuronium Bromide introduced in 1994 became the first drug to challenge the onset time of Succinylcholine Chloride, in that it produces good to excellent intubating conditions in 60 seconds. In addition to this Rocuronium Bromide is devoid of adverse effects of Succinylcholine Chloride. In view of this, the present study was undertaken to compare the intubating conditions of Rocuronium Bromide with that of Succinylcholine Chloride at 60 seconds. So Rocuronium is safer alternative to succinylcholine where succinylcholine is contraindicated.

REFERENCE:

- Trann DTT, Newton EK, Mount VAH, Lee JS, Wells GA, Perry JJ. Comparison of two muscle relaxants, rocuronium and succinylcholine, to facilitate rapid sequence induction
- Lyon R, Perkins Z, Chatterjee D, Lockey D, Russell M, Kent, Surrey & Sussex Air Ambulance Trust. Significant modification of traditional rapid sequence induction improves safety and effectiveness of pre-hospital trauma anesthesia. Critical Care 2015; Apr 1;19:134.
- Gowda V, Ranganath N, Asha N, Henjarappa KS, Arathi BH, Sowmya MJ. A

- comparative study of Rocuronium Bromide and Succinylcholine for endotracheal intubation using neuromuscular monitoring. *International journal of recent trends in science and technology* 2015;15(2): 345-350.
4. Sabo D, Jahr J, Pavlin J, Philip B, Shimode N, Rowe E, Woo T, Soto R in 2014. The increases in potassium concentrations are greater with succinylcholine than with rocuronium-sugammadex in outpatient surgery: a randomized, multicentre trial. *Canadian journal of anesthesia*. 2014 May;61(5):423-432
 5. Madhusudan M, Rao MH, Reddy AKS, Kadiyala V, Samantaray A, Hemanth N, Charupalli K. Comparison of intubating conditions and haemodynamic responses during rapid tracheal intubation using either suxamethonium or rocuronium with ephedrine pretreatment. *J Clin Sci Res* 2014;3:174-180.
 6. Khamankar S, Belekar V. Comparison of equipotent doses of rocuronium and vecuronium. *Anesth Essays Res*. 2015 Jan-Apr; 9(1): 88-91.
 7. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid- sequence induction of anesthesia in adult patients. *Anesthesiology*. 1993 Nov; 79(5): 913-8.