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KEY WORDS: vecuronium, rocuronium, heart rate, systolic blood pressure, diastolic blood pressure, time of onset

COMPARISON OF TIME OF ONSET AND HAEMODYNAMIC EFFECTS OF VECURONIUM BROMIDE WITH ROCURONIUM BROMIDE UNDER GENERAL ANAESTHESIA

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ABSTRACT

Introduction : Intubation is one of the means of securing airway . Muscle relaxants are useful in providing adequate muscle relaxation to enable laryngoscopy and intubation.the aim of this study was to compare the time of onset of Vecuronium bromide with Rocuronium bromide for endotracheal intubation and to compare the hemodynamic effects of Vecuronium bromide with Rocuronium bromide during endotracheal intubation.

Method : a total of 50 patientsof ASA G1 and 2 selected for elective surgery are divided into two groups according to randomization plan. One group (Rocuronium group) of 25 patients received Rocuronium 0.6 mg/kg body weight and the other group (Vecuronium group) of 25 patients received Vecuronium 0.1 mg/kg body weight. Parameters observed are Time of onset which is obtained by monitoring for the time from the end of the injection of muscle relaxant until maximum blockade of the first twitch response (T1) of the TOF and Haemodynamic changes which are monitored at 5 settings i.e. 0 min (Base line), 1, 3, 5 and 10 mins .

Result : The mean value of onset of action for Rocuronium is 73.6 ± 14.11 and for Vecuronium is 119.2 ± 19.13. In Rocuronium group there is increase in HR from base line which showed a peak at 5 min and decreased at 10 min, but in Vecuronium group there is decrease in HR from base line through out. There was no significant difference of SBP ,DBP and MAP at baseline between the mean values of the two groups.This statistical insignificance has continued at 1, 3, 5 and 10 min after giving relaxants .

Conclusion : Both the drugs are found to be equally good for maintaining hemodynamic stability in patients undergoing various surgeries. Rocuronium bromide can therefore be advocated as drug of choice where rapid intubation will be beneficial without compromise of haemodynamic stability.

INTRODUCTION:

Intubation is one of the means of securing airway.Muscle relaxants are useful in providing adequate muscle relaxation to enable laryngoscopy and intubation.Succinyl choline is introduced for intubation[1] and still preferred eventhough it has side effects. Of all the available relaxants, Rocuronium and Vecuronium come close to ideal muscle relaxant. Among these two, Rocuronium places itself ahead because of its rapid onset of action[2] in addition to having all the beneficial effects of Vecuronium, thus making it an ideal drug for endotracheal intubation.

AIMS AND OBJECTIVES:

1) To compare the time of onset of Vecuronium bromide with Rocuronium bromide for endotracheal intubation.
2) To compare the hemodynamic effects of Vecuronium bromide with Rocuronium bromide during endotracheal intubation.

MATERIALS AND METHODS:

This is a hospital based study invoving a total of 50 patients, ASRAMS Eluru

INCLUSION CRITERIA:

1. ASA Grade I and II.
2. Age between 15 and 60 years.
3. Mallampatti grade I or II airway anatomy.
4. Patients not suffering from neuromuscular disease.
5. Patients not receiving any medication known to interact with neuromuscular blocking drugs, for example- aminoglycoside antibiotics.

EXCLUSION CRITERIA:

1. ASA grade III and IV.
2. Age less than 15years and more than 60 years.
3. Uncontrolled hypertensives.
4. Patients with potential airway problems and anticipated difficult intubations, (other than Mallampatti grade I or II airway anatomy).
5. Patients suffering from neuromuscular diseases.

The patients selected for elective surgery are divided into two groups according to randomization plan. One group (Rocuronium group) of 25 patients received Rocuronium 0.6 mg/kg body weight and the other group (Vecuronium group) of 25 patients received Vecuronium 0.1 mg/kg body weight.

PROCEDURE:

Each patient was premedicated the night before and the morning of surgery with Cap. Omeprazole 40mg and Tab. Alprazolam 0.5mg. Inj. Tramadol 1mg/kg and Inj. Ondensetron 4mg intramuscularly one hour were given before shifting to the operation theatre. Atropine and promethazine are deliberately avoided since they alter the haemodynamics.

Pre operative investigations included hemoglobin perce ntage, haematocrit, total count, differential count, ESR, Urine analysis, blood area, serum creatinine and random blood sugar, ECG and chest x-ray.

All the patients are starved from midnight. Pulse rate and blood pressure are recorded prior to and after administration of premedication.

Upon arrival in the operation theater, an I.V line is secured .Heart rate, blood pressure and ECG are recorded prior to induction .

Preoxygenation is done for 3 minutes with 100% O2. Patents are given Inj. Midazolam 0.04mg/kg and Inj. Fentanyl 1-2 micrograms/kg. All patients are induced with 3-5 mg/kg of Thiopentone, the endpoint being the loss of the eyelash reflex. Intubation is done after suppression of TOF response using a well lubricated cuffed endotracheal tube of appropriate size after giving 0.6 mg/kg of Rocuronium to the patients in the study group and 0.1 mg/kg of Vecuronium to the patients in the control group .Neuromuscular monitoring was done using

a peripheral nerve stimulator and stimulating the ulnar nerve at the wrist via surface electrodes placed along the course of the nerve. Supra maximal square wave impulses of 0.2 mSec duration in a train-of-four sequence (2 Hz) were delivered. Baseline evoked mechanical response of the adductor pollicis muscle was assessed visually/manually. The evoked response to ulnar nerve TOF stimulation every 10 seconds was recorded. Time of onset is monitored by time gap between injecting vecuronium or rocuronium and complete ablation of first twitch response (T_1) of TOF response.

All the patients were ventilated with nitrous oxide-oxygen using closed circuit in the ratio 50:50%. Anaesthesia being maintained with 0.2-0.4% of isoflurane and repeat doses of 1/4th the original dose of muscle relaxants are given in both the groups. Heart rate and SBP, DBP and MAP are recorded one minute after administration of the drug and every five minutes till the end of the surgery. ECG is monitored throughout surgery.

Residual paralysis at the end of surgery is reversed with 0.05 mg/kg of neostigmine and 0.01 mg/kg of glycopyrolate. After clearing the throat, extubation was done at the onset of adequate respiration and good limb movements.

Parameters observed:

1. Time of onset is obtained by monitoring for the time from the end of the injection of muscle relaxant until maximum blockade of the first twitch response (T_1) of the TOF.
2. Haemodynamic changes are monitored at 5 settings i.e. 0 min (Base line), 1, 3, 5 and 10 mins

a. Heart rate recorded by ECG at regular intervals
b. Systolic blood pressure, Diastolic blood pressure and Mean arterial pressure recorded at regular intervals using a NIBP monitor.
c. ECG

RESULTS:

Demographic data like Age, Weight, Sex and ASA Grade were similar in both groups.

TABLE 1: ONSET OF ACTION PRESENTED AS Mean± S.D

Parameter	Rocuronium	Vecuronium	p value
Onset of action	73.6 ± 14.11	119.2 ± 19.13	< 0.0001 (HS)

The mean value of onset of action for Rocuronium is 73.6 ± 14.11 and for Vecuronium is 119.2 ± 19.13.Student unpaired t test was applied and found that there was high significant difference between two groups. (p= < 0.0001)

TABLE-II: Heart rate changes presented as Mean ±SD
(Student's Unpaired t-test)

Comparison of HR between Rocuronium and Vecuronium groups:

There was a significant difference in HR between the two groups at base line i.e. p= 0.0007. This significant difference

Heart rate	Rocuronium	Vecuronium	p value
0 min	82.72± 10.64	73.28± 7.55	0.0007(S)
1 min	83.6± 10.52	72.72± 6.95	< 0.0001(HS)
3 min	85.8± 10.05	71.6± 6.43	< 0.0001(HS)
5 min	88.72 ±10.06	65.68± 6.155	< 0.0001(HS)
10 min	87.76± 10.1	64.24± 5.78	< 0.0001(HS)

in HR between two groups has continued at 1 ,3 ,5 and 10 mins i.e. p < 0.0001 respectively.

How ever in Rocuronium group there is increase in HR from base line which showed a peak at 5 min and decreased at 10 min, but in Vecuronium group there is decrease in HR from base line through out.

TABLE-III : Systolic Blood Pressure(SBP) presented as Mean ± SD
(Student's Unpaired t-test)

SBP	Rocuronium	Vecoronium	p value
0 min	131.76 ±14.24	128 ±12.33	0.323(NS)
1 min	130.88± 13.93	125.48± 11.31	0.138(NS)
3 min	127.76± 10.47	124.2± 8.93	0.202(NS)
5 min	127.76 ±11.38	121± 12.64	0.052(NS)
10 min	129 ±11.343	124.4± 10.15	0.137(NS)

Comparison of SBP between Rocuronium and Vecuronium:

There was no significant difference of SBP at baseline between the mean values of the two groups at base line (p= 0.323). This statistical insignificance has continued at 1, 3, 5 and 10 min i.e p = 0.138, 0.202, 0.052 and 0.137 respectively.The change of SBP in Rocuronium group is less when compared to Vecuronium group.

TABLE-IV: Diastolic Blood Pressure (DBP) presented as Mean ±SD
(Student's Unpaired t-test)

DBP	Rocuronium	Vecuronium	p value
0 min	86.64 ± 13.55	84.52 ± 13.28	0.282 (NS)
1 min	89.16 ± 9.69	86.88 ± 9.37	0.401 (NS)
3 min	84.36 ± 9.95	82.84 ± 9.81	0.589 (NS)
5min	82.84 ± 8.21	80.48 ± 12.17	0.0764 (NS)
10 min	87.4 ± 9.19	85.16 ± 9.19	0.393 (NS)

Comparison of DBP between Rocuronium and Vecuronium: There was no significant difference of DBP between the mean values of the two groups at base line (p= 0.282).This statistical insignificance has continued at 1, 3, 5 and 10 min i.e p = 0.401, 0.589, 0.076, 0.393 respectively. The change of DBP in Rocuronium group is less when compared to Vecuronium group.

TABLE-V: Mean Arterial Pressure (MAP) presented as Mean ±SD
(Student's Unpaired t-test)

MAP	Rocuronium	Vecuronium	p value
0 min	103.01 ± 12.67	99.01 ± 12.48	0.266 (NS)
1 min	103.06 ± 10.57	99.74 ± 9.56	0.249 (NS)
3 min	98.82 ± 8.9	96.62 ± 8.6	0.38 (NS)
5 min	99.78 ± 8.45	93.98 ± 11.88	0.052 (NS)
10 min	101.26 ± 9.1	98.24 ± 9.15	0.246 (NS)

Comparison of MAP between Rocuronium and Vecuronium :

There was no significant difference of MAP between the mean ± SD values of the two groups at base line (p= 0.266). This statistical insignificance has continued at 1, 3, 5 and 10 min after giving relaxants i.e. p = 0.249, 0.38, 0.052, 0.246 respectively.The change of MAP in Rocuronium group is less when compared to Vecuronium group.

DISCUSSION:

Endotracheal intubation is an integral part of administration of general anaesthesia during surgical procedures. Suxamethonium, a depolarizing muscle relaxant with its rapid onset and short duration of action is still relaxant of choice to facilitate tracheal intubation. In addition to fasciculations, suxamethonium has got many side effects such as bradycardia and other dysrhythmias, rise in serum potassium, post operative myalgia, rise in intraocular, intragastric and intracranial pressure, incidences of prolonged recovery in patients with pseudo-cholinesterase deficiency and triggering of malignant hyperthermia. Because most of the side effects of suxamethonium reflect its depolarizing mechanism of action, search for ideal neuromuscular blocking agent focused on nondepolarising type of relaxants which has rapid onset time and offers good to excellent intubation conditions, as rapidly as suxame thonium and which lacks the above mentioned adverse effects is continuing[3].

An ideal muscle relaxant should have non-depolarizing mechanism of action, rapid onset and short duration of action, rapid recovery, non-cumulative, no histamine release, no cardiovascular side effects, high potency, and prompt reversibility by cholinesterase inhibitors and pharmaco logically inactive metabolites[4].

Haemodynamic stability is an integral and essential goal of any anaesthetic management plan . Rocuronium and Vecuronium come closer to the characteristics of ideal muscle relaxant inmaintaining hemodynamics.

Intravenous Vecuronium bromide, is considered as the "gold standard" among muscle relaxants for its cardiovascular stability. It also has a large margin of safety between neuromuscular and vagal blocking effects[5,6]. Intravenous Vecuronium though being cardiostable has a slow onset and causes bradycardia when used with narcotics[7]. Intravenous Rocuronium bromide is a relatively new steroidal intermediate acting non-depolarising neuromuscular blocking agent with a faster onset of action[2] . It has proved to have minimal cardiovascular side effects in animal studies[8].Some human studies have shown that Rocuronium has minimal effects on heart rate and arterial pressures with the dose of 2-3 x ED_{95}[2].

Thus we under took this study to evaluate the comparative properties of Rocuronium bromide with routinely used Vecuronium bromide for an agent with shorter onset of action and good haemodynamic stability.

In our study the mean onset of action of Rocuronium (73.6 ± 14.11) is shorter when compared to vecuronium (119.2 ± 19.13) which was highly significant (p = < 0.0005) This finding was similar to studies done by Booth MG et al. in 1992[9] Mayer M et al in 1992[10], Magorian T, Flannery KB, Miller RD in 1993 and Malhotra P, Saxena N , Kiran U and Choudhary M in 2002[11].

With regard to haemodynamics in our study we observed a significant change in HR in each of the two groups during 5 settings. A significant increase in HR by 7.47% at 5 min (88.72 ± 10.06) after giving rocuronium from base line (82.72 ± 10.64) was observed. Similarly we noticed a significant decrease in HR by 12.11 % at 10 min (64.24 ± 5.78) after giving vecuronium from base line (73.28 ± 7.55). The probable reason for the increase in HR in Rocuronium group is attributed to vagolytic or perhaps, sympathomimetic effect of rocuronium[12] .Vecuronium per se do not have any tendency to decrease HR[13,14] but the probable reason for decrease in HR in Vecuronium group is when combined with other drugs that do cause bradycardia (e.g., fentanyl).

In the Rocuronium group we observed no significant changes in SBP at any of the 5 settings but the maximum decrease in SBP was found at 5 mins by 2.48 % when compared to base line. Similarly in Vecuronium group we observed no significant changes in SBP at any of the 5 settings but the maximum decrease in SBP was found at 5 mins by 5.43 % when compared to base line. Thus the decrease in SBP was statistically insignificant when comparing different settings within the same group. In the Rocuronium group we observed no significant changes in DBP at any of the 5 settings but the maximum decrease in DBP was found at 3 mins by 3.35 % when compared to base line. Similarly in Vecuronium group we observed no significant changes in DBP at any of the 5 settings but the maximum decrease in DBP was found at 5 mins by 4.11 % when compared to base line. Thus the decrease in DBP was statistically insignificant when comparing different settings within the same group In our study we did not find any statistically significant difference in the SBP, DBP and MAP between Rocuronium and Vecuronium at any of the 5 settings.

Our findings are similar to findings studied by Robertson EN et al (1994)[12] who compared cardiovascular effects with 3X ED_{95} of rocuronium and vecuronium , he found that there were statistically significant increases from baseline in one or more (heart rate, BP) hemodynamic parameters in the Rocuronium group when compared to Vecuronium group.

CONCLUSION:

Rocuronium is devoid of any significant cardiovascular changes causing haemodynamic instability when compared with Vecuronium. Both the drugs are found to be equally good for maintaining hemodynamic stability in patients undergoing various surgeries. Rocuronium bromide can therefore be advocated as drug of choice where rapid intubation will be beneficial without compromise of haemodynamic stability

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