Original research article

Comparative Study of Vecuronium, Rocuronium and its Combination for Haemodynamics and Acceptable Intubating Conditions

Nitish Kumar[1], Supriya Suman[2]

[1]Senior resident, Department of Anaesthesiology ANMMCH Gaya

[2]Senior resident, Department of Anaesthesiology ANMMCH Gaya

Corresponding Author: Supriya Suman

Abstract

Background and Objectives: Vecuronium has a slow onset of action (2-3min) which limits its use in situations requiring rapid establishment of airway. Rocuronium can provide good intubating conditions within 90sec but it is not used routinely because of high cost. Combination of rocuronium with vecuronium is known to produce synergism without producing any side effects. It provides rapid onset of action and acceptable intubating conditions. This study was undertaken to evaluate the clinical benefits of the combination of rocuronium and vecuronium in terms of better haemodynamics and acceptable intubating conditions over individual drugs.

Methods: 90 ASA grade I and II patients in the age group 20-60 years of either sex scheduled for elective surgeries done under general anaesthesia were recruited for the study. They were randomly allocated into three groups - group V, group R, group RV with the sample size of 30 in each. After induction with fentanyl-propofol-nitrous oxide- oxygen, group V received vecuronium 0.08 mg/kg, group R received rocuronium 0.6 mg/kg and group RV received a combination of rocuronium 0.3 mg/kg with vecuronium 0.04 mg/kg.

Conclusion: The combination of rocuronium and vecuronium can provide clinically comparable conditions for tracheal intubation as rocuronium alone without compromising haemodynamic stability, thus, can be an economic alternative to rocuronium for intubation.

Keywords: Neuromuscular relaxants; rocuronium, vecuronium. Pharmacology; synergism. Neuromuscular relaxants; haemodynamic effects.

Introduction

Rapid and safe endotracheal intubation is of paramount importance in practice of general anaesthesia. Securing patient's airway smoothly and quickly minimizes the chances of regurgitation and aspiration of gastric contents. Sir William Mac Ewen (1848-1924) was the first physician to intubate trachea orally in 1878 for the sole purpose of administering anaesthesia. Mac Ewen performed a blind oral intubation on an awake patient to permit continued administration of chloroform for the relief of obstruction in laryngeal diphtheria, and then for removal of carcinoma of the mouth.[1] Endotracheal anaesthesia was introduced into the clinical practice in early part of 20th century. Though endotracheal anaesthesia was practiced with metal tubes and chloroform anaesthesia, true concept of endotracheal intubation was actually introduced by Sir Ivan Magill during the World War I.[1] Most intubations were done using inhalational technique which was associated with its own problems like laryngospasm and bronchospasm when intubation was attempted with inadequate depth. Further making the patient sufficiently deep to obtain good intubating

conditions led to haemodynamic disturbances because of higher concentration of inhalational agents that were used. The use of neuromuscular blocking drugs to facilitate intubation was first introduced into clinical practice in 1942 by Harold Randall Griffith[2] and within several years gained widespread acceptance. Neuromuscular blocking drugs are frequently used for tracheal intubation as they facilitate laryngoscopy, open the vocal cords, and prevent coughing providing good intubating conditions rapidly in most patients. When used in doses sufficient to provide ideal conditions for endotracheal intubation, all neuromuscular blocking drugs in current practice produce cardiovascular changes. The administration of two neuromuscular blockers in combination was first introduced by Lebowitz and coworkers[3] in an attempt to reduce the cardiovascular side effects of neuromuscular blockers by giving smaller doses of each drug as a combination. Since then, various combinations of neuromuscular blockers have been studied by many authors and is proved to be beneficial. In the present anaesthetic practice; it is not uncommon for a patient to receive two or more neuromuscular blocking drugs in combination, with the objectives of maintenance of haemodynamic stability along with a rapid airway control.

Objectives

To study the clinical benefits of combination of rocuronium and vecuronium over individual drugs. To provide an economic alternative to rocuronium without compromising haemodynamic stability and intubating conditions.

Material and Method

A randomized double blind study was conducted on 90 ASA grade I and II patients in the age group 20-60 years of either sex scheduled for elective surgeries done under general anaesthesia in Anugrah Narayan Magadh Medical college and Hospital Gaya, Bihar. Study duration of Two years.

Patients were allocated into three groups with the sample size of 30 in each group.

Group V (n=30) received vecuronium 0.08 mg/kg.

Group R (n=30) received rocuronium 0.6 mg/kg.

Group RV (n=30) received rocuronium 0.3 mg/kg and vecuronium 0.04 mg/kg.

Exclusion criteria

*****Patients with anticipated difficult intubation; MPT 3 and 4.

*Patients with hepatic, renal and cardiac dysfunction.

*Pregnant women.

*Morbidly obese patients.

*Those receiving medications which could interfere with neuromuscular function and haemodynamics.

A detailed preanaesthetic evaluation including history of previous medical illness, previous surgeries, general examination and appropriate baseline investigations were carried out on the previous day of surgery and recorded in the proforma. An informed and written consent was taken after explaining the anaesthetic procedure in detail. Sedation with tab. diazepam 10mg orally was given in the night to allay the anxiety. All patients were pre-oxygenated with 100% oxygen by face mask for 3min. General anaesthesia was induced with Inj. propofol 2mg/kg body weight i. v. and patients ventilated with 50% O_2 in N_2O. After loss of eye lash reflex and confirming adequacy of mask ventilation, the patients randomly received either intubating dose of Inj. vecuronium 0.08mg/kg body weight i. v. or Inj. rocuronium 0.6mg/kg body weight i. v. or a combination of Inj. vecuronium 0.04 mg/kg and Inj. rocuronium 0.3 mg/kg i. v. Intubation was attempted at 90sec after administration of relaxant, intubating conditions were evaluated and haemodynamic changes

were monitored. All laryngoscopies and intubations were done by the same anaesthesiologist to avoid subjective errors. In patients who had impossible intubating conditions, assisted ventilation was reinstituted and intubation was attempted 30sec later.

Table 1 Grading of intubating conditions as per Goldberg and colleagues

GRADE	DESCRIPTION
1=EXCELLENT	Easy passage of ETT without coughing, vocal cords relaxed
2=GOOD	Slight coughing, vocal cords relaxed
3=POOR	Passage of ETT with coughing, bucking, some movement of vocal cords present
4=IMPOSSIBLE	Vocal cords adducted or not visualized, jaw not relaxed

Heart rate, systolic and diastolic blood pressure, mean arterial pressure and SpO2 were recorded by the blinded observer, at baseline, post induction, post muscle relaxant and at 1,2,3,5 and 10 minutes after intubation. Any side effects if observed during intubation were noted. Anaesthesia was maintained with 50% oxygen in nitrous oxide with IPPV (intermittent positive pressure ventilation) in the three groups.

Results

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean SD (min-max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients and to find the homogeneity of parameters on continuous scale. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups and to find the homogeneity of samples on categorical scale. $p<0.05$ was considered to be significant.

Table 2: Comparison of age distribution

Age in years	Group V		Group R		Group RV	
	No.	%	No.	%	No.	%
21-30	4	13.3	4	13.3	7	23.3
31-40	8	26.7	8	26.7	12	40.0
41-50	13	43.3	13	43.3	9	30.0
51-60	5	16.7	5	16.7	2	6.7
Total	30	100.0	30	100.0	30	100.0
Mean ± SD	41.90±8.75		41.90±8.75		37.87±9.81	

Samples are age matched

The majority of the patients were in the age group of 31-50 (70%) years in each group. The mean age in group V and group R was 41.90 years whereas in group RV it was 37.87

years. The difference in the mean age of the patients between the three groups was not statistically significant..

Table 3: Comparison of gender distribution

Gender	Group V		Group R		Group RV	
	No.	%	No.	%	No.	%
Male	15	50.0	12	40.0	19	63.3
Female	15	50.0	18	60.0	11	36.7
Total	30	100.0	30	100.0	30	100.0

Samples are gender matched.
The study comprised of 46 males and 44 females. Group V comprised of 15 (50%) males and 15 (50%) females, group R comprised of 12 (40%) males and 18 (60%) females whereas group RV comprised of 19 (63.3%) males and 11 (36.7%) females. The three groups were comparable.

Table 4: Comparison of MPT Grade

MPT	Group V		Group R		Group RV	
	No.	%	No.	%	No.	%
1	22	73.3	22	73.3	22	73.3
2	8	26.7	8	26.7	8	26.7
Total	30	100.0	30	100.0	30	100.0

MPT grade is statistically similar between three groups.
All the patients selected for the study had MPT grade of 1 and 2. Group V, R, RV had 22 (73.3%) patients with MPT grade 1 and 8 (26.7%) patients with MPT grade 2. MPT grade was statistically similar between three groups.

There was no significant difference in the baseline heart rate between the three groups. After administration of muscle relaxant, there was no significant change in HR in group V and group RV, but there was a statistically significant (p value <0.05) increase in the mean HR in group R (from 90.80±16.02 to 99.73±15.10). There was statistically significant increase ($p<0.05$) in HR after intubation in all the three groups which persisted up to 5min in group R, 3min in group RV and returned to baseline, whereas in group V it persisted up to 10min. There was no significant change in SBP after administration of muscle relaxant in all the three groups. However, there was statistically significant ($p<0.05$) rise in SBP after intubation in both groups V and R which persisted up to 3min and thereafter returned to baseline. There was statistically insignificant change in DBP after the administration of muscle relaxant in all the three groups.

After intubation, DBP increased in group R at 1min and reached the baseline by 2min. However, the changes in group V and group RV remained statistically insignificant. While comparing the MAP, after administration of relaxant, there was no statistically significant change in this parameter in all the three groups. There was a statistically significant (p 0.05) rise in MAP after intubation which persisted upto 3min in group V and 1min group R, however it returned to baseline by 10min.

Discussion
In our study, we combined rocuronium and vecuronium to evaluate the clinical benefits of the combination in terms of better haemodynamics and acceptable intubating conditions over

individual drugs. The concept behind using combination of rocuronium and vecuronium, is that, when rocuronium is combined in equipotent doses with vecuronium it is found to act synergystically in the early part of blockade.[4,5] Nigrovic and colleagues[6] have postulated that the neuromuscular blocking agents belonging to different chemical groups (isoquionoline or aminosteroid) display an inverse pattern of affinities for the two D-subunits and, when present together, produce a synergistic neuromuscular block. This hypothesis does not satisfactorily explain the synergistic behaviour of the combination of structurally similar rocuronium and vecuronium. A marked pre-synaptic action developing rapidly after administration of a paralysing dose of rocuronium and which is subsequently swamped by a more slowly developing post synaptic effect has been postulated as an explanation of the unique properties of this drug. The proposed early presynaptic action could explain synergism between rocuronium and vecuronium developing during early stages of blockade.[4] Our study population consisted of 90 ASA grade I and II patients in the age group 20–60 years who were allocated into three groups - Group V, Group R, Group RV with the sample size of 30 in each group. Cooper and colleagues[7] reported excellent to good intubating conditions in 100% of patients at 90sec with use of rocuronium 0.6 mg/kg. Misra and colleagues[8], also noted excellent to good intubating conditions in all patients receiving rocuronium 0.6 mg/kg at 90sec. In our study, intubating conditions at 90sec were excellent to good in 93.3% of patients in group R and concurs with the results of above studies. Misra and colleagues[8] also noted excellent intubating conditions in 33.3% of patients receiving vecuronium 0.1 mg/kg at 90sec. In our study, we noted excellent to good intubating conditions in only 13.3% of patients in group V. This marginal decrease in percentage may be attributed to the lower dosage of vecuronium used in our study. In our study, we noted excellent to good intubating conditions in 93.3% of patients in group RV. The similarity of intubating conditions with rocuronium and the combination of rocuronium and vecuronium implies that these two drugs act synergistically during the early part of blockade. The synergistic action of rocuronium during the early stage of blockade was also seen in priming studies. Abdulatif M and colleagues[9] concluded that the priming dose of rocuronium 0.1 mg/kg reduced the priming interval to 1 minute, accelerating the onset time of atracurium and also provided intubating conditions comparable with succinylcholine and rocuronium. Man TT and colleagues[10] suggested that good intubating conditions were achieved in 58% patients of the rocuronium group, 63% of the patients receiving equipotent dose combination of rocuronium and atracurium. Following intubation, there was clinically and statistically significant increase in heart rate in all three groups. This persisted for 5min in group R, 3min in group RV which concurs with observations of Neeti M.[5] There was no clinically or statistically significant change in MAP after administration of muscle relaxants in all the three groups. Following intubation, there was statistically significant increase in MAP in group R persisting for 1min. This concurs with the study of Neeti M.[5] There was an increase in MAP in group V after intubation which persisted upto 3min.This can be attributed to the suboptimal intubating conditions at 90sec in this group requiring repeat laryngoscopy 30sec later. There was no increase in MAP following intubation in group RV.

Conclusion

Neuromuscular blocking drugs are an integral part of intubation process as they facilitate laryngoscopy, relax the vocal cords and provide excellent intubating conditions. Succinylcholine, is the gold standard muscle relaxant for rapid sequence induction. Though vecuronium is considered to be the drug of choice for cardiovascular stability it is often not a favoured choice for rapid sequence induction, due to the slow onset of action (2-3min). Rocuronium with faster onset of action (within 90sec) provides ideal conditions for rapid intubation when succinylcholine is undesirable or contraindicated. But presently the

high cost restricts its use on routine basis. In our study, we evaluated the clinical benefits of the combination of rocuronium with vecuronium in terms of providing optimal intubating conditions without compromising haemodynamic stability.

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