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ORIGINAL ARTICLE

A COMPARATIVE STUDY OF INTUBATING CONDITIONS AND HAEMODYNAMIC EFFECTS FOLLOWING VECURONIUM, ROCURONIUM AND ITS COMBINATION

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ABSTRACT: BACKGROUND: Vecuronium has a slow onset of action (2-3 mins) 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 its high cost. Combination of rocuronium with vecuronium is known to produce synergism without producing any side effects. This study was under taken 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 & II patients in the age group 20-60 years of either sex scheduled for elective surgeries 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. Intubation was attempted at 90sec after administration of muscle relaxant and scored according to four step scale proposed by Goldberg and colleagues. Heart rate and blood pressure were recorded before and after induction, after administration of muscle relaxant, and at 1, 2, 3, 5 and 10 minutes after intubation. **RESULTS:** Rocuronium and the combination group produced acceptable intubating conditions in 93.3% patients which was significantly better than that of vecuronium group (acceptable intubating conditions only in 13.3%). There were no significant changes in heart rate and mean arterial pressure (MAP) in the three groups. **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 rapid sequence induction.

KEYWORDS: Neuromuscular relaxants; rocuronium, vecuronium. Pharmacology; synergism. Neuromuscular relaxants; haemodynamic effects. Pharmacodynamics; relaxant combination. Intubation; tracheal.

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. Neuromuscular blocking drugs are frequently used for tracheal intubation. The administration of two neuromuscular blockers in combination was first introduced by Lebowitz and coworkers[1] 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[2,3,4,5] with the objectives of maintenance of haemodynamic stability along with a rapid airway control.

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In the present study we combined rocuronium with vecuronium to evaluate the clinical benefits of the combination in terms of better haemodynamics and acceptable intubating conditions over individual drugs.

METHODS: After obtaining ethical committee meeting approval a randomized double blind study was conducted on 90 ASA grade I & II patients in the age group 20–60 years of either sex scheduled for elective surgeries done under general anaesthesia. Patients with anticipated difficult intubation, hepatic, renal and cardiac dysfunction, pregnant women, morbidly obese patients and patients those receiving medications which could interfere with neuromuscular function and haemodynamics were excluded from the study. A detailed preanaesthetic evaluation and appropriate baseline investigations were carried out on the previous day of surgery. 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. Patients were allocated into three groups with the sample size of 30 in each group. Group V (n=30) received 0.08mg/kg vecuronium, Group R (n=30) received rocuronium 0.6 mg/kg and Group RV (n=30) received rocuronium 0.3 mg/kg and vecuronium 0.04 mg/kg.

On the day of surgery a preoperative heart rate, SpO2, noninvasive blood pressure, respiratory rate readings were recorded. On the operation table intravenous line was secured with 18G cannula and ringer lactate 500ml infusion was started. Patients were connected to non-invasive monitoring with 5-lead electrocardiograph (ECG), pulse oximeter, non-invasive sphygmomanometer and etco2 monitor all patients were pre-oxygenated with 100% oxygen by face mask for 3mins. Inj. glycopyrrolate 0.2mg iv slowly was administered and 1 minute later the patients received sedation with inj. midazolam 0.03 mg/kg body weight iv and analgesia with inj. fentanyl 2µg/kg body weight iv. General anaesthesia was induced with inj. propofol 2mg/kg body weight iv and patients ventilated with 50% O2 in N2O. 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 iv or inj. rocuronium 0.6mg/kg body weight iv or a combination of inj. vecuronium 0.04 mg/kg and inj. rocuronium 0.3 mg/kg iv. 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. However in all patients the first attempt of intubation was evaluated and scored according to the four step scale proposed by Goldberg and his colleagues.[6]

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

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and 10 minutes after intubation. Any side effect 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.

At the end of surgery, patients were reversed with inj. neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.01 mg/kg and extubated after recovery of adequate muscle power and consciousness.

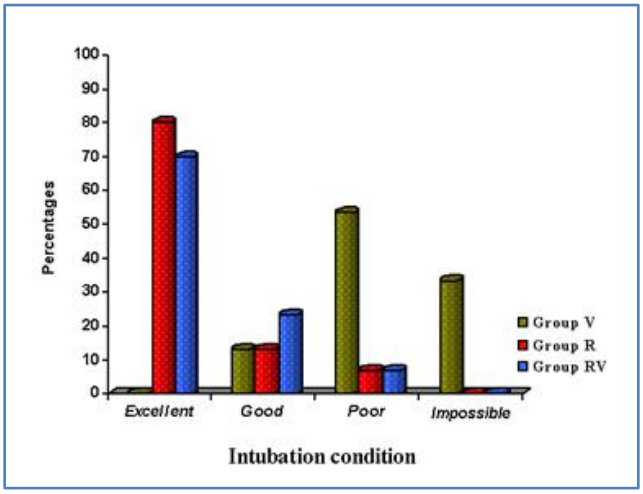
RESULTS: Statistical analysis was done using students 't' test, one way anova, two way anova and Chi-Square test. A value of p below 0.05 was considered significant. The patients in all three groups were statistically comparable with regards to their demographic and physical characteristics.

	Group V (n=30)	Group R (n=30)	Group RV (n=30)
Male: Female	15:15	12:18	19:11
Age (years)	41.90±8.75	41.90±8.75	37.87±9.81
Weight (kg)	55.37±9.14	55.37±9.14	56.47±8.17

Table 2: Demographic data (Mean ± SD)

Intubation score	Group V (n=30)	Group R (n=30)	Group RV (n=30)
1= Excellent	0	24(80.0%)	21(70.0%)
2= Good	4(13.3%)	4(13.3%)	7(23.3%)
3= Poor	16(53.3%)	2(6.7%)	2(6.7%)
4= Impossible	10(33.3%)	0	0
Mean ± SD	3.20±0.66	1.27±0.58	1.37±0.62

Table 3: Comparison of intubation score between three groups



Graph 1: Intubating condition at 90 seconds

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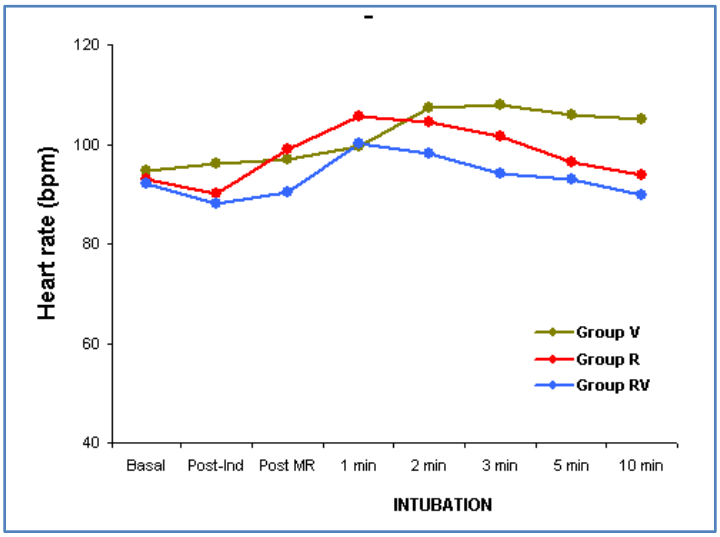
The intubating conditions were excellent to good in 93.3% of both groups R and RV, as compared to only 13.3% in group V. 86.6% patients in group V had impossible or poor intubating conditions compared to only 6.7% intubating in group R and group RV. The mean intubation score in group V was 3.20±0.66 (poor to impossible), in group R it was 1.27±0.58(excellent to good) and group RV it was 1.37±0.62 (excellent to good).

Heart rate (bpm)		Group V (n=30)	Group R (n=30)	Group RV (n=30)
Basal		94.80±17.46	93.07±15.38	92.33±7.36
Post induction		96.30±18.15	90.80±16.02	88.27±5.39
Post Muscle Relaxation		96.07±17.81	99.73±15.10	90.40±14.61
Post intubation	1 min	99.57±23.08	105.63±13.39	100.23±12.74
	2 min	107.27±18.56	104.53±15.23	98.07±14.02
	3 min	107.83±18.08	101.60±11.9	94.00±13.68
	5 min	106.00±16.44	96.47±10.63	92.007±11.00
	10 min	105.17±16.26	93.83±11.14	89.70±10.95
P value from induction				
Post Muscle Relaxation		0.348	<0.05	0.437
Post intubation	1 min	<0.05	<0.05	<0.05
	2 min	<0.05	<0.05	<0.05
	3 min	<0.05	<0.05	<0.05
	5 min	<0.05	<005	0.06
	10 min	<0.05	0.529	0.520

Table 4: Comparison of heart rate (HR) between three groups



Graph 2: Mean ± SD changes in heart rate (HR)

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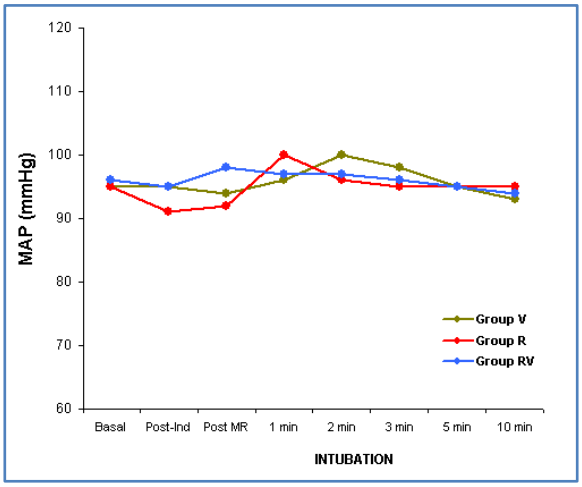
There was no significant difference in the baseline heart rate between the three groups. After administration of muscle relaxant, there was no significant change in HR in group V and group RV, but there was a statistically significant (p value <0.05) increase in the mean HR in group R (from 90.80±16.02 to 99.73±15.10). There was statistically significant increase (p value<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.

MAP (mm Hg)		Group V (n=30)	Group R (n=30)	Group RV (n=30)
Basal		95.60±6.72	95.11±8.39	96.47±8.23
Post induction		95.10±5.84	92.93±11.54	95.00±12.81
Post Muscle Relaxation		94.47±6.34	92.30±12.12	97.33±14.35
Post intubation	1 min	96.40±8.39	100.73±13.49	96.75±3.97
	2 min	100.03±12.98	95.75±3.97	97.37±4.45
	3 min	98.23±11.27	95.52±3.27	96.92±4.24
	5 min	95.43±6.91	95.70±14.15	95.41±3.97
	10 min	93.90±8.38	95.17±13.5	94.85±4.02
P value from induction				
Post Muscle Relaxation		0.237	0.89	0.878
Post intubation	1 min	0.138	<0.05	0.47
	2 min	<0.05	0.079	0.35
	3min	<0.05	0.08	0.52
	5 min	0.878	0.082	0.92
	10 min	0.628	0.095	0.32

Table 5: Comparison of Mean Arterial Pressure (MAP) between three groups



Graph 3: Mean ± SD changes in mean arterial pressure with time (MAP)

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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 value <0.05) rise in MAP after intubation which persisted up to 3mins in group V and 1min group R, however it returned to baseline by 10min. The changes in group RV were not significant.

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 synergistically in the early part of blockade.[7,8]

Nigrovic and colleagues[9] have postulated that the neuromuscular blocking agents belonging to different chemical groups (Isoquionoline or aminosteroid) display an inverse pattern of affinities for the two α-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 paralyzing 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.[7]

Our study population consisted of 90 ASA grade I & 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[10] reported excellent to good intubating conditions in 100% of patients at 90sec with use of rocuronium 0.6 mg/kg. Misra and colleagues,[11] also noted excellent to good intubating conditions in all patients receiving rocuronium 0.6 mg/kg at 90sec. In our study, intubating conditions at 9 sec were excellent to good in 93.3% of patients in group R and concurs with the results of above studies. Misra and colleagues[11] 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[12] concluded that the priming doses of rocuronium 0.1 mg/kg reduced the priming interval to 1 minute, accelerated the onset time of atracurium and also provided intubating conditions comparable with succinylcholine and rocuronium. Man TT and colleagues[13] suggested that good intubating conditions were achieved in 58% patients of the rocuronium group and 63% of the patients receiving equipotent dose combination of rocuronium and atracurium.

Synergism of combination of rocuronium and vecuronium was also observed by England AJ and colleagues,[7] who noted excellent to good intubating conditions at 60sec in 90% of patients receiving combination of vecuronium and rocuronium. Neeti M and colleagues[8] also noted excellent

to good intubating conditions at 60sec in 93.3% of patients receiving combination of vecuronium and rocuronium. In our study, we noted excellent to good intubating conditions in 93.3% of patients in group RV and this is consistent with the results of above studies.

We noted that the intubating conditions produced by the combination of rocuronium with vecuronium were comparable with rocuronium alone at 90sec and this concurs well with the studies of England A[7] and Neeti M.[8]

In our study, the haemodynamic parameters measured at baseline were comparable in all the three groups. There was no clinically or statistically significant change in heart rate following administration of muscle relaxant in group RV and V. However there was a slight increase in heart rate following administration of rocuronium which was clinically insignificant though significant statistically. This is consistent with the study of Neeti M and colleagues,[8] who attributed it to the weak vagolytic property of rocuronium. 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.[8] However in group V, the increase in heart rate was persistent for more than 10min. This may be due to suboptimal intubating conditions at 90sec in this group requiring repeat laryngoscopy 30sec later.

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.[8] There was an increase in MAP in group V after intubation which persisted up to 3mins. 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. The knowledge of the advantage of combination of two non-depolarizing neuromuscular blocking drugs producing additive and synergistic effect can be utilised clinically in such situations. The unique property of early pre-synaptic action of rocuronium produces synergism with vecuronium during the early part of blockade, thus accelerates the speed of onset and provides good intubating conditions.

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