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Original Research Article

Comparison of Intubating Conditions and Haemodynamic Responses in Rapid Sequence Induction using Rocuronium Verses Rocuronium with Ephedrine Pre-Treatment

Madhavi Latha Pinnelli[1], Voviliveni Srikala[2], B Srinivas[3]

[1]Assistant Professor, Department of Anesthesiology, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State

[2]Assistant Professor, Department of Anesthaesiology, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State

[3]Assistant Professor, Department of Anesthaesiology, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State

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Corresponding author: Dr. Madhavi Latha Pinnelli
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Abstract

Background: The fastest acting non-depolarizing muscle relaxant currently is rocuronium, it may be used instead of suxamethonium for rapid sequence intubation. According to reports, rocuronium at doses more than 0.9 mg/kg provides intubating circumstances at 60 seconds that are comparable to those seen with suxamethonium, but with a longer duration of action.

Methods: Based on the inclusion and exclusion criteria a total of n=60 cases were included in the study, and they were allotted in two separate groups randomly by a computer-generated random number. Group I n=30 cases patients received rocuronium 0.6mg/kg with pre-treatment of saline. Group II n=30 cases received rocuronium 0.6mg/kg with pre-treatment of ephedrine 100mcg/kg.

Results: In group I, the patient's heart rate increased from the baseline up to 3 min after intubation (P<0.05) and came to below the baseline value during the fourth and fifth minute after intubation *(*P>0.05). In group II patients, heart rate was significantly high from the baseline value during all the time intervals (P<0.05) and heart rate did not reach the baseline or below the baseline when compared to group I, which can be explained by the fact that group II received ephedrine pre-treatment which might have counteracted the fall in heart rate when compared to group I. When compared clinically heart rate variability was within 30% of the baseline value in both groups.

Conclusion: In this study the hemodynamic responses, but for raise of 25% in the heart rate in the ephedrine group other parameters were normal in both groups. Although both groups had clinically acceptable intubating conditions, rocuronium with ephedrine pre-treatment group had better intubation scores. Therefore, the quality of intubation with rocuronium – ephedrine group is better than with rocuronium. None of the patients had any adverse reaction to the drugs used and no critical incident was encountered during the study.

Keywords: Haemodynamic Responses, Rocuronium, Ephedrine, Rapid SequenceInduction

Introduction

Rapid sequence intubation is an established technique in patients considered to be at risk for aspiration of gastric contents. The goal of rapid sequence intubation is to secure the patient's airway smoothly and quickly minimizing the chances of regurgitation and aspiration of gastric contents. Traditionally Suxamethonium (Sch) has been the neuromuscular blocking drug of choice in rapid sequence intubation technique. Yet, its use is associated with several undesirable side effects like sinus bradycardia, arrhythmias, hyperkalemia, fasciculations, and myalgia which prompted the search for alternative drugs for rapid sequence intubation. [1] Amongst the currently available non-depolarizing muscle relaxants rocuronium has the most rapid onset of action and may provide an alternative to suxamethonium for rapid sequence intubation. Rocuronium is a monoquaternary amino steroidal non-depolarizing neuromuscular blocking agent with a shorter onset and intermediate duration of action. Rocuronium in a dose of >0.9 mg/kg has been reported to offer intubating conditions at 60 sec that are similar to those observed with suxamethonium but with a prolonged duration of action. [2] However, in a dose of 0.6 mg/ kg, 20–25% of the patients had a movement of vocal cords and also a diaphragmatic response to intubation. [1] This may be due to the slower onset of action of rocuronium at the laryngeal muscles and may also be due to the decrease in the cardiac output (CO) caused by the induction agents. Speed of onset of neuromuscular block is one of the requirements to rapidly secure the airway, which is affected by several factors like the rate of delivery of the drug to the neuromuscular junction, receptor affinity, plasma clearance, and the mechanism of neuromuscular block (depolarizing Vsnondepolarizing). [1] The speed of the drug's access to the receptors appears to be proportional to the cardiac output. In this respect, ephedrine has been shown to reduce the variability of the onset of non-depolarizing agents at the laryngeal muscles by increasing cardiac output. This drug may also reduce hypotension following rapid propofol administration. Any reduction in onset of intubating conditions without prolongation of duration action of muscle relaxants would be extremely useful. Hence the present study was undertaken to compare the intubating conditions and hemodynamic responses during rapid tracheal intubation using rocuronium versus rocuronium with ephedrine pre-treatment.

Material and Methods

A prospective, study was conducted in the Department of Anesthesiology, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language.

Inclusion criteria

1. ASA Grade I & II
2. 18-65 years of age
3. Elective non-cardiac surgical procedures
4. General anesthesia expected to last for more than 1 hour

Exclusion criteria

1. Allergy to study drugs
2. Anticipated difficult airway
3. Morbid obesity
4. Neuromuscular disorders
5. Pregnancy
6. ASA grade III and IV

Based on the inclusion and exclusion criteria a total of n=60 cases were included in the study, and they were allotted to two separate groups randomly by a computer-generated random number. Group I n=30 cases patients received rocuronium

0.6mg/kg with pre-treatment of saline. Group II n=30 cases received rocuronium 0.6mg/kg with pre-treatment of ephedrine 100mcg/kg.

All the patients underwent a thorough preoperative evaluation. Informed written consent was obtained from all the patients willing to participate in the study. All the

patients were pre-medicated with tablet alprazolam 0.5 mg night before surgery and 2 hrs before the scheduled time of surgery. Patients were kept nil per orally for 6 hrs for solids and 2 hrs for clear liquids on the day of surgery. Standard routine monitoring was done (ECG, NIBP, SPO_2). All patients were pre-oxygenated with 100% O_2 for 3 minutes. One minute after pre-oxygenation, fentanyl 1µg/ kg was given. One minute after fentanyl, the study drug comprising either 0.9% saline for group I or ephedrine in the dosage of 100 µg/ kg for group II was given intravenously. One minute after giving the study drug, anesthesia was induced with propofol 2 mg/kg and rocuronium 0.6 mg/kg. Mask ventilation was not done till endotracheal intubation or unless the oxygen saturation dropped below 95%. The anesthesiologist assessing intubating conditions was allowed into the Operation Theatre 40 seconds after the rocuronium was administered. Sixty seconds after injecting the rocuronium intubation was done. Intubating conditions were assessed as per the intubation scoring system of consensus conference (Copenhagen) 60 on good clinical research practice in pharmacodynamic studies of neuromuscular blocking agents. Cuffed oro-tracheal Poly Vinyl Chloride (PVC) tube of appropriate size was used for intubation and the cuff was inflated gradually by simultaneously feeling for air leak. The endotracheal tube was fixed after confirming the position of the endotracheal tube by auscultation of the chest and $ETCO_2$ monitor. The hemodynamic variables (systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, and oxygen saturation) were monitored continuously and recorded at 7-time intervals for analysis.

Duration of laryngoscopy and response60 of the patient during endotracheal intubation was observed at the time of intubation. Any change in hemodynamic variables of 30% from the baseline value was considered significant and managed accordingly. Anesthesia was maintained with 50% O_2, 50% N_2O, and halothane O.5-1% after intubation for 5 minutes with positive pressure ventilation. No noxious stimulus or incision was allowed during the study period of 5 minutes after intubation. All statistical analysis was done by using SPSS (Statistical Packages for Social Sciences, Chicago) 21.0 software. *A* p-value of < 0.05 was considered statistically significant. Analysis of variance (ANOVA) test. If the ANOVA test was found significant further analysis was done for each pair with paired t-test.

Results

The mean age in Group I (rocuronium with NS) n=30 cases was 37.6 ± 12.8 years and the mean age in group II (rocuronium with ephedrine) was 41.3 ± 11.6 years the p values were 0.293 hence the differences were insignificant. The number of males in group I was n=12(40%) and females were n=18(60%) and similarly, the number of males in group II was n=14(46.67%) and females was n=16(53.33%). The mean age in rocuronium with NS group (group I) is 55.6 ± 11.6 kg and in rocuronium with ephedrine group (group II) is 56.6 ± 10.8 kg given in figure 1. The difference between the two groups was not statistically significant (P value 0.768).

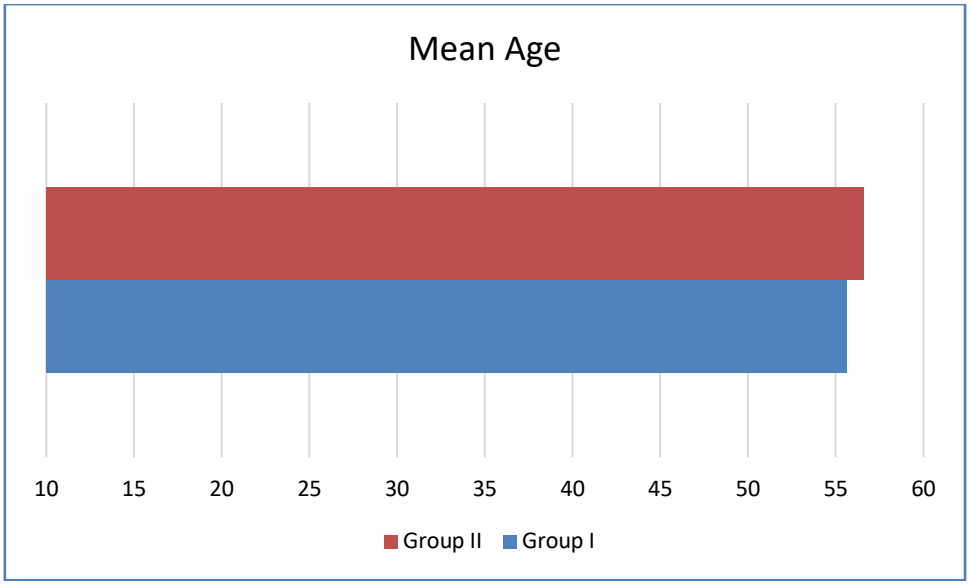

Figure 1: Comparison of mean age of two groups of patients included in the study

The number of patients in Group I with Mallampati class I was 83.33% and in group II was 86.67%. Based on the Cormack and Lehane grades out of all 4 grades no patients were found to be present in grades 3 and grade 4. In group I 56.67% were present in Cormack and Lehane grade I. In group II 60% of cases were in Cormack and Lehane grade I as depicted in table 1.

Table 1: Distribution of cases based on Mallampati class and Cormack-Lehane grades

Variables	*Group I*	*Group II*
Mallampati Class		
I	25	26
II	05	04
Total	30	30
Cormack Lehane Grade		
I	17	18
II	13	12
III	00	00
IV	00	00
Total	30	30

The mean duration of laryngoscopy in rocuronium with ephedrine (group II) was 19.32 ± 8.38 seconds and in rocuronium with NS (group I) is 21.48 ± 7.62 seconds. The difference between the two groups was not statistically significant (P value 0.435).

Table 2: Intubating Conditions and Duration of Laryngoscopy

Variable	Group I	Group II	p-value
Intubation conditions			
0	0	0	0.0014*
1	11	20	
2	19	10	
Mean duration of laryngoscopy (Seconds)	19.32	21.48	0.432

* Significant

The mean values of hemodynamic variables which included Heart rate, SBP, DBP, and MAP were compared in group I and group II. T1 is the baseline value, T2 is the value before intubation, T3 is one minute following intubation, T4 was two minutes after intubation, T5 was three minutes after intubation, and T6 values were collected 4 minutes after intubation, and T7 five minutes following intubation. Of all the hemodynamic variables there were significant variations in heart rates in group II and the group I at the interval of T4, T5, T6, and T7 ($p< 0.05$) even though clinically heart rate variability was within 30% from the baseline value in both groups. have been depicted in table 3.

Table 3: **Hemodynamic variables recorded and compared between two groups**

Variables	Group	T1	T2	T3	T4	T5	T6	T7
HR (BPM)	Group II	80 (14.4)	82.1 (15)	103 (18.3)	101.8 (19.1)	99.8 (18.5)	95.6 (16.6)	91.2 (15.2)
	Group I	79.5(16.7)	85.7 (14)	93 (14.1)	86.8 (14.5)	84.5 (16.4)	80.1 (14.6)	77.2 (15)
	P – Value	0.907	0.38	0.036	0.003*	0.003*	0.001*	0.002*
SBP (mmHg)	Group II	136.1 (20.6)	128.5 (22.5)	143.4 (31.1)	125.3 (28.2)	115.2 (24.8)	108.8 (19)	104.8 (14.6)
	Group I	139.9(22.0)	116.3 (18.7)	142.2 (30.2)	122 (24.5)	111.7 (23.2)	106.6 (22.8)	102 (18.2)
	P -Value	0.531	0.043	0.894	0.667	0.615	0.713	0.545
DBP (mmHg)	Group II	69 (11.2)	66.2 (13)	76.8 (20.7)	67.2 (17.7)	62.2 (15.8)	58.7 (12.7)	55.3 (10.6)
	Group I	71(11.3)	62.7 (11)	78.9 (14.6)	66.4 (15.7)	60.6 (13.9)	58 (11.4)	55.3 (10.1)
	P – Value	0.126	0.306	0.678	0.866	0.712	0.824	0.989
MAP (mmHg)	Group II	93.4 (13.4)	90 (14.6)	100.8 (24.9)	87.6 (20.8)	81.2 (18.5)	76 (14)	72.7 (11.1)
	Group I	98.4(13.3)	82.5 (13.3)	101.4 (19.3)	87.4 (18.5)	80 (16.6)	74.3 (14.1)	72.3 (12)
	P -Value	0.193	0.062	0.925	0.96	0.81	0.667	0.903

* Significant

In group I, the patient's heart rate increased from the baseline up to 3 min after intubation ($P<0.05$) and came to below the baseline value during the fourth and fifth minute after intubation ($P>0.05$). In group II patients, heart rate was significantly high from the baseline value during all the time intervals ($P<0.05$) and heart rate did not reach the baseline or below the baseline when compared to group I, which can be explained by the fact that group II received ephedrine pre-treatment which might have counteracted the fall in heart rate when compared to group I. When compared clinically heart rate variability was within 30% of the baseline value in both groups. When we compared the changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure we found that SBP, DBP, and MAP were comparable ($P> 0.05$) at all time intervals. In both groups when compared to baseline values SBP, DBP, and MAP values were significantly different in all time intervals except 1 min after intubation because we administered 0.5%-1% halothane immediately after intubation to all the study population. The rise in SBP, DBP, and

MAP at 1 min after intubation can be explained by the fact that the pressor response with laryngoscopy and endotracheal intubation. When compared clinically SBP, DBP, and MAP values are within 30% of the baseline value in both groups. Although both groups had clinically acceptable intubating conditions (good and excellent), in group II, there is significantly (*P* value=0.005) a greater number of patients had better intubation scores. In group II (rocuronium with ephedrine) patients (n=30) n=21 patients had excellent intubating conditions, n=9 patients had good intubating conditions and none of the patients had poor intubating conditions. In group I (rocuronium) (n=30) n=10 patients had excellent intubating conditions, n=20 patients had good intubating conditions and none of the patients had poor intubating conditions.

Discussion

Rapid sequence induction is an established technique in patients considered to be at risk for aspiration of gastric contents. The goal of rapid sequence induction is to secure the patients' airway smoothly and quickly minimizing the chances of regurgitation and aspiration of gastric contents. Traditionally suxamethonium has been the neuromuscular blocking drug of choice in rapid sequence induction and intubation techniques but is associated with several undesirable side effects. [1] like sinus bradycardia, arrhythmias, hyperkalemia, fasciculations, and myalgia. A substitute for suxamethonium for rapid sequence intubation may be rocuronium bromide, a monoquaternary amino steroidal non-depolarizing neuromuscular blocking drug having a quicker onset of action and an intermediate duration of action. According to reports, rocuronium provides similar intubating circumstances to suxamethonium but with a longer half-life. [2] Attempts were undertaken to lower the rocuronium dosage without sacrificing the drug's onset time or intubating circumstances. Speed of onset of neuromuscular block is one of the essential requirements to rapidly secure the airway. The rate at which a medication reaches receptors seems to be inversely related to cardiac output.

It has been demonstrated that ephedrine increases cardiac output, which lowers the variability of rocuronium onset at the laryngeal muscles. Additionally, it might lessen the hypotension that occurs after taking propofol quickly. Ephedrine improves intubating conditions and hastens the onset of rocuronium's action without extending the duration of muscle relaxants' action. Propofol has several potential benefits over other induction agents, including a quicker onset of action, reduction of reflexes in the pharynx, larynx, and trachea, appropriate depth of anesthesia during intubation, and quicker recovery. [3]. During the induction of anesthesia, propofol's most notable side effect is a reduction in arterial blood pressure. A 2-2.5 mg/kg induction dose results in a 25–40% reduction in systolic blood pressure and a slower transport of the muscle relaxant to the receptors, delaying the commencement of effect regardless of the presence of cardiovascular illness. [4] Propofol'svasodilatory action seems to be brought about by a decline in sympathetic activity as well as a direct impact on intracellular calcium mobilization. [5, 6] In this study, we compared the intubating conditions and hemodynamic responses during rapid sequence induction using rocuronium versus rocuronium with ephedrine pre-treatment. In this study, we found that heart rate was comparable between both groups, (group I and group II) at baseline, after induction, and one minute after intubation. In group I patient's heart rate increased from the baseline up to 3 min after intubation ($P < 0.05$) and came to below the baseline value during the fourth and fifth minute after intubation *(P*>0.05). In group II patient's heart rate was significantly high from the baseline value during all the time intervals (*P*<0.05) and

the heart rate did not reach the baseline or below the baseline when compared to group I, which can be explained by the fact that group II received ephedrine pre-treatment which might have counteracted the fall in heart rate when compared to group I. When compared clinically heart rate variability was within 30% of the baseline value in both groups. But caution needs to be exercised in the subset of patients in whom ephedrine-induced tachycardia might be detrimental (eg. ischaemic heart disease patients and valvular heart disease). The intubation conditions in group II (rocuronium with ephedrine) patients (n=30) n=21 patients had excellent intubating conditions, n=9 patients had good intubating conditions and none of the patients had poor intubating conditions. In group I (rocuronium) (n=30) n=10 patients had excellent intubating conditions, n=20 patients had good intubating conditions and none of the patients had poor intubating conditions.

Ephedrine 75 and 100 mcg/kg given before rapid tracheal intubation with propofol and rocuronium enhances the intubating circumstances, but it is ineffective in reducing the hypotension that occurs after inducing anesthesia with propofol, according to G Krishna et al., [7]. Additionally, they claimed that increasing the ephedrine dosage from 100 to 150 mcg/kg had no beneficial effects on the intubating circumstances. Ephedrine may, in overdoses, cause vasoconstriction of the blood vessels supplying the laryngeal muscles, preventing the relaxant from reaching the area of action. For this reason, we decided on an ephedrine dose of 100 mcg per kilogram. In our study, both groups had clinically acceptable intubating conditions (only one patient had a poor intubating condition in group I). However, in terms of intubation scores, the rocuronium with ephedrine group had better intubation scores and the rocuronium (good and excellent intubation conditions) group is not better for intubation. In this study, the confounding factors of other studies were presumably eliminated and both groups were comparable to patient characteristics i.e.; age, sex, weight distribution, type of surgical procedures (surgeries of minimum 1-hour duration), and also the type of anesthesia (all are given general anesthesia). W Ittichaikuthol et al., [8] AL. Kovac et al., [9]

Santiveri X et al., [10] studied the effect of ephedrine on the onset time of rocuronium. They concluded that intravenous ephedrine shortened the onset time of rocuronium with no significant adverse hemodynamic effects. Studies were done by Gopalakrishna et al., [7] Michelsen I et al., [11] Gamlin F et al., [12] have also proved that ephedrine pre-treatment before rapid tracheal intubation using propofol and rocuronium improved the intubating conditions without causing hypotension. Han D.W et al., [13] Ezri T et al., [14] Leykin. Y et al., [15] found the significance of injection timing of ephedrine to reduce the onset time of rocuronium. The onset time of rocuronium can be accelerated effectively if it is administered at the time when the effect of ephedrine on cardiac output has reached its maximum. No adverse effect or any critical incident was encountered during the study.

Conclusion

In this study the hemodynamic responses, but for raise of 25% in the heart rate in the ephedrine group, other parameters were normal in both groups. Although both groups had clinically acceptable intubating conditions, rocuronium with ephedrine pre-treatment group had better intubation scores. Therefore, the quality of intubation with rocuronium – ephedrine group is better than with rocuronium. None of the patients had any adverse reaction to the drugs used and no critical incident was encountered during the study.

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