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Efficacy of Sevoflurane on Intubating Conditions In General Anesthesia under Rocuronium-A Comparative Study

Dr. Pratibha Kumari[1], Dr. Ramu Valluri[2], Dr. Priyanka Gotluru[3*]
[1]Assistant professor, Department of Anesthesia, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad, Telangana, India
[2]Professor and Head, Department of anesthesia, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad, Telangana, India
[3]Senior resident, Department of anesthesia, Kamineni Academy of Medical Sciences and Research Centre, L.B. Nagar, Hyderabad, Telangana, India

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***Corresponding author**
Dr. Priyanka Gotluru

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Abstract: The ease with which endotracheal intubation is performed depends upon degree of muscle relaxation, depth of anaesthesia and skill of anaesthesiologist. This is prospective, randomised; double-blind study conducted at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad.The aim of this study is to compare the effect of sevoflurane on intubation time and intubating conditions when used along with rocuronium. A 70 patients aged between 30 to 50 year of both genders, weighting from 40 to 70kg coming for elective surgeries under general anaesthesia included. They are divided in two groups, Group R received 0.8 mg/kg rocuronium, and Group RS received 0.8 mg/kg of rocuronium with 2% sevoflurane. Intubating conditions were assessed by cooper scoring system. In Group R, 18patients showed excellent, 14 patients good and 3 patients poor intubation conditions and in group RS 21patients showed excellent, 6 patients good and 1 patient poor intubation conditions respectively. The time for loss of thumb adduction was 99.81±9.3 in Group R compared with 62.03±5.2s in Group RS and The onset time of intubation was 100.65±8.6s in Group R compared with 58.62±6.5 in Group RS. These timings were significantly reduced in the Group RS compared to Group R. Rocuronium 0.8 mg/kg produces good intubation conditions at 100 sec when compared with Rocuronium 0.8 mg/kg along with 2% sevoflurane provides excellent intubating conditions within 60–66 s without any adverse effects in elective surgeries in patients with stable haemodynamics.

INTRODUCTION

The ease with which endotracheal intubation is performed depends upon degree of muscle relaxation, depth of anaesthesia and skill of anaesthesiologist [1]. One characteristic of the ideal muscle relaxant is a rapid onset of action. Different techniques that have been used to decrease the effective onset time of non-depolarizing muscle relaxants include priming [2] and the administration of large doses [3]. Rocuronium, a non-depolarising aminosteroidal muscle relaxant is chemically 2-morpholino, 3-desacetyl, a 16-N-allyl pyrrolidino derivative of vecuronium, differing from it at three positions on steroid nucleus. Rocuronium has got intermediate duration of action with a rapid onset of action and is devoid of clinically significant cardiovascular side effects at effective neuromuscular blocking doses. Hence, it is considered better agent for endotracheal intubation among non-depolarizing neuromuscular blocking drugs. Volatile anaesthetics are known to potentiate the effects of nondepolarizing muscle relaxants [4]. The acceptance into clinical practice of newer potent volatile anaesthetics sevoflurane and desflurane has been, in part, a function of their low blood gas solubility that permits more rapid induction and emergence from anaesthesia and more rapid control of anaesthetic depth. Pre medication with 2% sevoflurane along with rocuronium bromide provide excellent intubation conditions during induction in patients undergoing different elective surgeries under general anaesthesia

MATERIALS AND METHODS

This prospective, randomised, double-blind study conducted after obtaining institutional ethical committee approval and a written informed consent from seventy five patients aged 18-50 years of ASA Grade I and II, scheduled to undergo various surgeries under general anaesthesia were selected. Exclusion

criteria were: increased risk of pulmonary aspiration, neuromuscular disease, Mallampatti grade III and IV, medications known to influence neuromuscular function, anticipated difficulty with airway management, and contraindications to recurronium, patient's refusal, pregnancy and breastfeeding, hepatic, renal diseases, patients receiving drugs interfering with neuromuscular function and psychiatric patients. The patients were divided randomly into two groups of 25 each as follows: GROUP-R- Patients received rocuronium bromide 0.6mg kg^{-1} intravenously and anaesthesia was induced at the onset of clinical weakness using propofol 2.5mg kg^{-1} and Group RS Patients received 0.8 mg/kg of rocuronium and 2% sevoflurane during induction using propofol 2.5mg kg^{-1}.

The nature of anaesthesia and nerve stimulation technique was explained in details to all the patients. Patients were kept fasted for 8 h before surgery. In the operation theatre, electrocardiogram, pulse oximeter, non-invasive blood pressure and train-of-four (TOF) neuromuscular function monitor (TOF watch, attached to the limb contra lateral to that with NIBP cuff) were attached, and baseline readings were obtained from each patient. Intravenous (IV) Ringer's lactatewas started at the rate of 250 ml/h after securing an 18-gauge IV cannula. The patients were pre-medicated with intravenous ranitidine 50 mg, metoclopramide10 mg, midazolam 0.02 mg/kg, glycopyrrolate 0.005 mg/ kg and fentanyl 2 µg/kg in the theatre. Patients were pre-oxygenated with 100% oxygen with a face mask in a circle system at a flow rate of 6 L/min for 3 min. In Group R, IV induction was carried out with propofol 2 mg/kg. In Group RS, induction was done using a face mask with 2% sevoflurane in oxygen with an initial total fresh gas flow of 6 L/min and propofol 2 mg/kg IV. Later fresh gas flow was reduced to 3 L/min during maintenance.

Neuromuscular monitoring using train of four counts at adductor pollicis muscle was commenced from time of loss of eyelash reflex using train of four (TOF) pattern of stimulation viz, supra maximal square wave stimuli applied to the ulnar nerve at the wrist at 2Hz for 2 seconds. The TOF stimulus was repeated at 12 second intervals until TOF count became 0 and this time was noted. In group-A TOF count at 60 second after administration of propofol was recorded and tracheal intubation performed by observer unaware of the group to which patient belonged. Time to loss of TOF response was calculated as the time between administration of rocuronium and complete abolition of response to TOF stimulation.

Intubating conditions were graded as excellent when intubating scores were between 8 and 9, good with 6–7, fair with 3–5 and poor with 0–2. Excellent and good intubating conditions were considered clinically acceptable as per Cooper *et al*.[5] Data noted included loss of thumb adduction, onset time of intubation, conditions at the time of intubation (using Cooper's scoring system), heart rate, mean arterial pressure, oxygen saturation (using pulse oximetry) at baseline, post-induction, at intubation, immediately after intubation, 1 min, 3min and 5 min after intubation.

Table-1: Cooper's intubation scoring systematic

Jaw relaxation	Vocal cords	Response to intubation	Score
Poor (impossible)	Closed	Severe coughing or bucking	0
Minimal (difficult)	Closing	Mild coughing	1
Moderate (fair)	Moving Slight	diaphragmatic movement	2
Good (easy)	Open	None	3

The data from the present study was systematically collected, compiled and statistically analyzed to draw relevant conclusions. Parameters like Age, Weight, Time to intubation, Time between relaxant and intubation were analyzed with Anova test. Intubating conditions, Train of four count at intubation were analyzed statistically with Chi-square test. Haemodynamics were analyzed with Anova with post hoc test and paired t test was used for- Time to onset of clinical weakness, Time to loss of Train of four. Differences were considered to be significant if p value was < 0.05

RESULTS

The present study was conducted in a sample of 70 participants, who were randomly divided into two groups, comprising of 35 participants each, Group R (Rocuronium) (n=35) and Group Rs (Rocuronium with 2% sevoflurane) (n=30). The study was conducted at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad during the period Febraury 2016 to Febraury 2018, results are as follows.

The patients in this study were aged between 30 to 50 year of both genders weighting from 40 to 70kg coming for elective surgeries under general anaesthesia were included. There were no significant demographic differences among groups with respect to age, weight, height, sex and ASA grade I and II patients and was shown in table 2.

Table-2: Demographic data

Variables	Group-R (mean+SD)	Group-RS (mean+SD)
Age(Yrs)	47.5 ± 20.03	45.9 ± 16.83
Wt(Kg)	57.6 ± 22.27	61.1 ± 12.35
Height(cm)	159.8 ± 11.53	158.5 ± 5.84
Sex (M/F)	17/18	20/15
ASA grade I/II	19/15	16/21

Patients undergone through different surgical procedures like Hemithyroidectomy, Cholecystectomy, Tonsillectomy, Laminectomy etc were mentioned in table 3.

Table-3: Surgical procedures

Surgical procedure	Group-R(No=35)	Group-RS(No=35)
Hemithyroidectomy	5	4
Cholecystectomy	6	4
Orthopaedic procedures	7	8
Diagnostic laparoscopy	5	6
Tonsillectomy	8	7
Laminectomy	4	6

Intubating conditions were assessed by cooper scoring system and were shown in table 4. In both groups patients were showed excellent intubating response but in group RS 28 member which is significantly higher than group R.

Table-4: Intubating conditions

Intubating condition	Group-R (No=35)	Group-RS (No=35)
Excellent	18	28
Good	14	6
poor	3	1

The time for loss of thumb adduction was 99.81±9.3 in Group R compared with 62.03±5.2s in Group RS and the onset time of intubation was 100.65±8.6s in Group R compared with 58.62±6.5 in Group RS. These timings were significantly reduced in the Group RS compared to Group R (Table 5).

Table-5: Neuro muscular monitoring data

Neuromuscular monitoring	Group-R (mean+SD)	Group-RS (mean+SD)	p-value
Time for loss of thumb adduction (seconds)	99.81±9.3	62.03±5.2	<0.001*
Onset time of intubation (seconds)	100.65±8.6	58.62±6.5	<0.001*

Heart rate, systolic and diastolic blood pressure were significantly more in all the three groups at 1 minute after intubation($p<.05$). All the haemodynamic variables had decreased at 3 minutes after intubation in all groups. But at 5 minutes after intubation all the haemodynamic parameters had come near baseline in group R and RS. The results between Group R and RS are not statistically significant ($p>.05$). Heart rate, systolic and diastolic blood pressure was shown in table 6.

All patients were satisfied with the induction technique used in this study and none of them complained of any discomfort or shortness of breath during induction of anaesthesia. There was no complaint of muscle pain in the postoperative period in group R, but 1 patient complained of muscle pain in group RS.

DISCUSSION

Muscle relaxation is used to serve two purposes: one to facilitate endotracheal intubation and other to provide surgical relaxation[6]. The ideal neuromuscular blocking agent is one which has brief duration of action, provides profound relaxation and is free from haemodynamic changes. rocuronium reliably produces muscle relaxation within 60 seconds of its administration with fewer side effects. Rocuronium is an aminosteroid nondepolarizing muscle relaxant with rapid onset and intermediate duration of action. It has a faster neuromuscular blockade onset time compared to other NDMRs[7]. It provides clinically acceptable

intubating conditions within 60–90 s in dose range of 0.6–1.2 mg/kg,[8] but large doses unduly prolong its duration of action, making it unsuitable for short surgical procedures.

Table-6: Haemodynamic parameters in two groups

Parameter	Group-R	Group-RS
Heart rate/minute		
0	76.23	76.52
1	90.24	88.35
3	84.83	82.68
5	75.35	74.39
Systolic blood pressure((mm of Hg)		
0	123.42	123.23
1	137.82	135.78
3	130.59	128.56
5	121.58	121.32
Diastolic blood pressure (mm of Hg)		
0	77.69	77.85
1	86.56	85.62
3	84.32	83.23
5	80.63	80.23

In our study mean Onset time of intubation was 100.65±8.6 sec in group R and 58.62±6.5 sec in group RS and Time for loss of thumb adduction was 99.81±9.3 and 62.03±5.2 respectively in group R and group RS. This is consistent with the study done by Seiber TJ et al[9] who evaluated intubating conditions 45 and 60 seconds after administration of intravenous induction agent following rocuronium 0.6mg kg^{-1} in 45 patients who were randomly assigned to three groups. He concluded that rocuronium 0.6 mg kg^{-1} provides good to excellent intubating conditions 45 and 60 s after the induction of anesthesia using the timing principle.

Studies comparing effects of rocuronium and succinylcholine on the intubating time and conditions have shown varying results In the Veena et al[10] study, rocuronium administered in the dose of 0.6mg kg^{-1} using timing principle and tracheal intubation was performed at 60 seconds after induction with propofol provided intubating conditions that were excellent to good in all patients(21-excellent,4-good) and this was comparable to succinylcholine 2mg kg^{-1} (22-excellent, 3-good) and the difference was statistically insignificant. None of the patient had poor intubating conditions with both the drugs. . Rocuronium at doses of 0.9 mg/kg and 1.2 mg/kg has been shown to result in rapid onset of action with comparable intubating conditions to that of succinylcholine 1 mg/kg for rapid sequence induction with endotracheal intubation [8]. The time to achieve maximum blockade was 89 s with rocuronium 0.6 mg/kg with clinically acceptable intubating conditions at 60–90 s in a previous study. Wright *et al*.[11]concluded that the onset time of rocuronium, in doses more than 0.8 mg/kg was comparable to that of succinylcholine 1 mg/kg at the adductor pollicis but was significantly delayed at the laryngeal adductors.

Potent inhalational anaesthetic like sevoflurane is known to potentiate the neuromuscular blocking effects of aminosteroid neuromuscular blocking agents. Under sevoflurane induction, a dose of 0.3 mg/kg rocuronium is found to provide ideal intubating conditions in children aged 1–6 years.[12].In a study using sevoflurane with rocuronium, and compared to only using rocuronium, the effective doses of rocuronium required to produce 50%, 90% and 95% twitch depression decreased by 30.5%, 26.7% and 25.2%, respectively; the duration of action and the recovery characteristics after administration of a total dose of rocuronium 0.4 mg/kg were both significantly prolonged by sevoflurane[13].

In our study in concern of haemodynamics, in group R and RS the haemodynamics were increased at 1 minute after intubation due to stress response of intubation but the heart rate, systolic Blood pressure and diastolic Blood pressure in group R and S returns back to baseline at 5 minutes.

Elderly patients being treated with rocuronium 0.9 mg/kg showed no clinically significant change in heart rate, arterial blood pressure or plasma catecholamine concentrations[13]. Slight to moderate increase in heart rate after rocuronium injection may be attributed to either pain on injection or to its weak vagolytic effect. The heart rate increase may be controlled by the prior administration of fentanyl.

In study conducted by Veena *et al.* [10] in group rocuronium(A), vecuronium(B) and Succinylcholine(C) the haemodynamics were increased at 1 minute after intubation due to stress response of intubation but the heart rate, systolic Blood pressure and diastolic Blood pressure in group A and B returns back to baseline at 5 minutes but not in Group C

showing that rocuronium and vecuronium when used with timing principle produces minimal circulatory changes and are haemodynamically stable drugs as compared to Succinylcholine which shows increase in all the parameters at 5 minute and this change was statistically significant. In another study by Koyama *et al.* [14] who also observed that increase in systemic blood pressure, heart rate and rate pressure product were significantly lower in patients in timing principle group than in those in SCC group. Intubating conditions were almost excellent in both groups, and there were no complications in this study.

CONCLUSION

Rocuronium 0.8 mg/kg produces good intubation conditions at 100 sec when compared with Rocuronium 0.8 mg/kg along with 2% sevoflurane provides excellent intubating conditions within 60–66 s without any adverse effects in elective surgeries in patients with stable haemodynamics.

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