

# A Comparative Study of the Effect of Priming and Sevoflurane on Intubating time and Intubating Conditions with Rocuronium as Intubating Agent in Neurosurgical Patients.

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Received: August 2016

Accepted: August 2016

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## ABSTRACT

**Background:** Rocuronium provides good intubating conditions but large doses causes prolongation of its duration of action, making it unsuitable for short surgical procedures. **Aims:** This study was designed to compare the effects of rocuronium with 3min priming interval and 2% sevoflurane on the time of intubation and intubating conditions. **Methods:** the study design is that of randomized, prospective double-blind trial. Forty five adult patients were randomly allocated into three equal groups: Group R received 0.8 mg/kg rocuronium, Group RS received 0.8 mg/kg of rocuronium with 2% sevoflurane and Group RP patients received a priming dose of 0.08 mg/kg of rocuronium followed by 0.72 mg/kg rocuronium 3 min later. Onset time of intubation, intubating conditions and time for loss of thumb adduction were assessed. Analysis of variance (ANOVA) test was used to compare the demographic data and intubating conditions among the groups. Intergroup comparison between R and RS, R and RP, RS and RP of the time for intubation and time for the loss of thumb adduction were done using student t test. A P value <0.05 was considered significant. **Results:** The onset time of intubation (loss of T1 of TOF) was 100.53±2.03s in group R, 62.9±1.9 s in-group RS, and 61.88±1.9s in group RP. The time for the loss of thumb adduction in R,RS,RP were 98.53±2.03, 60.93±1.9, 60±2.12 respectively. There is statistical significance p=0.001 between R and RS, R and RP group while comparing the onset time for intubation and time for the loss of thumb adduction. Mean intubating scores were excellent in all the three groups. **Conclusion:** Both rocuronium (0.08mg/kg) along with 2% sevoflurane and priming principle for rocuronium provide excellent intubating conditions within 60-66 sec in neurosurgical patients.

**Keywords:** Intubating conditions, priming, rocuronium, sevoflurane.

## INTRODUCTION

Endotracheal intubation using succinylcholine is an established technique for rapid sequence intubation in patients at risk of gastric aspiration. Succinylcholine has a number of undesirable side-effects like hyperkalaemia<sup>[1]</sup>, bradyarrhythmias<sup>[2]</sup>, increased intraocular tension, increased intracranial tension<sup>[3]</sup>, malignant hyperthermia and masseter spasm. Hence, it is not suitable in conditions like neuromuscular disorders, burns, acute head injury, open eye injury, intracranial haemorrhage<sup>[4]</sup> spinal cord injury<sup>[5]</sup>, cerebrovascular accidents and renal disease.

Non-depolarizing muscle relaxants (NDMRs) are used for rapid sequence intubation (RSI) using various principles such (1) timing principles, (2) combination of relaxant, (3) high dose of non-depolarizing muscle relaxants, (4) inhalational agents to augment the effect of non-depolarizing muscle relaxants, (5) use of intravenous anaesthetic agents with non-depolarizing muscle relaxants to augment neuromuscular blockade<sup>[6-10]</sup> and (6) priming principle.

Rocuronium has rapid onset and intermediate duration of action. It provides good intubating conditions within 60–90 s in dose range of 0.6–1.2 mg/kg<sup>[13]</sup> but large doses causes prolongation of its duration of action, making it unsuitable for short surgical procedures.

Thus, this study was taken up with the primary objective of evaluating the effects of rocuronium alone, along with 3min priming interval and along with 2% sevoflurane on the time of intubation and

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the secondary objective of evaluating the intubating conditions.

## MATERIALS AND METHODS

This prospective, randomized, double-blind study was conducted after Institute Ethics Committee approval and written informed consent in 45 adult patients belonging to American Society of Anesthesiologists (ASA) physical status Grades 1 and 2 aged between 20 and 50 years, of either gender in patients posted for elective neurosurgical procedures. Exclusion criteria included patient's refusal, patients with neuromuscular diseases, anticipated difficult intubation, systemic diseases, patients receiving drugs interfering with neuromuscular function, history of allergic reaction to rocuronium, pregnancy and breastfeeding and psychiatric patients.

Patients were assigned to one of the following three groups R, RS and RP randomly according to computer generated numbers:

Group RP: Priming with 0.08 mg/kg of rocuronium followed by 0.72 mg/kg of rocuronium after 3 min of priming interval

Group RS: received 0.8 mg/kg of rocuronium and 2% sevoflurane during induction.

Group R: received 0.8 mg/kg of rocuronium.

A standard anaesthesia protocol was followed. In the operation theatre, intravenous cannula was secured in the hand opposite to neuromuscular monitoring and a balanced salt infusion was started. Electrocardiogram (ECG), non-invasive blood pressure (NIBP), and oxygen saturation (SpO<sub>2</sub>) were monitored. The nerve stimulation technique was explained to the patient. A supramaximal stimulus was set with a peripheral nerve stimulator.

All the patients were given intravenous ranitidine 50 mg and metoclopramide 10 mg 1 hour prior to surgery. The patients were pre-medicated with midazolam 0.02 mg/kg, glycopyrrolate 0.005 mg/kg and fentanyl 2 mcg/kg in the theatre. Patients were pre-oxygenated with 100% oxygen at a flow rate of 6 L/min for 3 minute with a facemask in a circle system. In Group R, IV induction was carried out with propofol 2 mg/kg. Group RS was induced using a face mask with sevoflurane 2% in oxygen with an initial total fresh gas flow of 6 L/min and propofol 2 mg/kg IV and subsequently fresh gas flow was reduced to 3 L/min during maintenance. End-tidal sevoflurane concentration 1- 1.5 minimum alveolar concentrations (MAC) was maintained between in all the patients of Group RS. After the loss of verbal response, a supramaximal TOF stimulus was set and applied to the ulnar nerve at the wrist through surface electrodes (stimulation current set at 50 mA) and baseline TOF ratio percentage was noted in both group R and RS. In group R and RS ,after giving an intubating dose of rocuronium 0.8 mg/kg, supramaximally set TOF stimulus was again applied

and repeated every 10 s to evaluate visually for loss of adduction of thumb and disappearance of the first response (T1) of TOF stimuli. In group RP after preoxygenation, a priming dose of rocuronium (0.08mg/kg) was given. The patients were enquired about ptosis, vision problems, difficulty in swallowing, and difficulty in breathing. Anaesthesia was induced with propofol 2 mg/kg. After the loss of verbal response, a supramaximally set TOF stimulus was applied in-group RP also and baseline TOF ratio percentage noted. An intubating dose of rocuronium of 0.72 mg/kg was given after 3 min. Supramaximally set TOF stimulus was again applied and repeated every 10 s to evaluate for loss of adduction of thumb and disappearance of the first response (T1) of TOF stimuli. Onset time of intubation was taken as the time interval between the administration of intubating dose and the loss of T1 of TOF stimuli. After the loss of T1, tracheal intubation was done. Intubating conditions were assessed and recorded using Cooper's intubation scoring system [Table 1].

**Table 1: Cooper's Intubation Scoring System**

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

Intubating conditions were excellent when intubating scores were between 8 and 9, good 6–7, fair 3–5 and poor 0–2. Excellent and good intubating conditions were considered clinically acceptable as per Cooper et al [12].

The observations were recorded in Microsoft excel spread sheet and analysis was done using the SPSS 21 software. A P value <0.05 was considered significant. Data noted includes loss of thumb adduction, onset time of intubation and conditions at the time of intubation (using Cooper's scoring system). Based on results of the pilot study conducted by us, sample size was calculated. At 5% level of significance and power 90% and taking difference in mean onset time of intubation to be 28.5s and standard deviation 18, the sample size of 10 subjects was calculated in each group. For study purpose, 15 subjects were taken in each of the three groups. Continuous measurements were presented as mean ± standard deviation (SD). One way analysis of variance (ANOVA) test was used for comparing intubating conditions among the groups and demographic data. Intergroup comparison between R and RS, R and RP, RS and RP of the time for intubation and time for the loss of thumb adduction were done using student t test.

**RESULTS**

[Table 2] shows the demographic data. All the groups were statistically comparable with respect to age, sex, weight(p >0.05). Onset time for intubation were also compared between the groups. The onset

time of intubation (loss of T1 of TOF) was 100.53±2.03 sin group R, 62.9±1.9s in group RS and 61.88±1.9s in group RP.

[Table 3] shows comparison of times of intubation between group R and RS and it is statistically significant (p=0.001).

**Table 2: Demographic data.**

Parameter	Total	Group R	Group RS	Group RP	P value
Age	38.4±8.8	37.9±9.8	37.8±9.5	38.9±9.8	0.63 <sup>#</sup>
Sex(male/female)	25/20	9/6	8/7	8/7	0.14 <sup>#</sup>
Weight	61.5±8.4	60.2±8	61.2±7.4	63.3±10	0.43 <sup>#</sup>

Values expressed in mean (SD) and proportions applicable.# ANOVA test

**Table 3: Comparison of times of intubation (time interval between intubating dose and loss of T1 of TOF stimuli) between R and RS group.**

Group	Time of intubation(in sec)	P value
R	100.53±2.03	0.001*
RS	62.9±1.9	

Values expressed in mean±SD and proportions applicable.\*independent t test.

[Table 4] shows comparison of times of intubation between group R and RP and it is statistically significant (p=0.001)

**Table 4: Comparison of times of intubation (time interval between intubating dose and loss of T1 of TOF stimuli) between R AND RP group.**

Group	Time of intubation(in sec)	P value
R	100.53±2.03	0.001*
RP	61.88±1.9	

Values expressed in mean±SD and proportions applicable.\*independent t test.

[Table 5] shows comparison of times of intubation between group RS and RP and it is not statistically significant (p=0.143)

**Table 5: Comparison of times of intubation (time interval between intubating dose and loss of T1 of TOF stimuli) between RS AND RP group.**

Group	Time of intubation(in sec)	P value
RS	62.9±1.9	0.143*
RP	61.88±1.9	

Values expressed in mean±SD and proportions applicable.\*independent t test

Time of loss of thumb adduction was compared between the group R and RS and was found to be significant (p=0.001) [Table 6].

**Table 6: Comparison of time for loss of thumb adduction between group R and RS.**

Group	Time for loss of thumb adduction	P value
R	98.53±2.03	0.001*
RS	60.93±1.9	

Values expressed in mean±SD and proportions applicable.\*independent t test.

Time of loss of thumb adduction was compared between the group R and RP and was found to be significant (p=0.001) [Table 7].

**Table 7: Comparison of time for loss of thumb adduction between group R and RP.**

Group	Time for loss of thumb adduction	P value
R	98.53±2.03	0.001*
RP	60±2.12	

Values expressed in mean±SD and proportions applicable.\*independent t test.

Time of loss of thumb adduction was compared between the group RS and RP and was not found to be significant (p=0.21) [Table 8].

**Table 8: Comparison of time for loss of thumb adduction between group RS and RP.**

Group	Time for loss of thumb adduction	P value
RS	60.93±1.9	0.21*
RP	60±2.12	

Values expressed in mean±SD and proportions applicable.\*independent t test

In all the groups intubating conditions were good [Table 9].

**Table 9: Mean intubation score (mean± standard deviation).**

Data	Group R	Group RS	Group RP	P value
Mean intubating scores	8.47±0.52	8.5±0.5	8.4±0.52	0.95 <sup>#</sup>

Values expressed in mean±SD and proportions applicable.# ANOVA test

**DISCUSSION**

Rocuronium is derivative of vecuronium, differing from it at three positions on steroid nucleus. Rocuronium has got a rapid onset of action intermediate duration of action and is devoid of any clinically significant cardiovascular side effects at effective neuromuscular blocking doses which makes it a better agent for endotracheal intubation among non-depolarizing neuromuscular blocking drugs. Potent inhalational anaesthetic like sevoflurane is known to potentiate neuromuscular blocking agents. The priming principle can be advocated to shorten the onset time of non depolarizing muscle relaxants. The priming principle entails a divided-dose technique with a priming dose (10% of intubating dose),so as not to cause any

unpleasant side effects and to cause moderate inhibition of neuromuscular transmission. Our study was conducted to compare the intubating time and conditions of rocuronium alone, along with 2% sevoflurane and after 3min priming.

Cooper *et al*<sup>[12]</sup> compared the intubating conditions with rocuronium (0.6 mg/kg) and succinylcholine (1 mg/kg) in 50 patients. In the study, 95% of patients generated clinically acceptable intubating conditions at 60 s and 100% patients at 90 s with rocuronium. Intubating conditions were excellent in all cases. They concluded that rocuronium can be used as a safe alternative to succinylcholine in RSI.

A priming dose of 10% of the standard intubating dose ( $2 \times ED_{95}$ )<sup>[14]</sup> and a priming interval of 3-4 min has been recommended as a safe and effective technique. Wright *et al*<sup>[15]</sup> concluded that the onset time of rocuronium, in doses more than 0.8 mg/kg was comparable to that of succinylcholine at a dose of 1 mg/kg at the adductor pollicis and it was significantly delayed at the laryngeal adductors.

In our study, intubating time while using rocuronium alone is  $100.53 \pm 2.03$  s. On combination with 2% sevoflurane it was found to be  $62.9 \pm 1.9$  s and by priming principle, it was found to be  $61.88 \pm 1.9$  s. In our study there is no significant difference between sevoflurane group and 3min priming group. Both reduce the intubating time when compared to rocuronium alone. Time for the loss of thumb adduction in R,RS and RP group were found to be  $98.53 \pm 2.03$ ,  $60.93 \pm 1.9$  and  $60 \pm 2.12$  respectively. Compared to rocuronium alone, sevoflurane group and 3min priming group showed significant reduction in time for the loss of thumb adduction. There is no significant difference in time for loss of thumb adduction between sevoflurane group and priming group. Intubating conditions were good in all the three groups. The intubating dose (0.8mg/kg) used for our study is 2.6 times  $ED_{95}$  dose. Studies have found that effect of rocuronium 0.6 mg/kg was enhanced by 1.5 MAC of sevoflurane in comparison with isoflurane or propofol anaesthesia<sup>[16]</sup>.

In our study, we also noted no definite advantage of 3min priming principle over use of 2% sevoflurane along with rocuronium. Both provide excellent intubating conditions and reduce the intubating time almost to the same extent (60-65sec).

The autonomic margin of safety of rocuronium for the vagal block is 3-5. No haemodynamic changes were observed in humans without associated increase in plasma histamine levels even after doses of up to 4 times  $ED_{95}$ . In our study, we did not observe any increase in heart rate or blood pressure after rocuronium administration. This may be due to prior administration of fentanyl.

One of the major drawbacks of a priming dose is the occurrence of adverse effects such as generalized discomfort, weakness, diplopia, dysphagia and breathing difficulties.<sup>[14]</sup> Aziz *et al*<sup>[14]</sup> studied the effects of priming with vecuronium and rocuronium

on young and elderly patients. In the study, they monitored for the presence of muscle weakness by monitoring symptoms of diplopia, dysphagia, and ptosis, oxygen saturation and pulmonary function tests following priming. They concluded that there is a greater decrease in oxygen saturation and pulmonary function tests in the elderly (aged 65-73 years) following priming doses of vecuronium and rocuronium when compared to their younger (25-35 years) counterparts. However, in our study, we didn't observe any of the above side effects in 3min priming group.

The limitations of our study are we used the adductor pollicis muscle for neuromuscular monitoring in our study, which has delayed onset of blockade compared to the laryngeal and diaphragmatic muscles and we chose to include only elective neurosurgery patients in our study.

## CONCLUSION

Both rocuronium (0.08mg/kg) along with 2% sevoflurane and 3min priming principle for rocuronium provide excellent intubating conditions within 60-66 sec in neurosurgical patients. This approach can be considered for rapid sequence intubation during anaesthesia in neurosurgical patients.

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**How to cite this article:** Nitha CS, Nayak K. A Comparative Study of the Effect of Priming and Sevoflurane on Intubating time and Intubating Conditions with Rocuronium as Intubating Agent in Neurosurgical Patients. *Ann. Int. Med. Den. Res.* 2016; 2(6):AN11-AN15.

**Source of Support:** Nil, **Conflict of Interest:** None declared