Clinical Investigation

A comparative study of effect of sevoflurane on intubating conditions with rocuronium in neurosurgical patients

Address for correspondence:
Dr. Saikat Mitra,
Department of Anaesthesiology,
SMS Medical College, Jaipur,
Rajasthan, India.
E-mail: smsaikatmitra1@gmail.com

Saikat Mitra, Shobha Purohit, Sonali Bhatia, Poonam Kalra, Satya Prakash Sharma
Department of Anaesthesiology, SMS Medical College, Jaipur, Rajasthan, India

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/0019-5049.171557

Quick response code

ABSTRACT

Background and Aims: Rocuronium may not always be the preferred relaxant for rapid sequence intubation. When 2% sevoflurane is used in conjunction with rocuronium, it may reduce the time required for achieving complete skeletal muscle relaxation with the intubating dose of rocuronium. **Methods:** This study was prospective, randomised, double-blind in nature and compared the effect of sevoflurane on intubation time and intubating conditions when used along with rocuronium. Thirty adult patients belonging to American Society of Anesthesiologists physical status Grades 1 and 2, of either gender aged between 30 and 65 years undergoing neurosurgical operations were randomly allocated into two equal groups: Group R received 0.8 mg/kg rocuronium, and Group RS received 0.8 mg/kg of rocuronium with 2% sevoflurane. Onset time of intubation was assessed using train-of-four stimuli. The intubating conditions were compared using the Cooper scoring system and the haemodynamic responses were compared between the two groups. **Results:** The onset time of intubation was 101.73 ± 10.28 s in Group R and 60.4 ± 4.1 s in Group RS ($P < 0.001$), with excellent intubating conditions in both groups and without any adverse effects. Significant differences in heart rate and mean arterial pressure were seen immediately after intubation, at 1 and 3 min ($P < 0.05$) between the two groups. **Conclusion:** Rocuronium 0.8 mg/kg along with 2% sevoflurane provides excellent intubating conditions within 60–66 s from its administration.

Key words: Intubating conditions, rocuronium, sevoflurane

INTRODUCTION

Ever since the discovery of anaesthesia, anaesthesiologists are in quest of a muscle relaxant which might provide ideal intubating conditions in ultrashort duration with least side effects. Rapid sequence induction with endotracheal intubation is a well-known technique in patients at risk of gastric aspiration to protect the airway within 60–90 s following induction.

Nondepolarizing muscle relaxants (NDMRs) are used for rapid sequence intubation using various principles such as (1) timing principle, (2) priming principle, (3) high dose NDMR, (4) combination of relaxants and (5) inhalational agents to supplement the effect of NDMR on intubating conditions.

Rocuronium is an aminosteroid NDMR with rapid onset and intermediate duration of action. It has a faster neuromuscular blockade onset time compared to other NDMRs.[1] It provides clinically acceptable intubating conditions within 60–90 s in dose range of 0.6–1.2 mg/kg,[2] but large doses unduly prolong its duration of action, making it unsuitable for short surgical procedures. Hence, it may not be preferable for rapid sequence induction and endotracheal intubation.

How to cite this article: Mitra S, Purohit S, Bhatia S, Kalra P, Sharma SP. A comparative study of effect of sevoflurane on intubating conditions with rocuronium in neurosurgical patients. Indian J Anaesth 2015;59:774-8.

Volatile anaesthetics are known to potentiate the effects of NDMRs.[3] We used 2% sevoflurane with rocuronium bromide (at intubating dose of 0.8 mg/kg) during induction in patients undergoing elective lumbar disc surgeries under general anaesthesia. We assessed the efficacy of sevoflurane with rocuronium during induction in terms of reducing the onset time for intubation, evaluating intubating conditions and haemodynamic responses during intubation, so that it can be used for rapid sequence intubation.

METHODS

This prospective, randomised, double-blind study was conducted after Institute Ethics Committee approval and written informed consent in 30 adult patients belonging to American Society of Anesthesiologists (ASA) physical status Grades 1 and 2 aged between 30 and 65 years, of either gender. Exclusion criteria were patient's refusal, patients with neuromuscular diseases, anticipated difficult intubation, pregnancy and breastfeeding, hepatic, renal diseases, patients receiving drugs interfering with neuromuscular function, history of allergic reaction to rocuronium and psychiatric patients.

The patients undergoing lumbar disc operations under general anaesthesia were randomly allocated into two equal groups by 'chit in box' method: namely Group R (received 0.8 mg/kg of rocuronium) and Group RS (received 0.8 mg/kg of rocuronium and 2% sevoflurane during induction).

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 (NIBP) and train-of-four (TOF) neuromuscular function monitor (TOF watch, attached to the limb contralateral to that with NIBP cuff) were attached, and baseline readings were obtained from each patient. Intravenous (IV) Ringer's lactate was 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, metoclopramide 10 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. End-tidal sevoflurane concentration was continuously monitored with 'Spacelabs Healthcare Ultraview SL® module' and it varied between 1 and 1.5 minimum alveolar concentration (MAC) in all the patients of Group RS. After the loss of verbal response, a supramaximally set TOF stimulus was applied to the ulnar nerve at the wrist through surface electrodes (stimulation current set at 50 mA) using acceleromyograph after automatic calibration and baseline TOF ratio percentage was noted. After giving an intubating dose of rocuronium 0.8 mg/kg, supramaximally set TOF stimulus was again applied and repeated every 15 s to evaluate visually 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 intubating dose and the loss of T1 of TOF stimuli.

After the loss of T1, tracheal intubation was done by an experienced anaesthesiologist who was blinded to the study methodology. Intubating conditions were assessed and recorded using Cooper's intubation scoring system [Table 1].

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*.[4]

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, 3 min and 5 min after intubation.

Data were analysed statistically using software Primer of Biostatistics (version 6.0.0.0) [Developer -McGraw-Hill Global Education Holdings, LLC]. The sample size was calculated based on results of the pilot study conducted by us. At alpha error 0.05 and power 90% and taking difference in mean onset time of intubation (in seconds)

Table 1: Cooper's Intubation Scoring System

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

to be 28.5 and standard deviation 18, the sample size was calculated to be 10 subjects in each group. For study purpose, 15 subjects were taken in each of the two groups. Demographic data were compared using the Chi-square test. Quantitative data, i.e., age, weight, loss of thumb adduction, onset time of intubation, and haemodynamic variables (heart rate and mean arterial pressure) were compared using the unpaired *t*-test. Paired *t*-test was used for comparison of haemodynamic parameters over multiple points. Statistical significance was considered if $P < 0.05$.

RESULTS

All thirty patients completed the study. The two groups were comparable with respect to age, sex, weight and ASA grade [Table 2, $P > 0.05$]. The time for loss of thumb adduction was 100.8 ± 10.1 s in Group R compared with 59.07 ± 4.3 s in Group RS [Table 3, $P < 0.001$]. The onset time of intubation was 101.73 ± 10.3 s in Group R compared with 60.4 ± 4.1 s in Group RS [Table 3, $P < 0.001$]. The mean intubation score was comparable in both the groups [Table 4, $P = 0.11$].

The baseline haemodynamic parameters in both the groups were comparable ($P > 0.05$). Significant differences in heart rate and mean arterial pressure were seen immediately after intubation, at 1 and 3 min after intubation ($P < 0.05$) between the two groups [Figures 1 and 2]. Heart rate increased significantly ($P < 0.05$) above baseline values immediately after intubation, at 1 min, 3 min and 5 min after intubation in Group R as compared to Group RS. Mean arterial pressure was significantly reduced from baseline values post-induction and at the time of intubation in Group RS as compared to Group R ($P = 0.001$). In Group R, mean arterial pressure increased immediately after intubation, at 1 and 3 min after intubation, though statistically not significant.

DISCUSSION

Anaesthesiologists are in quest for NDMRs having ideal neuromuscular blocking properties with rapid onset of action and offering good to excellent intubation conditions without any significant adverse effects. Rocuronium, a non-depolarising aminosteroidal muscle relaxant is chemically 2-morpholino, 3-desacetyl,

Table 2: Demographic data (data are expressed as mean±standard deviation for age and weight, and absolute numbers for gender and American Society of Anesthesiologists' grade)

Demographic data	Group R (*n*=15)	Group RS (*n*=15)
Age (yr)	51.4±10.7	48.8±8.44
Weight (kg)	57.133±12.26	58.733±14.77
Sex (M:F)	9:6	7:8
Asa grade (I:II)	9:6	11:4

Table 3: Neuromuscular monitoring data (mean±standard deviation)

Neuromuscular monitoring	Group R (*n*=15)	Group RS (*n*=15)	*P* value
Time for loss of thumb adduction (seconds)	100.8±10.1	59.07±4.3	<0.001*
Onset time of intubation (seconds)	101.73±10.3	60.4±4.1	<0.001*

*Statistically highly significant

Table 4: Mean intubation score (mean±standard deviation)

Data	Group R (*n*=15)	Group RS (*n*=15)	*P* value
Mean intubation scores	8.733±0.46	8.333±0.82	0.11

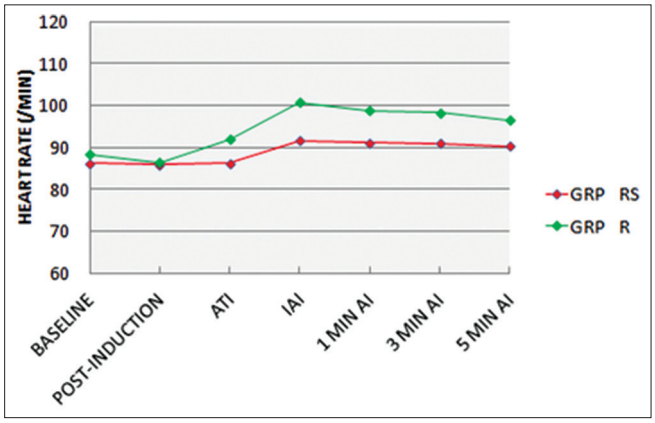

Figure 1: Comparison of changes in heart rate between the groups. IAI – Immediately after intubation; ATI – At intubation; AI – After intubation; GRP – Group

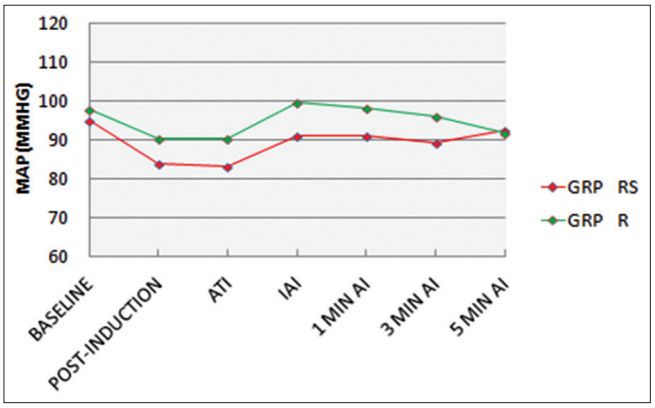

Figure 2: Comparison of changes in mean arterial pressure between the groups. IAI – Immediately after intubation; ATI – At intubation; AI – After intubation; GRP – Group

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. Potent inhalational anaesthetic like sevoflurane is known to potentiate the neuromuscular blocking effects of aminosteroid neuromuscular blocking agents. Our study was conducted to compare the intubating time and conditions of rocuronium with 2% sevoflurane.

Studies comparing effects of rocuronium and succinylcholine on the intubating time and conditions have shown varying results. 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[2]. 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.[4] Rocuronium at 1 mg/kg produces clinically acceptable intubating conditions at 60 s and it has been suggested as an alternative to succinylcholine 1 mg/kg in rapid sequence intubation in the absence of anticipated difficult airway conditions.[5] Similar conclusions regarding onset time and intubating conditions were obtained from other studies.[6,7] Wright *et al*.[8] 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.

In the present trial, the mean onset time for intubation in Group R was 101.73 ± 10.28 s which is higher compared to previous studies (74 ± 36 s).[8] The mean onset time for intubation in this trial was 60.4 ± 4.1 s using 2.6 × ED_{95} dose of rocuronium (0.8 mg/kg) with 2% sevoflurane during induction. However, intubating conditions were clinically acceptable in both the groups. 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[9]. There could be notable interactions between the neuromuscular blocking effects of rocuronium and 1.25 MAC of isoflurane, sevoflurane and desflurane resulting in a leftward shift of the dose-response curve.[10] 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.[11] 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]

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 after doses of up to 4 times ED_{95}. 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 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. However, heart rate was increased significantly above baseline values immediately after intubation, at 1 min, 3 min and 5 min after intubation in rocuronium group may be due to stress response to intubation.

The significant drop in mean arterial pressure from baseline values post-induction and at the time of intubation in Group RS in the present study may be a matter of concern in head injury patients. Longer onset time for intubation seen in Group R may be undesirable for rapid sequence intubation with 0.8 mg/kg dose of rocuronium alone.

One limitation of the present study was that the study groups included only patients undergoing elective surgeries; we felt it would be cumbersome to standardize the anaesthetic technique for emergency neurosurgical patients (like a head injury) with compromised haemodynamic status requiring a reduction in the drug doses. Hence, further studies need to be carried out with these drug combinations in other neurosurgical patients to establish stability in terms of haemodynamic parameters.

CONCLUSION

Rocuronium 0.8 mg/kg along with 2% sevoflurane provides excellent intubating conditions within 60–66 s without any adverse effects in elective neurosurgeries in patients belonging to ASA physical status I and II. This approach can be considered for rapid sequence intubation during anaesthesia in neurosurgical patients.

Financial support and sponsorship
Nil

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Rao MH, Venkatraman A, Mallleswari R. Comparison of intubating conditions between rocuronium with priming and without priming: Randomized and double-blind study. Indian J Anaesth 2011;55:494-8.
2. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Anesthesiology 1993;79:913-8.
3. Viby-Mogensen J. Dose-response relationship and time course of action of rocuronium bromide in perspective. Eur J Anaesthesiol Suppl 1994;9:28-32.
4. Cooper R, Mirakhur RK, Clarke RS, Boules Z. Comparison of intubating conditions after administration of Org 9246 (rocuronium) and suxamethonium. Br J Anaesth 1992;69:269-73.
5. McCourt KC, Salmela L, Mirakhur RK, Carroll M, Mäkinen MT, Kansanaho M, *et al*. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. Anaesthesia 1998;53:867-71.
6. Dubois MY, Lea DE, Kataria B, Gadde PL, Tran DQ, Shearrow T. Pharmacology of rocuronium with and suxamethonium. J Clin Anaesth 1995;7:44-8.
7. Huizinga AC, Vandenbrom RH, Wierda JM, Hommes FD, Hennis PJ. Intubating conditions and onset of neuromuscular block of rocuronium (Org 9426); a comparison with suxamethonium. Acta Anaesthesiol Scand 1992;36:463-8.
8. Wright PM, Caldwell JE, Miller RD. Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. Anesthesiology 1994;81:1110-5.
9. Lowry DW, Mirakhur RK, McCarthy GJ, Carroll MT, McCourt KC. Neuromuscular effects of rocuronium during sevoflurane, isoflurane, and intravenous anesthesia. Anesth Analg 1998;87:936-40.
10. Bock M, Klippel K, Nitsche B, Bach A, Martin E, Motsch J. Rocuronium potency and recovery characteristics during steady-state desflurane, sevoflurane, isoflurane or propofol anaesthesia. Br J Anaesth 2000;84:43-7.
11. Xue FS, Liao X, Tong SY, Liu JH, An G, Luo LK. Dose-response and time-course of the effect of rocuronium bromide during sevoflurane anaesthesia. Anaesthesia 1998;53:25-30.
12. Hung CT, Shih MH, Shih CJ, Liou SC, Kau YC, Chan C, *et al*. Intubation conditions with low dose rocuronium under sevoflurane induction for children. Chang Gung Med J 2005;28:174-9.
13. Shorten GD, Uppington J, Comunale ME. Changes in plasma catecholamine concentrations and haemodynamic effects of rocuronium and vecuronium in elderly patients. Eur J Anaesthesiol 1998;15:335-41.