Rapid Sequence Induction And Intubation With A Divided Dose Of Mivacurium Compared With Rocuronium: A Randomized, Controlled, Noninferiority Trial

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Research Article

Keywords: Mivacurium, Rocuronium, Rapid sequence induction and intubation, Neuromuscular blocking agents.

Posted Date: February 23rd, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1236107/v1

Abstract

Background Mivacurium is a short-acting nondepolarizing neuromuscular blocking agent (NMBA) with rapid and reliable metabolism. The aim of the present study was to investigate whether mivacurium provided tracheal intubation conditions noninferior to those of rocuronium for rapid sequence induction and intubation in patients undergoing general anesthesia.

Methods A total of 158 patients receiving elective surgery were recruited and randomized to the mivacurium group (Group Miva, n=79) or rocuronium group (Group Rocu, n=79). Mivacurium 0.25 mg/kg in divided doses or rocuronium 0.9 mg/kg were given to the patients in Group Miva or Group Rocu, respectively, in combination with propofol, lidocaine, remifentanil, and ephedrine. The primary outcome was the rate of excellent tracheal intubation condition evaluated by Cooper's scale 90 seconds after the initial dose of NMBAs. The secondary endpoints were mean arterial pressure and heart rate before and 10 minutes after induction at 1-minute intervals and adverse events. The non-inferiority margin was set as 10%.

Results The rates of excellent tracheal intubation conditions were 94.94% (75/79) in Group Miva and 100% (79/79) in Group Rocu. The difference was -5.06% (one-sided 97.5% confidence interval -9.96% to -∞), which satisfied the noninferiority hypothesis (P=0.024). Intubating conditions were clinically acceptable in all patients. Mean arterial pressure and heart rate were not significantly different during the induction period (P>0.05).

Conclusions Compared with rocuronium 0.9 mg/kg, mivacurium 0.25 mg/kg in divided doses in rapid sequence induction demonstrated noninferiority with regard to the rate of excellent intubation conditions and provided hemodynamic variations comparable to rocuronium.

Trial registration This study was registered with the Chinese Clinical Trial Registry on 02/05/2020 (URL: http://www.chictr.org.cn. Registry number: ChiCTR2000032571).

Background

Rapid sequence induction and intubation (RSII) is a general anesthesia induction technique recommended for patients at high risk of reflux and aspiration of gastric contents. The components of RSII are designed to protect the airway with a cuffed endotracheal tube as quickly as possible after induction. The ideal induction medication for RSII should have a rapid onset and metabolism with good intubation conditions and stable hemodynamic parameters [1].

Succinylcholine has traditionally been the preferred NMBA for RSII for a long time, with the advantages of fast onset, excellent intubation conditions, and rapid recovery of spontaneous ventilation, which is critical in the 'cannot intubate cannot ventilation' situation. However, it carries the side effects of triggering malignant hyperthermia, hyperkalemia, and postoperative myalgia and is contradictory in many clinical scenarios [2–7]. High doses of rocuronium (0.9–1.2 mg/kg, 3–4-fold of ED_{95}) have a similar onset time

to 1.0 mg/kg succinylcholine and have been advocated to be the surrogate muscle relaxant of succinylcholine for RSII [8, 9]. However, high doses of rocuronium delay recovery, prolong postoperative mechanical ventilation duration, and increase muscle relaxant antagonist use [10]. The duration is 122 ± 33 minutes from injection to recovery of the first twitch of train-of-four (TOF) to 75% of baseline after rocuronium 0.9 mg/kg bolus and 151 ± 29 minutes for 1.2 mg/kg [11]. Although sugammadex 16 mg/kg could re-establish spontaneous ventilation sooner from 1 mg/kg rocuronium-induced block than spontaneous recovery from 1 mg/kg succinylcholine-induced block [12], for some emergent short procedures, it is still worthy of investigating an anesthesia induction regimen for the purpose of fast recovery from neuromuscular block, reducing the demand for antagonism and benefiting those patients in countries or regions lack of or with limited access to sugammadex due to unbearable high price.

Mivacurium is a short-acting, benzylisoquinoline muscle relaxant that is degraded by butyrylcholinesterase in vivo. Rapid and reliable metabolism makes it a better choice for short-duration surgeries, while the disadvantages are the histamine release related to a rapid high-dose injection, unsatisfactory intubation conditions and unexpected delay in recovery in patients with butyrylcholinesterase deficiency [13, 14]. The most important factors affecting intubation are both the depth of general anesthesia and the level of neuromuscular block. Our hypothesis was mivacurium 0.25 mg/kg in divided doses in a modified RSII protocol with ephedrine priming, remifentanil, lidocaine and propofol provided excellent tracheal intubation conditions noninferior to that provided by rocuronium 0.9 mg/kg.

Methods

Ethics

The Institutional Research Ethics Board of Zhongshan Hospital, Fudan University (B2020-082) approved this prospective, randomized, controlled, patient- and assessor-blinded, noninferiority, single-center clinical study on April 26th, 2020. All patients signed informed consent forms before recruitment. This study was conducted in accordance with the Declaration of Helsinki. The authors adhered to the CONSORT statement for reporting randomized controlled trials.

Participants

A total of 158 patients aged between 18 and 65 years old with American Society of Anesthesiologists (ASA) grade I–II receiving elective surgery under general anesthesia with tracheal intubation in Zhongshan Hospital, Fudan University between April 2020 and August 2020 were enrolled. Exclusion criteria included predicted difficult airway; history of bronchial asthma; decompensated cardiac disease; abnormal hepatic or renal function; known neuromuscular disease; use of NMBAs within one week; known allergy to any of the induction medications; known butyrylcholinesterase deficiency; and pregnancy or lactating women. The withdrawal criterion was unexpected difficult airway requiring tools

other than a visual laryngoscope. The subjects were randomized to Group Miva (n = 79) or Group Rocu (n = 79) according to computer-generated random numbers by statistician and were concealed in opaque envelopes.

Anesthetia Protocol

Patients were placed in the supine position in the operating room, an 18-gauge indwelling needle was used to establish anterior cubital venous access, and lactated Ringer's solution was given. ECG, heart rate (HR), noninvasive blood pressure (NIBP) and oxygen saturation (SpO_2) were monitored. After sufficient preoxygenation with tidal volume breathing through a mask until the end-expiratory oxygen concentration reached ≥ 90% or above, lidocaine 1.5 mg/kg, propofol 2.0 mg/kg and ephedrine 6 mg were given sequentially. Then, for the patients in Group Miva, 0.25 mg/kg mivacurium (The Wellcome Foundation Limited; MIDDLESEX, UK) was given in divided doses (0.15 mg/kg injected in 10 s and 0.1 mg/kg in 5 s), separated by remifentanil 1 μg/kg injected in 30 s. Patients in Group Rocu were given rocuronium 0.9 mg/kg (N.V. Organon; Amsterdam, the Netherlands), followed by remifentanil 1 μg/kg injected in 30 s. Ideal body weight was used to calculate the dose of NMBAs for the patients whose actual weight was 30% or more above their ideal weight. Tracheal intubation was performed under a visual laryngoscope (TD-C-IV adult visual laryngoscope, Zhejiang Youyi Medical Apparatus Co., Ltd., Taizhou, China) 90 s after the completion of the initial dose in Group Miva and the completion of rocuronium in Group Rocu. Mechanical ventilation was started with a fraction of inspired oxygen (FiO_2) of 50%, tidal volume of 6–8 mL/kg, respiratory frequency of 10 times/min, and fresh gas flow of 1.0 L/min. Patient end-tidal carbon dioxide ($P_{ET}CO_2$) was kept in the range of 35–45 mmHg and 0.8–1.0 MAC sevoflurane inhalation was initiated. If MAP decreased by 30% or more from baseline while HR was < 60 beats per min (bpm), ephedrine 6 mg was given iv, while phenylephrine 100 μg was given if HR was > 60 bpm. If the HR dropped < 40 bpm without hypotension, 0.5 mg atropine was given. Patients whose MAP increased by 30% of baseline or HR > 100 bpm during or immediately after the intubation attempt were treated with propofol 0.5 mg/kg. For patients with choking or active vocal cord activity, an extra dose of propofol 0.5 mg/kg was given.

Data Collection

Blinded to the grouping information, the same attending anesthesiologist waited outside the operating room during anesthesia induction. After all medications were given, he was called into the operating room to perform tracheal intubation, and the intubation conditions of three variables were evaluated as per the intubation rating system of Cooper [15] immediately after intubation. Jaw relaxation or ease blade insertion was graded as easy (3), moderate (2), difficult (1) and impossible (0). Vocal cord positions were ranked as abducted (3), moving (2), closing (1) and closed (0). Response to intubation was graded as no movement (3), slight diaphragmatic movement (2), mild coughing (1) and severe coughing or bucking (0). The total scores of the three variables were rated as excellent (8–9), good (6–7), fair (3–5) and poor

(0–2). Good and excellent intubating conditions were considered 'clinically acceptable'. The MAP and HR were recorded minutely from the minute prior to induction (T0) to the 10th minute (T10) postinduction. RSII time was defined as the time from the start of lidocaine injection to the completion of cuff inflation. The tracheal intubation time was defined as the time from the placement of the blade between the upper and lower incisors to the completion of cuff inflation [16]. The need for additional vasopressors administered within T10 was recorded. Adverse reactions, including newly developed arrhythmia, skin manifestations of histamine release (macula, erythema, hives, flushing skin, etc.), and wheezes detected by auscultation after intubation were also recorded.

Sample Size

The primary outcome was the rate of excellent intubation conditions evaluated by Cooper's scale. According to the principle of choosing the margin of noninferiority, it was set to 1/10 − 1/5 of the rate of the comparator rocuronium and referring to equivalent studies, as well as the evaluation from our researchers and statisticians [17–19]. We chose a 10% difference as a clinically acceptable borderline with clinical relevance. The test level (α) was set as 0.025, the test power (1-β) was 0.80 and the ratio of patients enrolled in the two groups was 1:1. The number of patients was calculated to be 75 in each group, with an expected drop-out rate of 5%, and 158 patients were recruited.

Statistical Analysis

All statistical analyses were performed with IBM Statistics SPSS 22 (IBM Corp, Armonk, NY, USA), while SAS 9.4 statistical software (SAS Institute, Cary, NC, USA) was used for noninferiority testing. Quantitative data are expressed as the mean ± standard deviation and were compared by two independent sample t-tests, while $\chi 2$ tests were used for comparison of categorical variables. To explore whether the two groups had similar baseline hemodynamic variables, Student's t-tests were used to compare MAP and HR. Repeated measures analysis of variance (ANOVA) was used to compare the magnitude of MAP and HR responses to tracheal intubation. Analyses included fixed effects for time (T1 to T10), treatments (mivacurium and rocuronium), and treatments × time interactions. If the interaction was statistically significant, post hoc analysis using the Sidak correction method for mean differences was performed to determine whether there was any statistically significant difference between Group Miva and Group Rocu regarding the changes in MAP and HR between the longitudinal assessments. A $P < 0.05$ was considered statistically significant, while a $P < 0.025$ was considered significantly different for noninferiority testing.

Results

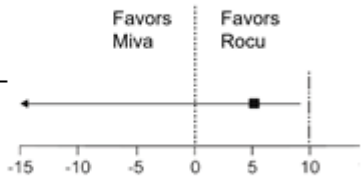
The flow chart of the study is shown in Fig. 1. A total of 158 patients were enrolled in the study. All patients were intubated successfully on the first attempt with a visual laryngoscope. The baseline characteristics of both groups were comparable (all $P > 0.05$, Table 1).

Table 1
Baseline demographics and patient characteristics

	Miva (n = 79)	Rocu (n = 79)	P
Sex (male/female)	37/42	40/39	0.633
Age (years)	49.6 ± 12.2	49.2 ± 12.0	0.828
Height (cm)	165.7 ± 7.5	165.8 ± 7.6	0.916
Weight (kg)	63.2 ± 9.8	64.4 ± 9.1	0.439
BMI (kg/m^2)	23.0 ± 3.1	23.4 ± 3.0	0.418
ASA grade (I/II)	47/32	46/33	0.872
Mallampati airway (I/II)	42/37	31/48	0.079
Surgical types (n %)			
General surgery	38(48.1)	40(50.6)	0.323
Thoracic surgery	5(6.3)	2(2.5)	
Orthopedics	11(13.9)	13(16.5)	
Urology	7(8.9)	10(12.7)	
Gynecology	7(8.9)	10(12.7)	
Digestive endoscopy surgery	11(13.9)	4(5.1)	
Previous history of hypertension (n %)	16(20.3)	15(19.0)	0.841
Data are shown as means ± SD and number (%). ASA, American Society of Anesthesiologists; BMI, body mass index.			

The rate of excellent tracheal intubation conditions was 94.94% (75/79) in Group Miva and 100% (79/79) in Group Rocu. The difference was − 5.06% [one-sided 97.5% confidence interval (CI), -9.96% to -∞], which met the noninferiority test (P = 0.024, Table 2). The rate of clinically acceptable intubation conditions was 100% in both groups.

Table 2 Difference in rate of excellent intubation condition between patients given mivacurium vs rocuronium under rapid sequence induction and intubation

	Miva (n=79)	Rocu (n=79)	Absolute difference (1-sided 97.5 CI) %	
Excellent rate (%)	75/79(94.94)	79/79(100)	-5.06 (-9.96 to -∞)	

For the individual variables of intubation conditions, a statistically significant between-group difference was found in the response to intubation ($P < 0.001$, Table 3). Diaphragmatic movement appeared during endotracheal tube passage. Three patients in Group Miva who experienced sustained diaphragmatic movement were treated with propofol 0.5 mg/kg immediately after intubation.

Table 3
Tracheal intubation condition according to Cooper's scale

Variables assessed	Miva (n = 79)	Rocu (n = 79)	P
Laryngoscopy			
Easy	77(97.5)	79(100)	0.155
Moderate	2(2.5)	0	
Difficult	0	0	
Impossible	0	0	
Vocal cords position			
Abducted	79(100)	79(100)	1
Moving	0	0	
Closing	0	0	
Closed	0	0	
Response to intubation			
No movement	58(73.4)	76(96.2)	< 0.001
Slight diaphragm movement	18(22.8)	3(3.8)	
Mild coughing	3(3.8)	0	
Severe coughing or bucking	0	0	
Overall rating			
Excellent	75(94.94)	79(100)	< 0.001
Good	4(5.06)	0	
Fair	0	0	
Poor	0	0	
Data are shown as number (%).			

ANOVA for MAP and HR revealed statistically significant time effects in MAP and HR. No group effect was found for either variable. The interaction effect (group × time) was significant for MAP but not for HR (Table 4). Analysis of MAP at each time point showed that in both groups, there was no difference in baseline MAP (101.4 ± 14.9 mmHg vs. 101.8 ± 13.5 mmHg, P = 0.841) or baseline HR (74.2 ± 12.5 bpm vs. 73.9 ± 13.8 bpm, P = 0.914). At T3, the MAP of Group Miva was significantly lower than that of Group Rocu (87.8 ± 14.4 mmHg vs. 94.0 ± 14.1 mmHg, P = 0.002). At T10, the between-group difference in HR (69.7 ± 14.1 bpm in Group Miva vs. 74.5 ± 15.9 bpm in Group Rocu) was statistically significant (P = 0.045). At all other time points, the between-group difference in MAP and HR was statistically

insignificant (Fig. 2A–2B). A total of 20 (25.3%) and 27 (34.2%) patients needed additional vasopressors during induction in Group Miva and Group Rocu, respectively, with no statistically significant difference (P = 0.223).

Table 4
Results of repeated measures ANOVA for MAP and HR variables

Variables	Time			Group			Interaction		
	F	df	P	F	df	P	F	df	P
MAP	34.735	10	< 0.001	0.343	1	0.559	2.414	10	0.011
HR	6.372	10	< 0.001	0.758	1	0.385	1.503	10	0.144
ANOVA, analysis of variance; HR, heart rate; MAP, mean arterial pressure.									

There was no statistically significant difference in the RSII time, tracheal intubation time or adverse reactions, including newly developed arrhythmia and wheezing, between the two groups (P > 0.05). However, more patients in Group Miva suffered from flushing on the upper chest than those in Group Rocu [18 (22.8%) vs 2 (2.5%), P < 0.001].

Discussion

Whether mivacurium is suitable for RSII is still debated due to unsatisfactory tracheal intubation conditions and the high incidence of hypotension related to histamine release. Dieck *et al.* [20] investigated intubation conditions after anesthesia induction 3 min after mivacurium administration with 0.2 mg/kg mivacurium, 2.5 mg/kg propofol and 1 μg/kg remifentanil, which led to poor intubating conditions, resulting in early study termination. Our randomized clinical trial demonstrated noninferiority for the rate of excellent intubation conditions of a modified RSII protocol employing 0.25 mg/kg mivacurium in divided doses with that of 0.9 mg/kg rocuronium in the context of propofol, remifentanil, lidocaine and ephedrine induction protocols. Mivacurium provided an excellent intubation condition rate of 94.94%, a clinically acceptable intubation condition rate of 100%, and hemodynamic fluctuation comparable to rocuronium 0.9 mg/kg.

Numerous scoring systems evaluating intubating conditions were available. Although other rating scales were at variance with Cooper's scale introduced in 1992, a total score of 9 in our study equals 'excellent' in Ali's study of 56% and Pino's study of 63%, and our induction regimen provided a higher rate of 72.15% than those reported by previous studies investigating the intubation condition in 90 s after mivacurium 0.25 mg/kg [21–23]. Modifications to the induction regimen might contribute to the improvement of intubation conditions. Intravenous lidocaine 1.5 mg/kg was given two minutes prior to intubation to blunt the sympathetic response and cough reflex to laryngoscopy [24–26]. Remifentanil, a fast onset ultrashort-acting narcotic, is particularly useful for intubation. Evidence has shown that propofol 2 to 2.5 mg/kg followed by a high dose of remifentanil 3 to 5 μg/kg provides good to excellent intubating

conditions at 1 to 2.5 minutes after induction without NMBA administration [26, 27]. We used remifentanil 1 μg/kg to facilitate intubation [28]. Pretreatment with ephedrine 70 μg/kg before rapid tracheal intubation improves intubating conditions [29]. Ephedrine creates superior intubation conditions one minute after anesthesia induction using propofol and rocuronium without extra side effects, and a low dose (i.e. 70–100 μg/kg) is recommended as the possible optimal dose [30]. According to a literature search, no clinical studies have regarded the effect of ephedrine pretreatment on intubation conditions after mivacurium. Therefore, we incorporated 6 mg ephedrine priming in our protocol to counteract the hypotension commonly seen after mivacurium administration.

In consideration of the short-acting property of mivacurium, we aimed to probe an induction regimen with mivacurium to find an alternative choice for short-duration surgeries without the availability of sugammadex. Current evidence showed that 0.9 mg/kg, 1.0 mg/kg or 1.2 mg/kg rocuronium administration provided statistically insignificant intubation conditions compared to 1 mg/kg succinylcholine, and a high dose of rocuronium was related to prolonged paralysis [9, 31]. Thus, we chose 0.9 mg/kg rocuronium in the control group. We chose the recommended maximum dose of mivacurium 0.25 mg/kg in divided doses and performed intubation 90 s after the 1st dose of mivacurium. All intubation was completed successfully without any episodes of hypoxia or hypoxemia.

Histamine release is another disadvantage of mivacurium [32]. Divided dose injection [22] and slow speed of injection over 30–60 s vs. 10–15 s during 0.25 mg/kg loading dose administration [13] could mitigate the hypotension due to histamine release. In this study, flushing on the upper chest was significantly more frequent in Group Miva than in the Rocu group.

We chose 90 s after the initial dose of mivacurium as the timing for intubation attempt. The onset time of NMBAs varies in different muscle groups. Hemmerling *et al*. employed noninvasive electrodes to investigate the onset time of 0.2 mg/kg mivacurium on different muscle groups [33]. The respiratory muscle group (laryngopharyngeal muscle and diaphragm) was found to reach the maximum block at 80–90 s, and the adductor pollicis muscle was at over 180 s. Although 60 s was usually considered the standard time point for the comparison study of other NMBAs to succinylcholine, taking the above findings into consideration, we chose 90 s as the trigger for intubation. A number of studies on mivacurium application in RSII also took 90 s as the time point of attempted intubation after NMBA administration [21–23].

One of the limitations of our study was that we did not employ quantitative neuromuscular monitoring. The adductor pollicis muscle is most commonly used to monitor the induced twitch response, and T1 inhibition at 95% is defined as the onset time of muscle relaxant [34]. Ali HH *et al*. [22] found that the TOF response reached 0 in only 2% of all patients during tracheal intubation with mivacurium. According to the package insert of mivacurium, when using a stimulator to monitor the onset of neuromuscular block of mivacurium, all four twitches of the TOF response may be present, with little or no fade, at the times recommended for intubation. As mivacurium is metabolized by butyrylcholinesterase, the plasma concentration of mivacurium might have dropped in laryngopharyngeal muscles and the diaphragm,

which have abundant blood supplies when the maximum blockade is reached in the adductor pollicis muscle. Since muscle relaxant monitoring is still not a routine clinical practice in many institutions due to resource shortages, an induction regimen with a fixed time interval for intubation will be easier to use. However, objective monitoring of neuromuscular blockage is crucial for determining the action of NMBAs. Objective neuromuscular monitoring should be used in future studies. Another limitation of this study was that it was a simulated RSII. Since even slight diaphragmatic movement could be disastrous for full stomach patients and histamine release might endanger critically ill patients, we chose ASA grade I–II and nothing by mouth (NPO) patients receiving elective surgery as study subjects.

It is premature to extrapolate our protocol to emergency settings. A total of 26.6% of the patients in Group Miva exhibited slight diaphragm movement or mild coughing, which might be catastrophic for full stomach patients. It is still worth further investigating whether strategies such as a high dose of ephedrine and/or magnesium priming [35] could improve the rate of excellent intubation conditions of mivacurium and the dose effect of ephedrine on the neuromuscular onset time and hemodynamic profiles to optimize the anesthesia induction protocol in future studies.

However, our induction regimen provided a rate of excellent and clinically acceptable intubation conditions higher than previous studies using the same dose of mivacurium and identical evaluation tools. Under current circumstances, we can recommend our induction regimen to patients who are NPOs, especially for patients receiving short-duration surgery since mivacurium is the only available short-acting nondepolarizing NMBA.

Conclusions

Mivacurium 0.25 mg/kg in divided doses in rapid sequence induction with lidocaine, ephedrine, propofol and remifentanil, compared with rocuronium 0.9 mg/kg, provided a noninferior rate of excellent intubation conditions 90 s after the initial dose of NMBAs. The mivacurium intubation regimen provided hemodynamic variations comparable to rocuronium.

Abbreviations

RSII: Rapid sequence induction and intubation; NMBAs: Nondepolarizing neuromuscular blocking agents; TOF: Train-of-four; NPO: Nothing by mouth; ASA: American Society of Anesthesiologists; ANOVA: Analysis of variance

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Research Ethics Board of Zhongshan Hospital, Fudan University (B2020-082). All patients signed informed consent forms before recruitment in accordance with the Helsinki Declaration.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the [mendeley data] repository, [Li, Yuxin (2022), “Rapid sequence induction and intubation with a divided dose of mivacurium compared with rocuronium: a randomized, controlled, non-inferiority trial Running title: RSII with mivacurium vs. rocuronium”, Mendeley Data, V2, doi: 10.17632/9d6vt645ty.2]

Competing interests

The authors certify that they have no competing interests.

Funding

This research was funded by the Fund for Young Scholars of Zhongshan Hospital, Fudan University (Fellowship Fund-010) and Shanghai Municipal Health Commission Clinical Research Program (202040177).

Authors’ contributions

ZXG and LYX have made substantial contributions to the conception and design of the manuscript. MYM, DF and SYC acquired, analysed and interpreted the data. All authors have participated in drafting the manuscript. ZXG revised it critically. All authors read and approved the final version of the manuscript.

Acknowledgments

We thank Hao CHEN, Department of Preventive Medicine, School of Public Health, Fudan University, for assisting in the statistical analysis and proofreading the manuscript.

References

1. Stollings JL, Diedrich DA, Oyen LJ, Brown DR. Rapid-Sequence Intubation: A Review of the Process and Considerations When Choosing Medications. Annals of Pharmacotherapy. 2013;48(1):62–76.
2. El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. Anesth Analg. 2010;110(5):1318–25.
3. Fuchs-Buder T, Schmartz D. The never ending story or the search for a nondepolarising alternative to succinylcholine. Eur J Anaesthesiol. 2013;30(10):583–4.
4. Girard T. Pro: rocuronium should replace succinylcholine for rapid sequence induction. Eur J Anaesthesiol. 2013;30(10):585–9.

5. Schreiber JU. Con: succinylcholine should not be replaced by rocuronium for rapid sequence induction. Eur J Anaesthesiol. 2013;30(10):590–3.
6. Perry J, Lee J, Sillberg V, Wells GJCDSR. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2008(2):CD002788.
7. Meek T. Traditional rapid sequence induction is an outmoded technique for Caesarean section and should be modified. Opposed. Int J Obstet Anesth. 2006;15(3):229–32.
8. Magorian T, Flannery K, Miller RJA. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Anesthesiology. 1993;79(5):913–8.
9. Tran D, Newton E, Mount V, Lee J, Mansour C, Wells G, et al. Rocuronium vs. succinylcholine for rapid sequence intubation: a Cochrane systematic review. Anaesthesia. 2017;72(6):765–77.
10. Lee S, Ro YJ, Koh WU, Nishiyama T, Yang HS. The neuromuscular effects of rocuronium under sevoflurane-remifentanil or propofol-remifentanil anesthesia: a randomized clinical comparative study in an Asian population. BMC Anesthesiol. 2016;16(1):65.
11. Han T, Kim H, Bae J, Kim K, Martyn JA. Neuromuscular pharmacodynamics of rocuronium in patients with major burns. Anesth Analg. 2004;99(2):386–92.
12. Sorensen MK, Bretlau C, Gatke MR, Sorensen AM, Rasmussen LS. Rapid sequence induction and intubation with rocuronium-sugammadex compared with succinylcholine: a randomized trial. Br J Anaesth. 2012;108(4):682–9.
13. Savarese JJ, Ali HH, Basta SJ, Embree PB, Scott RP, Sunder N, et al. The clinical neuromuscular pharmacology of mivacurium chloride (BW B1090U). A short-acting nondepolarizing ester neuromuscular blocking drug. Anesthesiology. 1988;68(5):723–32.
14. Ostergaard D, Viby-Mogensen J, Rasmussen SN, Gatke MR, Varin F. Pharmacokinetics and pharmacodynamics of mivacurium in patients phenotypically homozygous for the atypical plasma cholinesterase variant: effect of injection of human cholinesterase. Anesthesiology. 2005;102(6):1124–32.
15. 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(3):269–73.
16. Platts-Mills TF, Campagne D, Chinnock B, Snowden B, Glickman LT, Hendey GW. A comparison of GlideScope video laryngoscopy versus direct laryngoscopy intubation in the emergency department. Acad Emerg Med. 2009;16(9):866–71.
17. McCourt KC, Salmela L, Mirakhur RK, Carroll M, Makinen MT, Kansanaho M, et al. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. Anaesthesia. 1998;53(9):867–71.
18. Andrews JI, Kumar N, van den Brom RH, Olkkola KT, Roest GJ, Wright PM. A large simple randomized trial of rocuronium versus succinylcholine in rapid-sequence induction of anaesthesia along with propofol. Acta Anaesthesiol Scand. 1999;43(1):4–8.
19. Shukla A, Misra S. Ease of intubation: A randomized, double-blind study to compare two doses of rocuronium bromide for endotracheal intubation. Anesth Essays Res. 2016;10(3):512–5.

20. Dieck T, Steffens J, Sander B, Krauss T, Hoffmann N, Leister V, et al. Propofol, remifentanil and mivacurium: fast track surgery with poor intubating conditions. Minerva Anestesiol. 2011;77(6):585–91.
21. Geldner GF, Schweiger S, Hetz W, Rugheimer E. Intubation conditions and circulatory effects 90 seconds after a divided mivacurium dose with three different TIVA induction methods. Anaesthesist. 1995;44(5):334–8.
22. Ali H, Lien C, Witkowski T, Brull S, Stout R, Bartkowski R, et al. Efficacy and safety of divided dose administration of mivacurium for a 90-second tracheal intubation. J Clin Anesth. 1996;8(4):276–81.
23. Pino RM, Ali HH, Denman WT, Barrett PS, Schwartz A. A comparison of the intubation conditions between mivacurium and rocuronium during balanced anesthesia. Anesthesiology. 1998;88(3):673–8.
24. Aouad MT, Sayyid SS, Zalaket MI, Baraka AS. Intravenous lidocaine as adjuvant to sevoflurane anesthesia for endotracheal intubation in children. Anesth Analg. 2003;96(5):1325–7.
25. Davidson JA, Gillespie JA. Tracheal intubation after induction of anaesthesia with propofol, alfentanil and i.v. lignocaine. Br J Anaesth. 1993;70(2):163–6.
26. Yukioka H, Hayashi M, Terai T, Fujimori M. Intravenous lidocaine as a suppressant of coughing during tracheal intubation in elderly patients. Anesth Analg. 1993;77(2):309–12.
27. Trabold F, Casetta M, Duranteau J, Albaladejo P, Mazoit JX, Samii K, et al. Propofol and remifentanil for intubation without muscle relaxant: the effect of the order of injection. Acta Anaesthesiol Scand. 2004;48(1):35–9.
28. Albertin A, Casati A, Deni F, Danelli G, Comotti L, Grifoni F, et al. Clinical comparison of either small doses of fentanyl or remifentanil for blunting cardiovascular changes induced by tracheal intubation. Minerva Anestesiol 2000;66(10):691–6.
29. Gopalakrishna MD, Krishna HM, Shenoy UK. The effect of ephedrine on intubating conditions and haemodynamics during rapid tracheal intubation using propofol and rocuronium. Br J Anaesth. 2007;99(2):191–4.
30. Sun R, Tian JH, Li L, Tian HL, Jia WQ, Yang KH, et al. Effect of ephedrine on intubating conditions created by propofol and rocuronium: a meta-analysis. J Evid Based Med. 2012;5(4):209–15.
31. Tran DT, Newton EK, Mount VA, Lee JS, Wells GA, Perry JJ. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2015(10):CD002788.
32. Bishop M, O'Donnell J, Salemi JJAA. Mivacurium and bronchospasm. Anesth Analg. 2003;97(2):484–5.
33. Hemmerling TM, Schmidt J, Hanusa C, Wolf T, Schmitt H. Simultaneous determination of neuromuscular block at the larynx, diaphragm, adductor pollicis, orbicularis oculi and corrugator supercilii muscles. Br J Anaesth. 2000;85(6):856–60.
34. Fuchs-Buder T, Claudius C, Skovgaard LT, Eriksson LI, Mirakhur RK, Viby-Mogensen J, et al. Good clinical research practice in pharmacodynamic studies of neuromuscular blocking agents II: the Stockholm revision. Acta Anaesthesiol Scand. 2007;51(7):789–808.

35. Kim MH, Oh AY, Jeon YT, Hwang JW, Do SH. A randomised controlled trial comparing rocuronium priming, magnesium pre-treatment and a combination of the two methods. Anaesthesia. 2012;67(7):748–54.

Figures

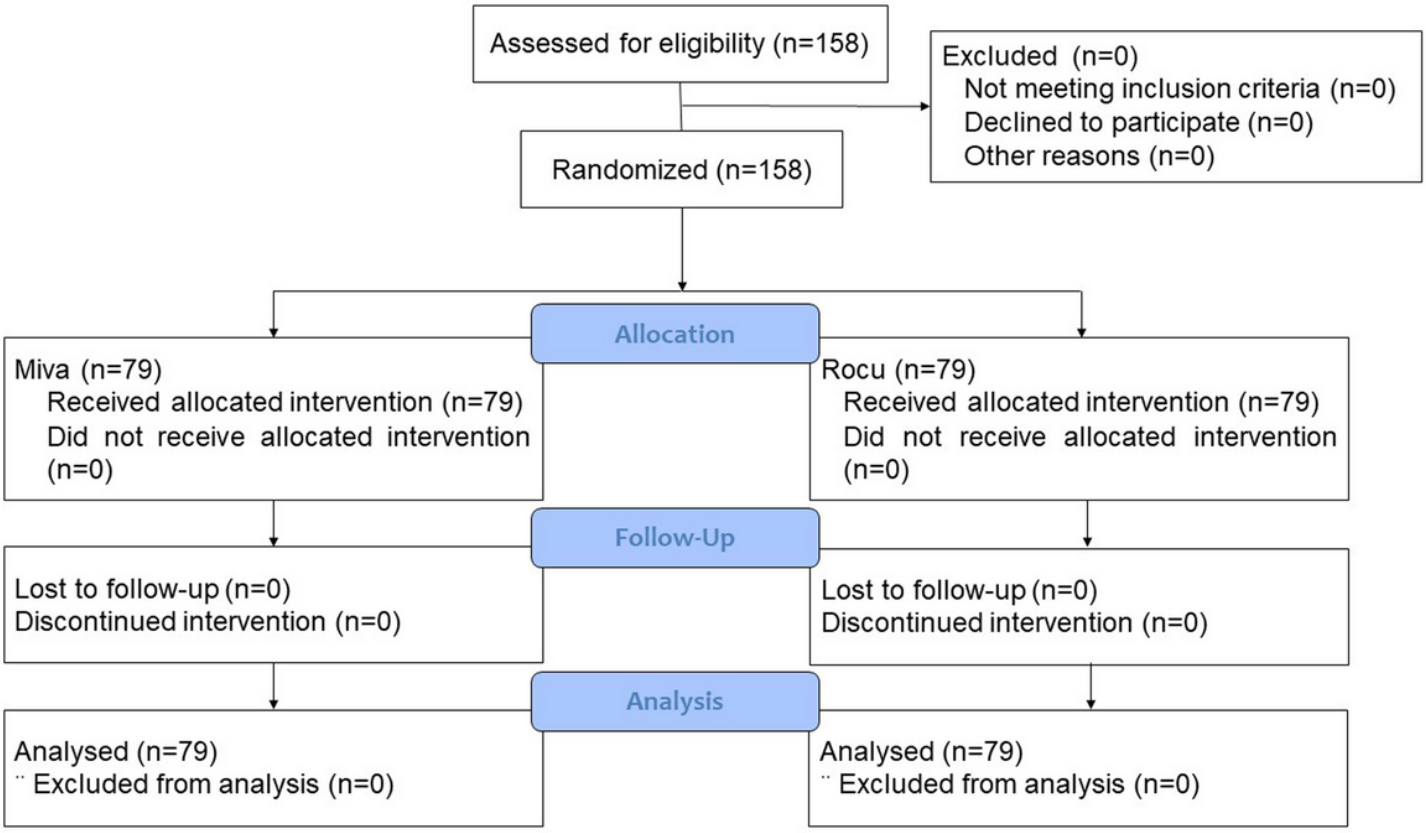


Figure 1

Study Flowchart

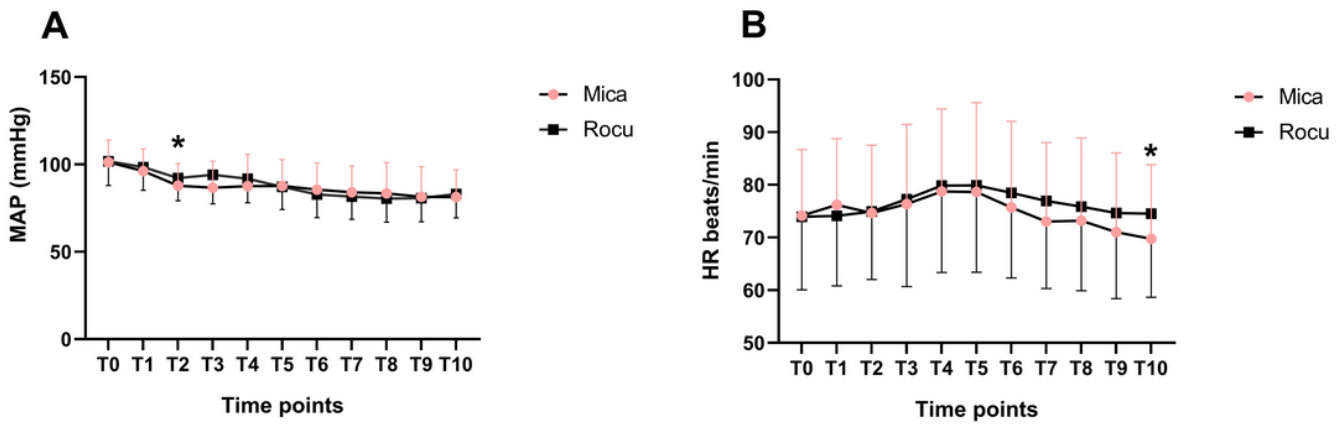


Figure 2

Group MAP (**A**) and HR (**B**) changes during the induction period. T0: prior to induction, T1-T10: 1-minute interval at 1 to 10 min after induction, data are represented as the means ± SD. *P<0.05 for between group comparison. HR, heart rate; MAP, mean arterial pressure.