Original Article

The Effect of Rocuronium Priming Dose Based on Actual Versus Corrected Body Weight in Modified Rapid Sequence Intubation

A Postaci, NN Ozcan, N Aydin- Guzey, UC Ersoy

Department of Anesthesiology and Reanimation, Ankara City Hospital, Health Application and Research Center, University of Health Sciences, Turkey

Abstract

Background: Rapid sequence intubation (RSI) is a technique that allows patients to be quickly intubated and have the airway secured. **Aims:** The purpose of this study was to investigate the effect of rocuronium priming and intubation dose calculated according to actual body weight (ABW) or corrected body weight (CBW) on the neuromuscular block and intubation quality in rapid sequence induction and intubation (RSII). **Patients and Methods:** This prospective randomized, double-blind study was conducted on a total of 60 patients randomized into two groups using the closed-envelope method between January 2021 and December 2021, with 30 individuals in each group. In group 1, CBW was used with the formula to calculate the neuromuscular blocking drug (NMBD) dose. The ABW of patients was used to calculate the NMBD dose in group 2. **Results:** The data of 50 female patients who underwent group 1 (CBW, n = 25) and group 2 (ABW, n = 25) were analyzed. Age, weight, height, body mass index (BMI), quality of laryngoscopy, post-priming side effects, mean arterial pressure (MAP), and heart rate (HR) values did not differ across the groups. When train-of-four (TOF) values, priming and intubation dose, and laryngoscopy time were compared, a statistically significant difference was found between the two groups of TOF count (TOF C) 1 (the duration of action). **Conclusion:** This study suggests that the application of rocuronium priming and intubation dose according to CBW in RSII, especially during the pandemic, provided similar intubation conditions as the application according to ABW, while its shorter duration of action shows that it can be preferred, especially in short-term surgical cases.

Keywords: *Priming, rapid sequence intubation, rocuronium*

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Introduction

A rapid sequence induction of anesthesia and endotracheal intubation (RSII) involves the fast delivery of a neuromuscular blocking agent after an induction agent to establish optimal intubating conditions and minimize the time the airway is left unprotected.[1] The modified RSII was used in cases of hemodynamic instability and can be defined as using a hypnotic agent, an opioid agent for reducing airway reflexes and sedatives to induce amnesia and avoiding positive pressure ventilation before intubation. Rapid sequence intubation (RSI) indications include emergency surgery under general anesthesia, cesarean section, trauma patients, gastrointestinal pathology, gastroesophageal reflux disease, neurological or neuromuscular disease, patients with increased intra-abdominal pressure, airway management outside the operating room, and patients with coronavirus disease 2019 (COVID-19).[2-6] Nondepolarizing neuromuscular blocking drugs (NMBDs) should be used in high doses for RSI. Increasing the dose of the NMBDs can shorten the onset time but will result in a prolonged block.[7-9] The onset time of nondepolarizing

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Address for correspondence: Assoc. Prof. A Postaci, Birlik Mah. 435 Cd 42/4, 06610, Cankaya/Ankara/Turkey.
E-mail: aysunposta@yahoo.com

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NMBDs can be shortened by priming. This consists of the administration of a small, sub-paralyzing dose of the NMBD several minutes before administering a larger intubating dose. Particularly in surgical cases during the pandemic, general anesthesia and airway manipulations are aerosol-producing procedures that could infect healthcare workers. The goals of airway management during this period were to rapidly secure the airway on the first attempt and to reduce or eliminate aerosolization of respiratory secretions.[1,2,10,11]

The primary aim of this study was to investigate the effect of rocuronium priming and induction dose calculated according to actual body weight (ABW) or corrected body weight (CBW) on the neuromuscular block and intubation quality in modified RSII.

Materials and Methods

After obtaining the Ankara City Hospital ethics committee approval (E1-20-10939), and the approval of the patient consent, 60 female patients with an American Society of Anesthesiologists (ASA) status of 1–2, aged 18–65 years, who will undergo elective gynecologic oncologic surgery, and be intubated as orotracheal have been included in this prospective randomized, double-blind study between January 2021 and December 2021. Patients were randomly allocated, by sealed envelope randomization, to two groups of 30 patients each. In group 1, CBW was used to calculate the dose of NMBD. The formula is CBW = ideal body weight (IBW) + [actual body weight (ABW) – IBW] X 0.4. The ideal body weight was calculated by removing 106 cm from the height of the body.[11]

Those aged 65 and over, patients with ASA 3 and above, pregnant women, those at risk of malignant hyperthermia, anticipated difficult airways, evidence of neuromuscular, cardiovascular, respiratory, hepatic, or renal disease, those with body weight 100 kg and above, and those who did not agree to participate in this study were not included.

Exclusion criteria during the rapid sequence procedure were patient's refusal to preoxygenation, refusal to cooperate, laryngoscopy time longer than 20 seconds, modified Cormack–Lehane (CL) score of 3 and above, and complication developed during the intubation procedure.

In the operating room, routine monitoring of blood pressure, electrocardiogram, pulse oximetry (Aisys CS^2 GE anesthesia device), and body temperature was initiated. After monitoring, the patients were premedicated with intravenous midazolam of 1 mg and 100 mcg fentanyl 10 minutes before induction. Neuromuscular function was monitored with kinemyography electrodes of the Aisys CS^2 GE anesthesia device. Before the nerve stimulator electrodes were placed for neuromuscular monitoring, the skin was cleaned and wiped with alcohol. The negative electrode of the nerve stimulator was placed 2–3 cm. proximal to the skin fold formed when the wrist was flexed, over the ulnar nerve trace, and the positive electrode was placed 2–3 cm proximal to the negative electrode.

The body weights of all patients were measured before entering the operating room. The priming (0.06 mg/kg) and intubation (0.94 mg/kg) dose of the drug was calculated according to the group patient included and was diluted to a total volume of 10 ml with normal saline, and syringes were labeled as priming and intubation for each patient. The anesthesiologist responsible for the anesthesia procedures was blinded to group allocation.

Pre-Oxygenization with a well-fitting mask, standard supine position and anesthetic circuit, with a 10 L/min fresh gas flow, FiO_2 = 100% for 3 minutes (tidal volume method) before priming. Rocuronium 0.06 mg/kg (priming dose) was administered for priming 2.5 minutes before anesthesia induction in both groups. Two minutes after priming, the patients were questioned in terms of ptosis, blurred-double vision, and difficulty in swallowing and breathing. After the administration of lidocaine of 20 mg, propofol (2-2, 5 mg/kg), and before the administration intubating dose of rocuronium (0.94 mg/kg), automatic calibration of the device was done and the supramaximal current of stimulation was set. Train-of-four (TOF) stimuli at the supramaximal current were applied at 20-s interval. After spontaneous respiratory depression, patients in both groups were not ventilated with a mask until intubation (apneic oxygenation). Patients in both groups were intubated 45 seconds after the intubation dose of rocuronium using a Macintosh laryngoscope and a 7.5-mm internal diameter (ID) cuffed endotracheal tube. Anesthesia was maintained with end-tidal sevoflurane 1.7–2% + remifentanil 0.01–0.5 mcg/kg. This study is completed when TOF count (TOF C) 1 (the duration of action) occurs. The parameters checked for the study during the operation were as follows.

- Hemodynamic data: mean arterial pressure (MAP) and heart rate (HR) before and after induction and one and three minutes after intubation.
- TOF data: TOF ratio (TOFR) during intubation, time-to-TOF ratio 0, time to TOF C 1.
  Priming side effects: ptosis, blurred-double vision, and difficulty in swallowing and breathing.
- Laryngoscopy time: time until the laryngoscope is

placed in the mouth and the endotracheal tube is passed through the vocal cords.
- Revisited CL score.[12]
- Intubating conditions (quality of laryngoscopy).[13]

Statistical analysis

The sample size was calculated based on a previous study reported by CS Meyhoff *et al*.[14] In calculation, G Power 3.1.9. 2 Package program was used. Time to reappearance of T1 (min) values, it was calculated that a total of 44 patients, including at least 22 patients in each group, should be included in the d = 0.87 effect size, 80% power, and α = 0.05 error level. Mean standard deviation, median, and minimum and maximum values were given in descriptive statistics for continuous data, and percentage values were given in discrete data. The Shapiro–Wilk test was used to examine the conformity of continuous data to normal distribution. In the comparison of continuous data in two groups, Student's t-test was used for data showing normal distribution, and the Mann–Whitney U-test was used for data that did not fit a normal distribution. In the comparison of the measurements of the patients at different times, the analysis of variance (ANOVA) (repeated) was used in the data showing normal distribution, and the time of the difference was examined with the Bonferroni test. The Friedman test was used to compare data that did not fit normal distribution with measurements at different times. The timing of the difference was analyzed with the Friedman multiple comparison test. The Chi-square and Fisher's exact tests were used for group comparisons (cross tables) of nominal variables. IBM Statistical Package for the Social Sciences (SPSS) version 20 (Chicago, IL, USA) program was used in the evaluations, and a $P < 0.05$ was accepted as the statistical significance limit.

Results

In our study, 60 female patients were included. Ten patients were excluded from the study, and the data of 25 patients who underwent group 1 and 25 patients who underwent group 2 were analyzed [Figure 1]. No difference was found in the age, weight, height, BMI, quality of laryngoscopy, post-priming side effects, MAP, and HR values [Tables 1,3-5] of the two groups ($P > 0.05$, Tables 1-3). However, diaphragmatic movement to laryngoscopy was observed in three patients in the ABW group, while it was observed in seven patients in the CBW group. Post-priming side effects were observed in seven patients in the ABW group and three patients in the CBW group. When TOF values, priming and intubation dose, and laryngoscopy time were compared, a statistically significant difference was found between the two groups of TOF C 1 [Table 2].

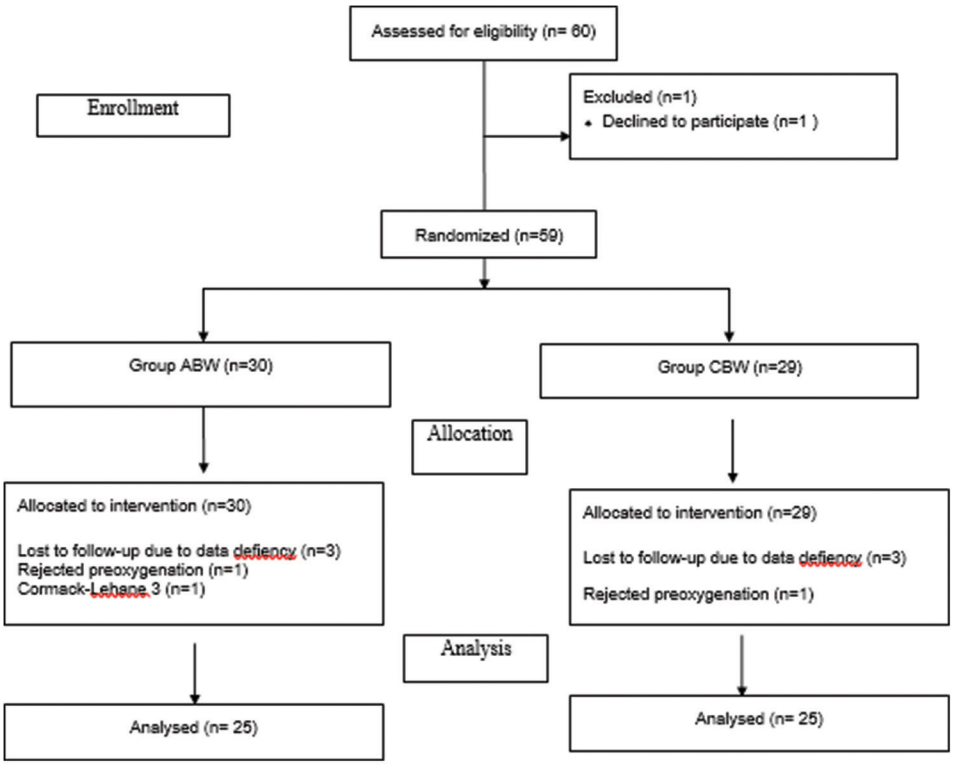

Figure 1: Research flowchart

Table 1: Demographic data of patients

	Total Mean±SD Median (Min-Max)	CBW (*n*=25) Mean±SD Median (Min-Max)	ABW (*n*=24) Mean±SD Median (Min-Max)	*P*
Age (year)	46.45±9.46 48 (23-63)	44.08±10.00 45 (25-63)	48.92±8.38 51 (23-58	0.074*
Weight (kg)	74.98±11.95 74 (54-98)	75.16±12.11 73 (58-98)	74.79±12.04 74.5 (54-95)	0.916*
Height (cm)	160.41±3.80 160 (154-172)	161.04±3.36 160 (156-168)	159.75±4.19 159 (154-172)	0.240*
BMI (kg/m^2)	29.18±4.43 29 (21-37)	28.94±4.59 27.6 (23-37)	29.42±4.35 30 (21-37)	0.709*

*P>0.05 not significantly different with Student's t-test

Table 2: Neuromuscular block value, laryngoscopy time, rocuronium priming, and induction dose in the two groups

	Total (*n*=49) Mean±SD Median (Min-Max)	CBW (*n*=25) Mean±SD Median (Min-Max)	ABW (*n*=24) Mean±SD Median (Min-Max)	*P*
Rocuronium priming dose (mg)	4.15±0.69 4 (3.2-6.0)	3.76±0.37 3.5 (3.2-4.5)	4.56±0.72 4.5 (3.3-6.0)	0.001**
Rocuronium intubation dose (mg)	64.84±10.22 62 (51-89)	59.72±5.17 58 (51-68.5)	70.18±11.49 69.75 (51-89)	0.001**
TOF ratio (%) during intubation	36.73±17.35 40 (0-65)	37.56±16.61 43 (0-65)	35.87±18.41 40 (0-60)	0.738
TOF ratio 0% time (sec)	135.18±46.85 135 (44-240)	143.56±44.35 140 (50-223)	126.46±48.71 123 (44-240)	0.205
TOF count 1 (min)	52.27±13.30 51 (26-90)	47.36±9.88 47 (26-62)	57.38±14.63 56 (37-90)	0.007*
Laryngoscopy time (sec)	13.08±2.70 13 (9-20)	13.92±2.79 14 (9-20)	12.21±2.35 12 (9-18)	0.025*

*P<0.05 significantly different with Student's t-test, **P<0.05 significantly different with Mann–Whitney U-test

Table 3: Patients intubating conditions, revisited Cormack–Lehane scores, and effect of priming doses

	Total		CBW (*n*=25)		ABW (*n*=24)		*P*
	n	%	*n*	%	*n*	%	
Intubating condition							
Excellent	39	79.6	18	72	21	87.5	0.289*
Good	10	20.4	7	28	3	12.5	
Priming side effects							
No	39	79.6	22	88	17	70.8	0.171*
Yes	10	20.4	3	12	7	29.2	
Revisited Cormack–Lehane score							
1	24	49	13	52	11	45.8	0.523*
2a	16	32.7	9	36	7	29.2	
2b	9	18.4	3	12	6	25	

*P>0.05 no significantly different with Fisher's exact test

Discussion

In our study, rocuronium priming and intubation dose administration according to ABW or CBW did not cause any difference in intubation quality and TOF values. However, a difference was observed in the duration of action (TOF C 1). The time of TOF C 1 was longer in the ABW group.

High doses of rocuronium are usually recommended, especially when tracheal intubation is required quickly. The priming technique with rocuronium has been

Table 4: Heart rate of the patient during the study period

	CBW (*n*=25) Mean±SD Median (Min-Max)	ABW (*n*=24) Mean±SD Median (Min-Max)	*P*
BI HR	82.76±14.55 80 (57-120)	79.14±10.96 81 (61-99)	0.335*
AI HR	84.16±12.60 83 (64-107)	81.00±11.94 80 (58-109)	0.373*
Int+1 HR	94.08±13.89 92 (71-130)	91.67±16.89 92 (55-118)	0.587*
Int+3 HR	88.56±11.56 86 (72-112)	86.29±14.58 86.5 (54-110)	0.548*
P	0.001**	<0.001**	

HR: heart rate, BI: before induction, AI: after induction, Int+1: 1 min after intubation, Int+3: 3 min after intubation. *: $P>0.05$ no significantly different (Student's *t*-test), **: $P<0.05$ significantly different [analysis of variance (ANOVA) (repeated)]

Table 5: Mean arterial pressure of patient during the study period

	CBW (*n*=25) Mean±SD Median (Min-Max)	ABW (*n*=24) Mean±SD Median (Min-Max)	*P*
BI MAP	105.16±12.82 107 (79-139)	100.54±12.67 96 (78-126)	0.211
AI MAP	91.92±15.27 92 (63-137)	85.92±8.71 85 (71-104)	0.100
Int+1 MAP	109.20±23.02 103 (73-170)	101.83±20.01 99.5 (66-140)	0.239
Int+3 MAP	94.36±14.77 90 (73-139)	86.83±11.58 88.5 (68-113)	0.054
P	<0.001**	<0.001**	

MAP: mean arterial pressure, BI: before induction, AI: after induction, Int+1: 1 min after intubation, Int+3: 3 min after intubation. *: $P<0.05$ significantly different (Student's *t*-test), **: $P<0.05$ significantly different [analysis of variance (ANOVA) (repeated)]

investigated in several studies, and a shortening of the onset of action has been demonstrated.[8,9] Studies have shown that the priming technique with rocuronium accelerates the onset of action compared with a single intubation dose.[7-9] We carried out our study by adding the priming technique to the RSII technique to provide intubation in a short time during the pandemic period.

Leykin *et al*.[9] conducted a study with 60 patients divided into four groups of 15 each. In the priming groups, they administered 0.04 mg/kg priming dose of rocuronium before ketamine or thiopentone induction; then, after ketamine or thiopentone induction, they administered 0.4 mg/kg rocuronium. Before ketamine or thiopentone induction, no priming was used in the control groups. In priming groups, intubation quality was found better. The combination of ketamine and priming improved the intubating conditions more than thiopentone and priming, or ketamine alone. In our study, anesthesia induction was performed with fentanyl 100 mcg and propofol 2–2.5 mg/kg in both groups, and no difference was found between the mean TOFR rates and intubating conditions of the two groups during the intubation procedure. Propofol is the intravenous (IV) anesthetic agent that reduces upper airway resistance the most.[15] Therefore, we think that it contributed to our difference in the intubation quality of the two groups.

Bock *et al*.[10] investigated the effects of the priming technique on rocuronium in 84 patients. They divided the patients into four groups: 0.45 mg/kg of rocuronium was administered 1 minute after the placebo saline injection in group 1; in group 2, 0.405 mg/kg of rocuronium was administered 1 minute after a priming dose with 0.045 mg/kg of rocuronium; 0.6 mg/kg of rocuronium was given 1 minute after placebo saline injection in group 3; and a priming dose of 0.06 mg/kg of rocuronium and 1 minute later 0.54 mg/kg of rocuronium were administered to group 4. The onset time was significantly shorter in group 2 (92.5 ± 24 sec) compared with group 1 (122.5 ± 54 sec). Likewise, the onset time of rocuronium was significantly shorter in group 4 (55 ± 17 sec) than in group 3 (85 ± 25 sec). Priming with rocuronium significantly shortened the onset of the T-95 effect; however, no difference was observed in terms of intubation quality in all four groups. In a recent study, Puri *et al*.[16] were divided to the patients into two groups and administered 0.06 mg/kg of rocuronium for priming and after 3 minutes 0.56 mg/kg of rocuronium was applied as an intubation dose in one of the groups. The same procedure was applied to the second group by injecting physiological saline instead of rocuronium for the priming dose. Excellent intubation conditions were achieved in 97% of patients in both groups.

Yavaşcaoğlu *et al*.[17] aimed to compare two different priming doses and priming intervals of rocuronium with a single dose of rocuronium in a study conducted with 75 patients and examined the effects of these on the onset of action times and intubation conditions. In this study, patients were divided into five groups; 0.06 mg/kg priming dose of rocuronium and 0.54 mg/kg of rocuronium 2 minutes later were administered in group I; 0.10 mg/kg priming dose of rocuronium followed by 0.5 mg/kg of rocuronium 2 minutes later was given to group II; 0.06 mg/kg priming dose of rocuronium and 0.54 mg/kg of rocuronium 3 minutes later were administered in group III; 0.10 mg/kg priming dose of rocuronium followed by

0.50 mg/kg of rocuronium 3 minutes later was given to group IV; and 3 minutes later after placebo priming with saline, 0.6 mg/kg priming dose of rocuronium was administered in group V. Another study by Schultz *et al*.[18] found durations of action of 37 min at 0.6 mg/kg and 73 min at 1.2 mg/kg when rocuronium was administered in nonobese patients.

Ideally, priming should accelerate neuromuscular blockade, while neuromuscular blockade should not cause side effects. While the maximum safe priming dose of a nondepolarizing relaxant should be equal to 10% of the effective dose, higher doses are not safe.[19] The priming dose used in our study was not more than 10% of the ED95 dose as in Donati's recommendations. Furthermore, in our study, although a statistically significant difference was found between the mean priming doses of two different groups, the difference between the mean priming doses was less than 1 mg. This result may be the reason why we did not detect any difference in priming side effects between the two groups. In a study by Schmidt *et al*.,[20] priming with 0.06 mg/kg dosage of rocuronium was investigated and no side effects were detected. In our study, also 0.06 mg/kg of rocuronium was used as the priming dose and although there was a difference between the priming doses of the two groups we did not observe any statistically significant difference between the two groups in terms of neuromuscular blocking symptoms (e.g., heavy eyelids, blurred vision, and difficulty in swallowing).

The secondary endpoint of our study was the duration of action in the two groups. Leykin *et al*.[21] studied a rocuronium dose of 0.6 mg/kg based on ideal body weight or real body weight in morbidly obese patients and found that the duration of action was 55.5 min when rocuronium was administered based on real body weight and 22.3 min when administered based on ideal body weight. However, Meyhoff *et al*.[14] used a rocuronium dose of 0.6 mg/kg in intubation without priming based on IBW or CBW in morbidly obese patients and found that the duration of action was shorter (21 min) in the IBW group than in the CBW group (28–31 min). In our study, the duration of action was 47,3 min administered based on CBW and 57,3 min when administered based on ABW, confirming that dosing based on CBW resulted in a shorter duration of action than dosing based on ABW. No further improvement in intubation conditions was observed at 45 s with the administration of rocuronium dose according to ABW versus CBW.

Although there was no statistical significance in the quality of intubation in our study, the fact that we detected diaphragmatic movement against intubation in three patients in the ABW group and seven patients in the CBW group may be the limitation of our study. We think this may be clinically important. Therefore, we think that further studies might be needed by increasing the sample size and including male patients due to possible gender difference.

In conclusion, the findings of this study suggest that applying a priming and intubation dose of rocuronium based on the patient's CBW in RSII, especially during the pandemic period, provides similar intubation conditions compared with the application based on ABW. Additionally, the shorter duration of the influence of CBW-based applications suggests that they may be preferred in short-term surgical cases.

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Conflicts of interest

There are no conflicts of interest.

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