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Effect of Priming Dose Rocuronium Use on Intubation Quality and Duration

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ABSTRACT

Introduction: This study aimed to investigate the effects of priming dose application with rocuronium, considering ideal body weight (IBW), on intubation quality and duration during the use of rocuronium and vecuronium as neuromuscular blockers.

Methods: Our study was conducted at University of Health Sciences Turkey, Haseki Training and Research Hospital on 60 patients who were in the American Society of Anesthesiology I-II group, aged between 20-70, Mallampati I-II-III, body mass index between 20-35, and planned for medium-term elective surgical intervention. The patients were randomly divided into four groups. Group I was administered a priming dose of rocuronium 0.06 mg/kg and rocuronium 0.54 mg/kg following anesthesia induction, and group II was administered a priming dose of saline and 0.1 mg/kg vecuronium following anesthesia induction, and group III was administered a priming dose of rocuronium 0.06 mg/kg and vecuronium 0.1 mg/kg following anesthesia induction, and group IV was administered a saline priming dose and rocuronium 0.6 mg/kg following anesthesia induction. Priming and intubation doses of neuromuscular blockers were calculated according to the IBW of the patients. In addition to routine monitoring, the TOF-Guard device was used for neuromonitoring, and the T95 onset time [the time from the end of the muscle relaxant injection until maximum neuromuscular block (95%) was achieved] was recorded. The same person intubated the patients when the TOF value decreased to 5% or below. The quality of endotracheal intubation was assessed using the Clarke and Mirakhur scale. Statistical analyses were performed using SPSS 18.0 software.

Results: The effect onset time of group 1, in which rocuronium was used as a neuromuscular blocker and priming application, was significantly shorter than that of group 4, in which bolus dose rocuronium was used. Although the effect onset time of vecuronium in group 3, primed with rocuronium, was shorter than that in group 2, where the bolus dose of vecuronium was used, the difference was not observed to be significant.

Conclusion: As a result, it was concluded that priming dose application with rocuronium accelerates the neuromuscular block created by rocuronium, has no significant effect on the rate of neuromuscular block created by vecuronium, and provides excellent intubation conditions. It provides fast, high quality, and safe intubation in rapid induction required cases.

Keywords: Priming dose application, intubation quality, rocuronium

Introduction

Endotracheal intubation is one of the most critical periods in anesthesia applications in terms of hypoxia and pulmonary aspiration, and it must be completed as soon as possible to ensure airway patency (1-3). Neuromuscular blocker drugs have become an indispensable part of anesthesia practices today, allowing surgical intervention to be performed more safely, comfortably, and in a shorter time by creating a suitable working environment in addition to rapid and atraumatic endotracheal intubation. An ideal neuromuscular blocker should be potent, rapid, and short-acting, should not be accumulative, should not have cardiovascular side effects, should disappear completely in a short time, should not release histamine, should be antagonized by anticholinesterases, should be broken down into pharmacologically inactive metabolites, and should have a non-depolarizing mechanism of action (4). Non-depolarizing blockers can provide reliable intubation in only 2-3 min (5). In cases where rapid intubation is required, succinylcholine, a depolarizing blocker, is used because it acts within 10-30 seconds. However, it has serious side effects such as triggering hyperkalemia, bradycardia, ventricular arrhythmia, and malignant hyperthermia, as well as muscle pain due to fasciculations caused by succinylcholine (6). Its routine use is controversial because of reported cases of serious arrhythmia and cardiac arrest (7). In recent studies, different methods have been tried using nondepolarizing blockers in endotracheal intubations and to shorten this time (8-11).

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The "priming principle", which has become widely used in recent years, is a method that aims to provide a faster effect when the actual drug dose is applied by reducing the sensitivity of acetylcholine receptors by administering non-depolarizing blockers in subparalytic doses (12). In this technique, a small portion of the intubation dose of the neuromuscular blocking drug is administered before the induction of anesthesia, and the remaining main intubation dose is administered after a certain time interval. This initial dose applied was called "priming dose" by Foldes (13). This application accelerates the effect onset time of neuromuscular drugs (14,15). Two theories have been proposed to explain this acceleration mechanism. The first one states that the priming dose retains some of the postsynaptic nicotinic receptors; and thus, when the actual intubation dose is applied, the number of receptors required for clinical paralysis is reached much faster. On the other and, the second theory states that the priming dose blocks the presynaptic nicotinic receptors, reducing the release of acetylcholine. As a result, the intubation dose causes paralysis much faster (12). If the nondepolarizing agent applied as the first dose is different from the basic nondepolarizing drug, the effect onset time of the drug main and the dose requirement may vary depending on the interaction between the two drugs (16). Excessive fat stores theoretically increase the volume of distribution of fat-soluble drugs, thus requiring a larger loading dose to maintain the same plasma concentration. This is the basic logic of adjusting some drug doses according to the actual body weight of obese patients. Maintenance doses should also be given less frequently because a larger volume of distribution is expected to further slow clearance. On the contrary, ideal body weight (IBW) should be considered when adjusting the dose of water-soluble drugs such as neuromuscular blocking drugs because they have more limited distribution volumes that are not affected by fat stores (17).

Our study aimed to investigate the effects of priming dose application with rocuronium, taking into account IBW, and the use of rocuronium and vecuronium as neuromuscular blockers on intubation quality and duration.

Methods

Obtained permission from University of Health Sciences Turkey, Haseki Training and Research Hospital Ethics Committee (approval number: 43-2023, date: 09.08.2023). Our study was carried out at University of Health Sciences Turkey, Haseki Training and Research Hospital on 60 patients who were in group I-II according to the American Society of Anesthesiology classification, aged between 20-70 Mallampati I-II-III, BMI between 20-35, and planned for medium-term elective surgical intervention.

Patients with neuromuscular, cardiovascular, renal, and hepatic diseases or those using medications that could affect neuromuscular function (polypeptide antibiotics, anticonvulsants, magnesium sulfate, etc.), those with malnutrition, those who received radiotherapy-chemotherapy, and those who were alcohol dependent were excluded from the study.

In the prospective, randomized, double-blind research, 60 patients included in the study were randomly divided into 4 groups of 15 patients. Vascular access was established on the patients who were taken to the operation room, and fluid infusion was started. Heart rate (HR), diastolic arterial pressure, systolic arterial pressure, mean arterial pressure (MAP), oxygen saturation (SpO_2), and end-tidal carbon dioxide (ETCO2) values were recorded. Acceleromyographic monitoring of the patient was provided noninvasively with a TOF watch device placed on the other arm (TOF watch-Organon Teknika).

For this purpose, the acceleromyography probe of the TOF watch was fixed to the pulp of the thumb with a patch. The negative electrode of the nerve stimulator was placed 2-3 cm proximal to the skin fold formed when the wrist was flexed on the ulnar nerve trace, and the positive electrode was placed 2-3 cm proximal to the negative electrode. The stimulator receiver was fixed to the pulp of the thumb, and the thermoreceiver was placed in the thenar region. The hand is fixed with the palm facing up and the thumb moving freely, but the other four fingers remain motionless. Single twitch T1 and TOF stimulation was chosen as neuromuscular stimulation.

The four patient groups areas follows:

Group I: Priming dose with 0.06 mg/kg rocuronium bromide and 0.54 mg/kg rocuronium bromide following anesthesia induction.

Group II: Priming dose with physiological saline and 0.1 mg/kg vecuronium following anesthesia induction.

Group III: Priming dose with 0.06 mg/kg rocuronium bromide and 0.1 mg/kg vecuronium followed by induction of anesthesia.

Group IV: Priming dose with physiological saline, and 0.6 mg/kg rocuronium bromide following anesthesia induction.

After premedication of 1-2 mcg/kg fentanyl and 0.03 mg/kg midazolam were administered to the patient, TOF was calibrated at 100% and stimulation was paused until muscle relaxants were administered. Primings and intubation doses of the neuromuscular blocker to be administered were calculated according to the patients' IBW.

IBWs were calculated according to Devine's formula (18):

IBW_MAN = 1.0× [Height(cm) – 100 + 0.25× [Height(cm) – 150]],

IBW_WOMEN = 0.9× [Height(cm) – 100 + 0.25× [Height(cm) – 150]].

Anesthesia induction was achieved with 4-6 mg/kg of thiopental sodium given three minutes after the priming dose. After the remaining part of the intubation dose of neuromuscular blockers was administered, the T95 onset of action time [the time from the end of the muscle relaxant injection until maximum neuromuscular block (95%) was achieved] was recorded with neuromuscular monitoring. When the TOF value dropped to 5% or below, the same person intubated the patients. The quality of endotracheal intubation was assessed using the Clarke and Mirakhur scale (Table 1).

Anesthesia maintenance of the patients was provided with 40% O_2/air and 2% sevoflurane. To maintain an end-tidal CO_2 pressure of 30-35 mmHg, mechanical ventilation was used. T95, T25 (time from the end of muscle relaxant injection to recovery of neuromuscular transmission to 25% of the initial value), recovery index (T25-75) and responses to a series of four stimuli at 15-second intervals were monitored and

recorded. MAP, HR, SpO_2, ETCO2 were recorded before induction, after induction, before intubation, after intubation, and on the 1st, 3rd, 5th and 10th minute of the operation. At the end of the operation, the inhalation agents were discontinued, and the patients were extubated and transferred to their services after being observed for half an hour.

Statistical Analysis

SPSS 18.0 program was used for statistical analysis. Descriptive statistics are given as numbers and percentages for categorical variables and as mean and standard deviation for numerical variables. When comparing groups, the chi-square and Fisher's exact test were used for categorical variables. Comparisons of numerical variables between the two groups were made with Student's t-test, provided that the normal distribution condition was met. The paired sample test was used to compare the same variables at different times within the group. More than two group comparisons were made with the Kruskal-Wallis test. In cases where statistical significance was found using the Kruskal-Wallis test, the Mann-Whitney U test was used as a post-hoc multiple comparison method. In evaluation, $p<0.05$ was accepted as the significance level.

Results

Demographic data of 60 patients in this study are given in Table 2. Between the groups, no statistically significant difference was detected in terms of age, height, weight, IBW, BMI, operation time, and gender ($p>0.05$) (Table 2).

With regard to Mallampati scoring, no statistically significant difference was detected between the groups ($p>0.05$) (Table 3).

The MAP between the groups were compared. While a statistically significant difference was detected in post-induction MAP between group 4 and group 2 ($p<0.05$), MAP at other times did not show a statistically significant difference ($p>0.05$).

The MAPs were compared according to the pre-induction values within the groups. Values in group 1, after intubation, 1st minute and 10th minute, in group 2, after intubation and 1st minute, in group 3, after intubation and 1st minute, and in group 4 in the pre-intubation, post-intubation, 1st minute and 5th minute showed a statistically significant difference ($p<0.05$), while no statistically significant difference was detected in the other values ($p>0.05$).

The HRs between the groups were compared, and a statistically significant difference was detected between 1st minute HR values of group 1 and group 2 ($p<0.05$). No statistically significant difference was detected between the groups for HR at other times ($p>0.05$).

No statistically significant difference was observed between the groups ($p>0.05$) when the O_2 saturation between the groups was compared at all times.

Table 1. Clarke and Mirakhur rating scale

Score	Jaw opening	Vocal cords	Reaction to intubation
0	Impossible	Closed	Severe coughing or straining
1	Difficult	Half closed	Moderate straining
2	Medium	Moving	Slight diaphragmatic movement
3	Easy	Open	No reaction

Scoring: 9-8: Excellent, 7-6: Is good, 5-3: Medium, 2-0: Bad

Table 2. Demographic data of the study group

	Group 1	Group 2	Group 3	Group 4	p
Age	47.27±13.64	50.4±15.22	52.53±13.22	47.4±14.15	0.71
Height	164.47±6.61	165.47±8.5	161.07±9.8	163.8±6.6	0.19
Weight	79.4±11.3	77.47±13.46	75.8±9.4	81.6±10.97	0.51
BMI	28.83±2.88	27.86±4.54	28.93±3.65	29.8±3.68	0.58
IBW	56.53±6.93	57.69±8.45	53.45±8.94	55.65±6.69	0.18
Operation duration	67.53±21.35	77.33±27.66	84.53±31.5	85.2±25.56	0.24
Gender					
Man	4 (28.6%)	5 (35.7%)	2 (14.3%)	3 (21.4%)	0.601
Women	11 (23.9%)	10 (21.7%)	13 (28.3%)	12 (26.1%)	

BMI: Body mass index, IBW: Ideal body weight

Table 3. Comparison of Mallampati score values between groups

	Group 1	Group 2	Group 3	Group 4	p
Mallampati					
1	7 (29.2%)	5 (20.8%)	7 (29.2%)	5 (20.8%)	0.774
2-3	8 (22.2%)	10 (27.7%)	8 (22.2%)	10 (27.7%)	

Table 4. Comparison of Clarke and Mirakhur Scale, T95, T25, and T25-75 values between groups

	Group 1	Group 2	Group 3	Group 4	p
T95 (SN)	**87±35.49**	130±46.63	122±35.7	146.6±46.1	**0.001**
T25 (DK)	62.6±20.6	67.9±22.3	75.7±31.5	74.6±24.9	0.50
T25-75 (SN)	247.3±113.2	324.8±148.9	315.6±135.1	282.2±64.1	0.30

Similarly, when the ETCO2 values between the groups were compared, no statistically significant difference was detected at all times ($p>0.05$).

With regard to neuromuscular block and intubation quality, T95(sec), T25(min) and T25-75(sec) values were compared. Considering the effect on-set time between group 1 and the other groups, T95 values were found to be statistically significantly shorter for group 1 ($p<0.05$).

No statistically significant difference was detected between the groups when comparing the clinical effect duration and recovery index (T25 and T25-75) values (Table 4).

It was determined that priming dose application with rocuronium significantly accelerated the neuromuscular block caused by rocuronium, had no statistically significant effect on the rate of neuromuscular block caused by vecuronium, and had no significant effect on the clinical effect duration, recovery index, and intubation conditions.

Discussion

The time between the administration of the priming dose and the administration of the actual intubation dose is called the "priming interval". It has been suggested that a priming dose of 10% of the intubation dose and a priming interval of 3-4 minutes is safe and effective (19-21). There have been different studies on the use of rocuronium with different priming doses and priming intervals (22-24).

In our study, the effects of priming with 0.06 mg/kg rocuronium based on IBW at a 3-minute interval on rocuronium and vecuronium block and intubation quality in patients who received intravenous premedication were investigated.

In their study on 60 patients, Rao et al. (25) compared priming application with rocuronium with the use of a single dose bolus and examined the effect of priming application on intubation conditions and intubation time. The control group was administered with 0.60 mg/kg rocuronium, whereas the priming group was administered a priming dose of 0.06 mg/kg rocuronium and an actual intubation dose of 0.54 mg/kg. Intubation time was measured using TOF stimulation, and it was reported that priming with rocuronium shortened the intubation effect onset time (T95) (50±7.3 s priming group, 94 s control group). In addition, it was reported that excellent intubation conditions were achieved in both control and priming groups, and priming with rocuronium did not have any side effects. Griffith et al. (20) also compared priming application with rocuronium with the use of bolus doses. As the priming dose, 0.06 mg/kg rocuronium was used, and the actual intubation dose was given 2 min after priming. In this study, it was shown that priming with rocuronium shortened the onset time of intubation. Martin et al. (26) explored the effects of a single dose of 100 µg/kg vecuronium with an initial dose of 10, 15 and 20 µg/kg and found the intubation times to be 165, 158, 141, and 220 s, respectively. In their study where Redai and Feldman (23) investigated the effects of the first dose of rocuronium and vecuronium in the vecuronium block, they found that both drugs shortened the effect onset time.

For our study, T95, T25, and T25-75 values we recorded for the muscle strength evaluation made with TOF monitoring. A shorter T95 (onset time) means that the patient is ready for intubation in a shorter time. Our study showed that the lowest T95 time was obtained in Group 1 (87±35.49 sec), which was primed with rocuronium in the rocuronium block. It was determined that priming application with rocuronium based on IBW significantly shortened the duration of action in the rocuronium block (group 1: 87±35.49, group 4: 146±46.1 sec), but priming application in the vecuronium block did not create a significant difference compared with the bolus dose of vecuronium (group 2: 130±46.6, group 3: 122±35.7 sec).

Abdulatif et al. (27) investigated intubation time and intubation quality with atracurium while priming with rocuronium. They applied 1, 1.5, and 2 minutes as priming intervals to different groups, and as a result, it was revealed that priming with rocuronium shortened the onset time of intubation, regardless of the priming interval, and similar times were obtained with rocuronium or succinylcholine. In addition, the intubation quality of the groups was investigated, and while good-excellent intubation quality was observed in the groups where priming was applied (more than 50%), excellent intubation quality was obtained in 100% of the groups where succinylcholine was applied.

In their study on 60 patients, Leykin et al. (28) found differences in intubation quality. They divided the patients into 2 groups; the first group was administered 0.4 mg/kg rocuronium after priming with 0.04 mg/kg rocuronium. The same procedure was applied to the second group by injecting saline as the priming dose. The intubation quality was recorded in the groups. Intubation quality was determined to be statistically significantly higher in the priming group.

In our study, intubation quality was assessed using CMS, and near-perfect intubation quality was achieved in the majority of patients (CMS 6 and above). It was determined that there was no significant difference between the groups in terms of CMS value. The highest CMS values were obtained in group 3, where rocuronium priming was applied to the vecuronium block; however, it was determined that priming with rocuronium did not create a significant difference in intubation quality.

The total duration of effect, defined as the time until 25% recovery of the T1 response, and the recovery index, defined as the time from 25% recovery to 75% recovery, were recorded in all patients. No significant difference was not found in our study in terms of clinical effect duration and recovery index. These findings are in agreement with other studies (20,29,30).

In their study, Griffith et al. (20) stated that while no difference was observed in terms of recovery index between the group primed with rocuronium and the group given saline placebo, priming with rocuronium shortened the onset time of intubation. In another study (30), 80 patients were divided into two groups: group 1 was administered 0.1 mg/kg priming dose rocuronium and 0.5 mg/kg rocuronium after a 4-min priming interval, and group 2 was administered 0.6 mg/kg single dose rocuronium. The clinical effect duration is noted to be 40±3.2 minutes in the priming group, whereas it was 39.3±2.4 minutes in the 0.6 mg/kg single dose rocuronium group. It was stated that priming application does not make a difference in terms of clinical effect duration.

In our study, it was determined that priming with rocuronium according to IBW did not create a significant difference in the duration of clinical effect. The clinical effect duration of groups 1 and group 3, in which rocuronium was used as the main neuromuscular blocker, was similar, and the clinical effect duration of groups 2 and group 3, in which vecuronium was used, was also similar. The difference in clinical effect durations is believed to be due to the different pharmacological effect durations of rocuronium and vecuronium, which are used as basic neuromuscular blockers.

Furthermore, in our study, cardiovascular system effects were evaluated by comparing hemodynamic parameters (MAP and HR) between groups. No clinically significant difference was detected in terms of MAP and HR values between the priming groups and the non-priming groups. In intragroup evaluations, it was thought that the statistically significant difference in MAP after intubation was an expected result of the stress response and sympathetic discharge that developed due to intubation. Similarly, the increase in HR values after the 1st minute in the intra-group evaluation was thought to be the result of the stress response that developed after intubation. In our study, it was observed that no side effects occurred in the priming groups.

Study Limitations

The limiting factor of our study was the small number of patients included in the study.

Conclusion

It was concluded that priming dose application with rocuronium accelerates the neuromuscular block created by rocuronium, has no significant effect on the rate of neuromuscular block created by vecuronium, and provides excellent intubation conditions. It provides fast, high quality, and safe intubation in rapid induction required cases.

Ethics Committee Approval: Obtained permission from University of Health Sciences Turkey, Haseki Training and Research Hospital Ethics Committee (approval number: 43-2023, date: 09.08.2023).

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