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The effect of low-dose rocuronium on rapid tracheal intubation using a video laryngoscope

A randomized double blind controlled study

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Abstract

Background: The aim of this study was to investigate the clinical effectiveness of rocuronium in low doses on conditions during rapid tracheal intubation using video laryngoscope.

Methods: Ninety-eight patients undergoing otolaryngologic surgery were randomly divided into 2 groups: group L using 0.3 mg/kg of rocuronium intravenously (n = 49) and group C using 0.6 mg/kg of rocuronium (n = 49). Sixty seconds after rocuronium administration, tracheal intubation was performed using a video laryngoscope. The overall intubation condition was evaluated along with specific conditions, including laryngoscopy condition, vocal cord position, and intubation response. Intubation profiles, including Cormack–Lehane grade, 1st attempt success rate, and intubation time, were also evaluated.

Results: Overall intubation conditions showed a significant difference between group L and group C ($P = .003$). Although the incidence of vigorous response after tracheal intubation was higher in group L than in group C ($P = .022$), laryngoscopy condition and vocal cord position were similar between the 2 groups ($P = .145$ and .070, respectively). Intubation profiles showed no differences between the 2 groups. The frequency and amount of additional rocuronium administration during surgery were also similar.

Conclusions: Low-dose rocuronium provided significantly worse overall intubation conditions compared to the conventional dose of rocuronium for rapid tracheal intubation. However, when using a video laryngoscope, it may provide clinically acceptable laryngeal muscle relaxation.

Abbreviations: DL = direct laryngoscope, NMBA = neuromuscular blocking agent, NMT = neuromuscular transmission, PACU = post-anesthesia care unit, SpO_2 = peripheral oxygen saturation, TOF = train-of-four, VL = video laryngoscope.

Keywords: intubation, intubation conditions, rocuronium, video aryngoscope

1. Introduction

The use of muscle relaxant can facilitate tracheal intubation, restrict patients' involuntary movement during surgery and improve the surgical field.[1] Rocuronium bromide, a steroidal neuromuscular blocking agent (NMBA), enables rapid tracheal intubation, but the duration of action can be prolonged when a larger dose is used.[2,3] Moreover, in cases of short surgery, not requiring full muscle relaxation, even the use of muscle relaxant for intubation dose may result in residual paralysis,[4] thereby causing complications such as patient anxiety and respiratory failure during the postoperative recovery.[4,5] Therefore, the appropriate use of a muscle relaxant depends on the type and extent of the surgery.

Compared with the traditional direct laryngoscope (DL), a video laryngoscope (VL) can improve the grade of intubation difficulty judging from the visual field of laryngeal view and facilitating tracheal intubation.[6–8] By using VL, the conventional dose of rocuronium may not be necessary for successful tracheal intubation, especially in an operation requiring rapid tracheal intubation. However, information on the effect of low doses of muscle relaxants on rapid tracheal intubation when using VL was largely unavailable. In the present study, we compared 2 different doses of rocuronium between the 2 groups on rapid tracheal intubation using VL and determined their clinical effectiveness in patients undergoing otolaryngologic surgery.

2. Methods

2.1. Patients

After obtaining approval from the Institutional Review Board of Dankook University Hospital (registered number: DKUH 2016-05-024-001), this study was conducted from July 2016 to May 2017. The study protocol was registered on an international clinical trials registry platform (http://cris.nih.go.kr, KCT0002000). The written informed consent for inclusion in this study was obtained from all of 98 patients (age range: 19–64

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years), with patients who met the American Society of Anesthesiologists physical status 1 or 2, and were scheduled for otolaryngologic surgery not requiring microscope.

Patients with cervical spine disorder, temporomandibular joint disorder, any abnormalities of the upper airway such as inflammation, abscess, trauma and tumor, or history of radiotherapy due to head and neck cancer were excluded. Patients with a history of compromised physical activity more than 6 months due to cerebrovascular disease or trauma were also excluded.

2.2. Randomization and group assignments, blindness

The randomization was sequenced into blocks of 4 and 6 patients using randomization software. The 98 patients were randomly allocated into 2 groups: a group using low-dose NMBA (0.3 mg/kg of rocuronium bromide) for tracheal intubation (group L, n = 49) and a group using NMBA (0.6 mg/kg of rocuronium bromide) for tracheal intubation (group C, n = 49).

Because the present study was double blind, it was not revealed to both patient and physician who provided general anesthesia which dose of NMBA was used. To maintain blindness, NMBAs were prepared just before general anesthesia induction by an independent nurse who did not participate in the surgery. To make the total volume of NMBA 10 mL, each dose of rocuronium bromide (0.3 or 0.6 mg/kg) was prepared in a 10 mL syringe and the remaining volume was filled with 0.9% NaCl.

2.3. Anesthesia protocol

Patient did not receive premedication. On arriving at the operating room, patients were monitored with bispectral index, noninvasive blood pressure, peripheral oxygen saturation (SpO_2), and an electrocardiogram. Neuromuscular transmission (NMT) was monitored by acceleromyographic response of the adductor pollicis muscle using surface electrodes (TOF-Watch SX, Organon Ireland Ltd. Dublin, Ireland). After preoxygenation with 100% oxygen via a facemask, anesthesia was induced with target-controlled infusion of remifentanil (effect site concentration 4.0 ng/mL) and propofol (effect site concentration 4.0 μg/mL) using a multidrug infusion device (Orchestra Base Primea; Fresenius Kabi, Bad Homburg, Germany). When bispectral index < 60 and patient did not respond to a verbal command, prepared NMBA (rocuronium bromide, Kabirocuronium, Fresenius Kabi, GmbH, Austria) corresponding to assigned group was given. Before initial NMBA administration, calibration of TOF-Watch SX was performed and train-of-four (TOF) ratio was repeatedly monitored every 15 seconds. Tracheal intubation was performed 60 seconds after NMBA administration using a video laryngoscope (Glideoscope or C-MAC). After tracheal intubation, anesthesia was maintained using a target controlled infusion of propofol and remifentanil by monitoring the bispectral index between 40 and 60. All patients were ventilated with tidal volume of 8 mL/kg and respiratory rate of 10 to 12 breaths/minute, maintaining end-tidal carbon dioxide concentration 35 to 40 mm Hg. When the gross spontaneous respiratory movement was observed or surgeon required a further muscle relaxation during surgery, additional doses of NMBA (10 mg of rocuronium bromide) was given each time. At the end of surgery, infusion of propofol and remifentanil was discontinued and sugammadex (Bridion, MSD, Oss, Netherlands) 200 mg was given intravenously when the TOF count more than 2. Tracheal extubation was performed when patients were responded to verbal command and showed TOF ratio more than 0.9. After extubation, patients were transferred to the post-anesthesia care unit (PACU). During the entire anesthesia period, a forced air warmer system (Bair Hugger; 3M, St. Paul, MN), which was set to 38°C, was applied to all patients' lower extremities.

2.4. Outcome measurement

Primary outcome was the overall intubation condition. The overall tracheal Intubation condition was assessed as excellent, good, and poor. Tracheal intubation condition consisted of 3 factors; laryngoscopy condition, vocal cord position, and intubation response. Ratings of each factors are based on a scoring system proposed for good clinical research practice in studies of neuromuscular blocking drugs.[9] The intubating anesthesiologist rated the ease of laryngoscopy, the movement and position of the vocal cords, and the reaction to intubation, as demonstrated in Table 1.

Secondary outcome was the incidence of 1st attempt intubation success rate, intubation time, extubation time, and TOF ratio at the end of surgery. Intubation time was the duration between at the time of insertion and removal of VL. Blood pressure and heart rate change before and after tracheal intubation were also recorded. Extubation time was the duration between anesthetic drug discontinuation and tracheal tube removal. Intubation related complication such as a postoperative sore throat and hoarseness was assessed at 1 hour after PACU admission.

2.5. Statistics

In the present study, anticipating a 20% difference of the poor intubation condition between 2 groups, 44 patients would be required in each group with a type 1 error of 0.05 and a power of 0.8. Considering a possible dropout rate of 10%, 49 patients per group were needed. Normality was tested using Shapiro–Wilk test. Continuous variables were compared using the Student's *t*-test or Mann–Whitney *U*-test; categorical variables were compared using the chi-square test or Fisher's exact test. A *P*-value of $< .05$ was considered to indicate statistical significance.

Table 1

Evaluation of intubation conditions.

Variables	
Laryngoscopy condition	
Easy	Jaw relaxed, no resistance to blade insertion
Fair	Jaw not fully relaxed, slight resistance to blade insertion
Difficult	Poor jaw relaxation, active resistance of the patient to laryngoscopy.
Vocal cord position	
Abducted	
Intermediated	
Closed	
Intubation response	
None	
Slight	One to 2 weak contractions or movement for <5 seconds
Vigorous	More than 2 contractions and/or movement for longer than 5 seconds

Excellent: all variables are high grade (easy, abducted, or none).
Good: all variables are either high or middle grade.
Poor: the presence of a single low grade (difficult, closed, or vigorous).

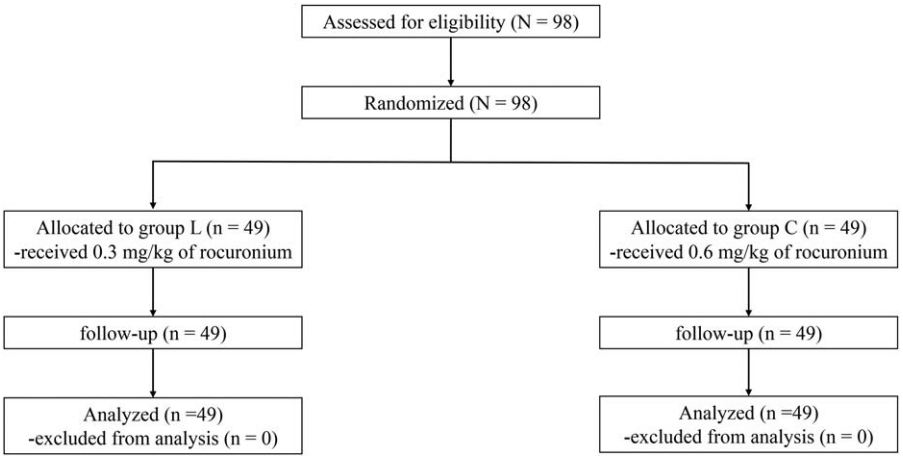

Figure 1. A CONSORT flowchart.

3. Results

A total of 98 patients were enrolled and randomly divided into 2 groups (Fig. 1). Patient's demographics are shown in Table 2 and there were no differences between the 2 groups.

3.1. Primary outcomes

Overall intubation condition showed a significant difference between group L and group C ($P = .003$). The incidence of excellent, good, and poor intubation condition was 18.4%, 46.9%, and 34.7% in group L (vs 55.1%, 34.7%, and 10.2% in group C, respectively). Each of the factors determining intubation condition is compared in Figure 2. Between the 2 groups, laryngoscopy condition and vocal cord position were similar ($P = .145$ and .070, respectively), but intubation response showed a statistical difference. The incidence of vigorous response after tracheal intubation was greater in group L than in group C ($P = .022$) and the incidence of no response was greater in group C than in group L ($P = .005$).

Table 2

Demographics.

	Group L (n = 49)	Group C (n = 49)	*P*
Age, years	47 [37–55]	44 [35–54]	.701
Gender (M/F)	31/18	31/18	1.000
ASA (1/2)	33/16	37/12	.374
Height, cm	168 [162–175]	168 [163–172]	.672
Weight, kg	67 [58–79]	68 [61–78]	.712
BMI, kg/m^2	24.6 [21.6–26.6]	24.3 [22.5–26.8]	.546
Type of surgery, n (%)			.677
Endoscopic sinus surgery	17 (34.7%)	19 (38.8%)	
Septoturbinoplasty	9 (18.4%)	5 (10.2%)	
Thyroidectomy	9 (18.4%)	9 (18.4%)	
Parotidectomy	4 (8.2%)	1 (2.0%)	
Uvulopalatopharygoplasty	4 (8.2%)	7 (14.3%)	
Submandibular gland resection	2 (4.1%)	4 (8.2%)	
Tonsilectomy	1 (2.0%)	1 (2.0%)	
Other neck mass	2 (4.1%)	3 (6.1%)	

Data were expressed as median [interquartile range] or number (%).

3.2. Secondary outcomes

Intraoperative and postoperative data are shown in Table 3. Intubation profiles, including Cormack–Lehane grade, 1st attempt success rate, and intubation time, had no differences between either group. During surgery, the frequency and amount of additional administration of rocuronium were also similar between the 2 groups. At the end of surgery, the incidence of TOF ratio < 0.9 was significantly higher in group C compared with group L ($P = .03$). In subgroup analysis with patients undergoing operation time < 60 minutes, TOF ratio at the end of surgery was significantly lower in group C than in group L (62% [43–88]% vs 94% [79–99]%, respectively, $P = .03$) Postoperative intubation related complication (sore throat and hoarseness) showed no difference between either group.

4. Discussion

We have demonstrated that the overall intubation condition was better in group C, using 0.6 mg/kg rocuronium for rapid tracheal intubation under VL. However, the laryngoscopy condition and vocal cord position were similar between the 2 groups.

Rapid tracheal intubation can be required for urgent airway access in cases of difficult airway management and protection of airway.[10,11] Traditionally, succinylcholine is the most commonly used because of its rapid onset and short duration, but it can have serious side effects.[12] Larger doses of rocuronium (more than 1 mg/kg) can allow rapid paralysis,[3] exacerbate side effects and prolong the duration of muscular blockade. Conventionally, 2 times of ED_{95} of NMBA can be used to facilitate tracheal intubation and, 0.6 mg/kg of rocuronium is used since the ED_{95} of rocuronium was 0.3 mg/kg.[13] Although 0.3 mg/kg of rocuronium was less than that conventionally used, it also may be effective dose and full relaxation might not be mandatory for rapid sequence intubation under VL. Moreover, it may be helpful to reduce the adverse effect of NMBA such as postoperative residual paralysis. In the present study, we compared 2 doses of rocuronium, which were ED_{95} (0.3 mg/kg) and 2 times of ED_{95} (0.6 mg/kg).

In our result, overall intubation condition was better in the group using 0.6 mg/kg of rocuronium. However, it may be necessary to discuss that intubation condition consists of 3 factors: laryngoscopy condition, relating to the resistance to the

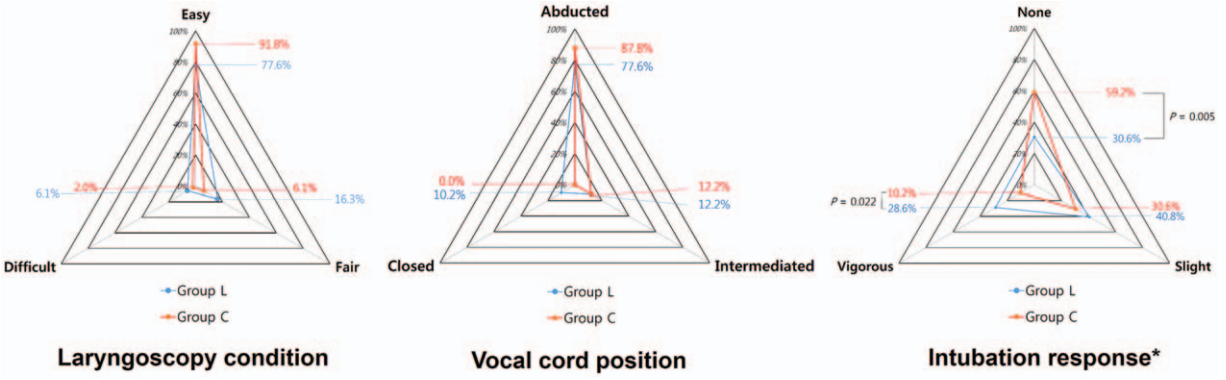

Figure 2. Comparison of the 2 groups in each factor of intubation condition. $^{*}P < .005$.

laryngoscope; vocal cord position having to do with the vocal cord movement during intubation; and intubation response, such as a patients' reaction to intubation like a cough or limb movement. Of the 3 factors, both of laryngoscopy condition and vocal cord position can be regarded as being more related to intubation condition than intubation response because those were evaluated before tracheal intubation. Laryngoscopy condition reflects the resistance of laryngeal muscles and vocal cord position reflects glottis opening to reduce damage by intubation. Intubation response can be caused by sympathetic stimulation or direct mucosal damage,[14] and effectively attenuated by intravenous administration of lidocaine, or opioids,[15–18] as well as by muscle relaxant. Thus, it would be better to take consideration in interpretation whether the intubation response parameter could be included in the overall intubation condition. Our result showed that similar laryngeal muscle relaxation and glottis opening were achieved by 0.3 mg/kg of rocuronium. 0.3 mg/kg dose of rocuronium was used in several studies with the various anesthetic drugs such as propofol, sevoflurane, and variable doses of opioids.[11,19,20] Some studies reported rocuronium 0.3 mg/kg with propofol and an opioid allows adequate intubating conditions.[21,22]

In addition to laryngeal muscle relaxation, the use of VL can contribute to the similar intubation profiles. Compared with direct laryngoscopy, VL can provide an extended view of 60% in the vertical plane and 80% in the vertical plane of the glottis area, which offers an advantage in cases of an anteriorly placed larynx.[23–25] In the present study, although 0.3 mg/kg of rocuronium was a low dose for intubation under conventional DL, acceptable laryngoscopy condition could be achieved in patients using VL.

Muscle relaxants may facilitate tracheal intubation but can also delay postoperative recovery or complications following residual paralysis when excessively used. As the action duration of rocuronium is 35 to 70 minutes, it is necessary to change the dose according to the duration of surgery. Schlaich et al[26] reported that the time to recover to TOF ratio 0.8 in patients who received 0.3 mg/kg of rocuronium was 34 minutes whereas that of 0.6 mg/kg rocuronium was 60 minutes. We performed subgroup analysis with patients undergoing surgery < 60 minutes and TOF

Table 3

Intraoperative data and intubation related postoperative outcomes.

Variables	Group L (n = 49)	Group C (n = 49)	*P*
Intraoperative period			
Intubation success rate at 1st attempt, n (%)	45 (91.8%)	45 (91.8%)	1.000
Intubation time, seconds	28 [19–38]	22 [15–31]	.062
Cormack–Lehane grade	2 [1–2]	2 [1–2]	.661
Required lifting force, n (%)	15 (30.6%)	7 (14.3%)	.058
Required laryngeal pressure, n (%)	9 (18.4%)	7 (14.3%)	.587
Mean blood pressure change after intubation (%)	27 [8–44]	14 [7–32]	.089
Heart rate change after intubation, beats/minutes	25 [12–36]	24 [11–40]	.881
Operation time, minutes	75 [49–106]	70 [40–95]	.402
Anesthesia time, minutes	120 [90–150]	105 [85–135]	.488
The number of additional rocuronium administration (n)	0 [0–2]	0 [0–1]	.153
The amount of additional rocuronium, mg	0 [0–16]	0 [0–10]	.139
Total propofol amount, g	1.0 [0.7–1.2]	0.8 [0.7–1.2]	.261
Total remifentanil amount, mg	0.8 [0.5–1.1]	0.7 [0.5–1.1]	.431
Postoperative period			
TOF ratio at the end of surgery (%)	96 [79–100]	87 [59–100]	.082
TOF ratio < 0.9 at the end of surgery, n (%)	12 (27.9%)	21 (51.2%)	.030
Extubation time, seconds	512 [415–623]	560 [415–669]	.647
Postoperative sore throat incidence, n (%)	27 (55.1%)	25 (51.0%)	.687
Postoperative sore throat score	3 [0–5]	2 [0–5]	.672
Postoperative hoarseness incidence, n (%)	5 (10.2%)	3 (6.1%)	.463

Data were expressed as median [interquartile range] or number (%).

ratio was much higher in group L than in group C, consistent with the previous studies.[26,27] Taken with our result of the lower incidence of TOF ratio < 0.9 at the end of surgery in group L, it can suggest that using low-dose rocuronium may be helpful for reducing the risk of residual paralysis in shorter surgeries.

Our study has several limitations. First, although this study evaluated patients who had no factors predicting difficult intubation at preanesthetic evaluation, there is a possibility of difficult intubation should a patient have a difficult airway and according to the type of surgery. In such cases, large dose of rocuronium can be helpful to secure patients' airway. Second, we here used a qualitative grading system to assess the intubation condition, not a scoring system. Although the scoring system, which sums up the score of both subjective and objective criteria, can assess comprehensive evaluation, qualitative measurement can be assessed for each of individual consisting parameters by grading. Had different scales been used, the study results may have been different. Third, anesthesia was induced and maintained with target-controlled infusion of remifentanil and propofol in our study. As inhalation anesthetics may have a potentiating effect on neuromuscular blocking effects of muscle relaxants,[28,29] total intravenous anesthesia was used in order not to influence the intubating conditions.

In conclusion, the use of low-dose rocuronium can provide significantly less overall intubation conditions compared to the conventional dose of rocuronium. However, when rapid tracheal intubation using a VL is necessary, it may provide clinically acceptable laryngeal muscle relaxation with a reduced risk of the adverse effect of NMBAs.

Author contributions

Author contributions: S.M.J.: acquisition and interpretation of data, and drafting of the manuscript. J.G.L: 0acquisition and interpretation of data. H.S.: study concept and design, interpretation of data, statistical analysis, critical revision of the manuscript, and study supervision. S.K. and B.J.L: critical revision of the manuscript, and study supervision.

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