

Intubating Conditions after High-Dose Cisatracurium Versus Standard-Dose Rocuronium for Rapid-Sequence Intubation: A Randomized Controlled Trial

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Background: Rapid-sequence intubation (RSI) involves administering an intravenous anesthetic agent and a rapid-onset neuromuscular blocking agent (NMBA) to facilitate rapid and secure intubation. The currently recommended NMBAs for RSI are succinylcholine or rocuronium.

Objective: To explore whether the alternative high-dose cisatracurium, which is eight times the 95% effective dose (8ED95), is comparable to standard-dose rocuronium (4ED95) for providing excellent intubating conditions during RSI.

Material and Methods: A double-blind randomized controlled trial study was designed to include 124 participants. All patients were randomly divided into two groups of 62 patients each, with one group receiving 0.4 mg/kg cisatracurium (CIS group) and the other receiving 1.2 mg/kg rocuronium (ROC group). Intubating conditions were assessed 90 seconds after induction, which was defined as excellent, characterized by easy laryngoscopy, wide-open vocal cords, and no coughing or limb movement. The primary outcome was the proportion of excellent intubating conditions, with a predefined non-inferiority (NI) margin of -10%. Secondary outcomes included anesthesiologist's satisfaction, train-of-four (TOF) count at 90 seconds, TOF count at successful intubation, time to TOF count of 0, time to TOF count of 1, hemodynamic parameters, and number of adverse events requiring treatment.

Results: Excellent intubating conditions were found in 91.94% (57 out of 62) and 95.16% (59 out of 62) of patients in the CIS and ROC groups, respectively. The risk ratio of non-excellent intubating conditions in the CIS group was 1.725 compared with the ROC group, without statistical significance (95% CI 0.394 to 7.555, $p=0.469$). However, the intervention could not demonstrate a NI margin of less than -10% to standard-dose rocuronium ($p=0.08$). The CIS group showed a significantly slower onset time than the ROC group, with a median time to TOF 0 of 215.5 seconds (IQR 183 to 270) versus 167 seconds (IQR 110 to 220) ($p=0.024$). The other secondary outcomes, including the anesthesiologist's satisfaction, showed no significant differences.

Conclusion: High-dose cisatracurium did not establish NI to standard-dose rocuronium for excellent intubating conditions during RSI at 90 seconds. Although clinically acceptable conditions were observed, the slower onset time of cisatracurium should be considered when rapid airway control is mandatory.

Trial registration: Thai Clinical Trials Registry, TCTR20210824007

Keywords: Rapid sequence intubation; Rapid sequence induction; RSI; Cisatracurium; Rocuronium; Intubating condition; Non-inferiority trial

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Rapid-sequence intubation (RSI) is a common medical practice technique and has become a standard approach during the COVID-19 pandemic⁽¹⁾. This

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procedure involves administering an intravenous anesthetic agent, a rapid-onset neuromuscular blocking agent (NMBA), and intubating the patient with an endotracheal tube. The advantages of RSI include the ability to perform intubation quickly and safely, an increased success rate of intubation, and a minimized risk of aerosol-transmissible diseases. In addition, compared with awake techniques, performing RSI can decrease patient discomfort and complications such as hypertension, tachycardia, and increased intracranial or intraocular pressure⁽²⁾.

However, the potential disadvantages of RSI are the side effects of each medication used during the procedure. In anesthetic practice, the drugs and dosages are selected according to the patient's

condition. The currently recommended NMBA for use during RSI is succinylcholine or rocuronium⁽²⁾.

Succinylcholine is a depolarizing NMBA with a rapid onset and a short duration. It can cause serious side effects such as hyperkalemia, malignant hyperthermia, bradycardia, and increased intracranial and intraocular pressure. Reports have indicated that succinylcholine can induce sore throat and trigger anaphylaxis^(3,4).

Rocuronium, a non-depolarizing NMBA, is an alternative agent for patients who need to avoid the side effects⁽⁵⁾. The duration of rocuronium is much longer than that of succinylcholine, and its effects depend on adequate hepatic and renal function⁽⁶⁾. This drug may prolong the duration of muscle relaxation in patients with hepatic or renal failure^(7,8). Rocuronium can also trigger an anaphylactic reaction⁽⁴⁾. However, a significant advantage of rocuronium is the availability of its specific reversal agent, sugammadex. This reversal agent is only available in select large-scale hospitals in Thailand due to its high cost.

Cisatracurium is a commonly used non-depolarizing NMBA in critical care medicine and operating rooms because it provides hemodynamic stability without chemically mediated histamine release, even at high doses^(5,9-16). However, the use of cisatracurium in RSI is limited because its onset time is longer at the recommended loading dose than at the equipotent dose, thus ED₉₅ at 0.05 mg/kg cisatracurium and 0.3 mg/kg rocuronium^(5,17-21). Cisatracurium differs from rocuronium in that it is eliminated by Hofmann degradation, which is an organ-independent elimination, and the patient's course of recovery is more predictable than after administering rocuronium⁽²²⁻²⁴⁾. Hepatic or renal disease may have little effect on the duration of action of cisatracurium. One study suggested that among advanced-age patients, cisatracurium had a shorter duration of action and recovery time than rocuronium at an equipotent dose, which may be explained by subclinical age-related changes in the function of vital organs⁽¹⁹⁾. Additionally, cisatracurium has a lower incidence of anaphylaxis than rocuronium⁽⁴⁾.

Previous studies have demonstrated that increasing the dosage of non-depolarizing NMBAs can accelerate the onset time^(9,13-16,21,25-29). A previous study suggested that high-dose cisatracurium (8ED₉₅) can be used in RSI⁽³⁰⁾, but no study to date has compared this intervention with patients who received standard-dose rocuronium (4ED₉₅). Therefore, the present study explored whether

high-dose cisatracurium (8ED₉₅) would provide a non-inferior intubating condition to standard-dose rocuronium (4ED₉₅) performing RSI.

MATERIAL AND METHODS

Study design

Study design adhered to the CONSORT guidelines. This interventional study was designed as a randomized controlled clinical trial and involved 124 patients at Ramadhibodi Chakri Naruebodindra Hospital, Chakri Naruebodindra Medical Institute, between August 2021 and May 2022. The study was approved by the Ramathibodi Ethics Committee (MURA2021/650, dated August 6, 2021) and registered at the Thai Clinical Trials Registry (TCTR20210824007, dated August 24, 2021). The researchers informed all enrolled patients about the research methods and provided written informed consent. The first patient was enrolled in the study on August 25, 2021.

Patients

Eligible patients included 18 to 65-year-old adults with an American Society of Anesthesiologists (ASA) physical status classification of I to III who were willing to participate in the study. They were planning to undergo elective surgery requiring general anesthesia for more than one hour. All patients skipped heavy meals for more than eight hours, light meals for more than six hours, and clear liquids for more than two hours before the induction of general anesthesia.

Exclusion criteria included pregnant or breastfeeding patients, patients who were predicted to have difficult intubation (including apparent facial anomalies and overall assessment from potential risk factors), patients at risk of aspiration, patients with severe diseases (such as cardiovascular disease, reactive airway disease, neuromuscular disease, and hepatic or renal dysfunction), and patients with cardiac pacemakers. The history of drug allergy related to the research or patients who currently use the medication that could affect the action of NMBAs, such as aminoglycosides, antidepressants, anticonvulsants, antiarrhythmic agents, or magnesium sulfate, was excluded.

Randomization, intervention, and blinding

Using a computer-generated randomization website, the researchers randomly divided the participants into two groups by a block-of-four randomization sequence, as the high-dose

cisatracurium group (CIS group) and the standard-dose rocuronium group (ROC group). The authors used sealed envelopes for allocation concealment and collected demographic data at enrollment. All patients underwent general anesthesia with the RSI technique under the service of two anesthesiologists and one nurse anesthetist. The first anesthesiologist to provide anesthetic care and perform the intubation was a certified anesthesiologist with at least three years of clinical experience in anesthesia and airway management. This anesthesiologist was blinded to the patients' groups while performing intubation and maintaining anesthetic care. The second anesthesiologist prepared the medication for RSI using the protocol noted in the envelope.

Before the anesthesiologist induced the patient into an anesthetic state, the subject underwent standard monitoring, including electrocardiography, blood pressure, and pulse oximetry. Additionally, neuromuscular transmission (NMT) monitoring was applied to monitor the train-of-four (TOF) count after the patient was anesthetized. After the nurse anesthetist measured and recorded the baseline hemodynamic data, the first anesthesiologist performed preoxygenation via facemask using 100% oxygen at 6 L/minute for three minutes. The second anesthesiologist prepared 2 mg/kg propofol and 1.5 mcg/kg fentanyl for both groups. The NMBA used in RSI was either 0.4 mg/kg cisatracurium in the CIS group or 1.2 mg/kg rocuronium in the ROC group, both administered in normal saline up to 20 mL and contained in identical 20-mL syringes for blinding purposes. After three minutes of preoxygenation, the second anesthesiologist administered all medications. The sequence of injection was fentanyl, propofol, the NMBA specific to the patient's group, and 10 mL of normal saline without interruption. The first anesthesiologist waited to perform endotracheal intubation 90 seconds after the drug administration, while the facemask remained sealed over the patient's face without assisted or controlled ventilation, and no volatile anesthetic drug was provided. The first anesthesiologist performed facemask ventilation only to rescue when the patient's oxygen saturation was below 94%. At 90 seconds after the drug administration, the first anesthesiologist performed intubation using an endotracheal tube with an intubating stylet by direct laryngoscopy. The nurse anesthetist measured and recorded the TOF count at 90 seconds after medication injection, then continued TOF monitoring every 12 seconds and recorded the TOF count upon completion of intubation.

After finishing intubation, the first anesthesiologist confirmed the position of the endotracheal tube, secured the tube, immediately rated the intubation's satisfaction using a numeric rating scale (NRS), and the intubating conditions using the intubating condition scale established by Goldberg et al.⁽³¹⁾ as excellent (easy passage of the tube without coughing, vocal cords relaxed), good (passage of the tube with slight cough, vocal cords relaxed), poor (passage of the tube with moderate coughing or bucking, some vocal cord movement), or not possible (vocal cords adducted or not visualized, jaw not relaxed). If the first attempt at intubation was unsuccessful, the anesthesiologist could perform facemask ventilation or use an alternative airway device to manage the patient's airway.

The patient was initially anesthetized with 2% sevoflurane, oxygen, and nitrous oxide with a 50% fraction of inspired oxygen. The sevoflurane and intravenous opioids could be adjusted by the first anesthesiologist to maintain the proper depth of anesthesia and to keep the patient within normal physiological conditions. The study was completed when the TOF count was back to 1, and the second anesthesiologist informed the first anesthesiologist about the NMBA used for anesthetic induction. During the maintenance phase of anesthesia, the nurse anesthetist recorded the patient's hemodynamic parameters and observed any adverse events that required treatment, such as rash, hypotension, hypertension, tachycardia, or bradycardia. If any adverse events occurred during the study, the primary anesthesiologist decided whether the patient needed treatment.

The primary outcome of the study was the proportion of patients with excellent intubating conditions at 90 seconds after administration of NMBA. The secondary outcomes were the anesthesiologist's satisfaction, TOF counts at 90 seconds (TOF90s), TOF counts at successful intubation (TOFint), time to a TOF count of 0 (TTOF0, estimated as the onset time of NMBA), time to a TOF count of 1 (TTOF1, calculated as the duration of NMBA), hemodynamic parameters, and the number of adverse events requiring treatment. A flow-chart of the study's progression was shown in Figure 1.

Statistical analysis

The authors calculated the sample size based on 100% excellent intubating conditions with 1.2 mg/kg rocuronium and an expected difference of less than

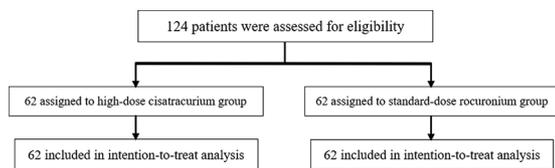


Figure 1. Flow chart of the study's progression.

–10% in excellent intubating conditions between the CIS and ROC groups. The sample size provided 80% power based on a type I error of 0.05. Considering a 10% dropout rate, the sample size was 62 patients in each group.

All patients who fulfilled the inclusion criteria underwent intention-to-treat analysis without missing data. Categorical variables were presented as the number count with percentage and were compared using the chi-square, Fisher's exact, or the Monte Carlo exact test. Continuous variables were presented as mean, median, standard deviation, and interquartile range, depending on the data distribution, as determined by the Kolmogorov-Smirnov test. The variables were compared using a t-test for data with a parametric distribution. The Mann-Whitney U test was employed for data with a non-parametric distribution.

Intubating conditions were assessed by a non-inferiority analysis using a non-inferiority margin of –10% as specified in the protocol. Univariable logistic regression was performed to identify various factors associated with non-excellent intubating conditions.

Hemodynamic profiles were analyzed using two-way repeated-measures ANOVA with the baseline as the covariate. Statistical analysis was done using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). A significance level of p-value of less than 0.05 was used for all statistical analyses.

RESULTS

One hundred twenty-four patients were enrolled, 44 men (35.48%) and 80 women (64.52%), and randomly assigned to the two study groups. Most demographic characteristics showed no difference between the two groups, as shown in Table 1. The exception was the ASA physical status, in which the CIS group had a higher proportion of patients with an ASA physical status of II than the ROC group. The predicted difficulty in airway management showed no significant difference between the two groups.

For the primary outcome, the proportion of patients achieving excellent intubating conditions

Table 1. Comparison of baseline characteristics between CIS group and ROC group

	CIS group (n=62)	ROC group (n=62)
Sex: male/female; n	41/21	39/23
Age (years); mean±SD	45.37±11.73	49.44±12.15
Weight (kg); mean±SD	64.06±11.49	64.11±11.06
Body mass index (kg/m ²); mean±SD	24.39±3.39	24.41±3.84
ASA physical status; n (%)		
III	4 (6.45)	18 (29.03)
II	41 (66.13)	30 (48.39)
I	17 (27.42)	14 (22.58)
Mallampati score; n (%)		
III	4 (6.45)	9 (14.52)
II	39 (62.9)	32 (51.61)
I	19 (30.65)	21 (33.87)
Potential risk factors for difficult intubation; n (%)		
Thyromental distance of <6 cm	1 (1.61)	2 (3.23)
Mouth opening of <3 cm	0 (0.0)	0 (0.0)
No patency of nares	1 (1.61)	1 (1.61)
Prominent incisor	1 (1.61)	0 (0.0)
Head and neck motility limitation	0 (0.0)	0 (0.0)

SD=standard deviation; CIS group=high-dose cisatracurium group; ROC group=standard-dose rocuronium group; ASA=American Society of Anesthesiologists

Table 2. Multivariable analysis for the excellent intubating condition

Factors	Adjusted OR (95%CI)	p-value
NMBA	1.57 (0.35 to 7.01)	0.554
ASA physical status	0.67 (0.21 to 2.15)	0.497

OR=odds ratio; CI=confidence interval; ASA=American Society of Anesthesiologists; NMBA=neuromuscular blocking agents

at 90 seconds was 91.94% (57 out of 62) in the CIS group and 95.16% (59 out of 62) in the ROC group. All remaining patients in both groups were rated as having good intubating conditions (8.06% in CIS and 4.84% in ROC); notably, no patients in either group were classified as having poor or non-intubatable conditions. Regarding procedural success, the first-attempt intubation rate was 100% (124 out of 124) for all participants, with no alternative airway devices or rescue techniques required. After multivariable analysis, due to the imbalance in the ASA classification, no association was found between the excellent intubating condition and the ASA classification (as shown in Table 2).

In the non-inferiority analysis, the difference in the proportion of excellent intubating conditions between the CIS and ROC groups was –3.22%, with a 95% confidence interval (CI) ranging from –13.0% to 6.6%. Although the univariable analysis showed

Table 3. Non-inferiority of CIS group over ROC group according to failure to meet excellent intubating conditions (margin ROC-CIS=-10% or difference in proportion=-0.1)

	Non-excellent (n=8)	Excellent (n=116)	Total (n=124)	Proportion
Agent; n (%)				
CIS group	5 (8.06)	57 (91.94)	62	0.08 (P1)
ROC group	3 (4.84)	59 (95.16)	62	0.05 (P2)
Confidence intervals of the difference (P2 - P1)				
H0: P2 - P1 = 0 vs. Ha: P2 - P1 ≠ 0				
Wald Z (cc)	P2 - P1 = -0.03 [(-0.13) - 0.07], width=0.2, p=0.717			
Upper non-inferiority tests of the difference (P2 - P1)				
H0: P2 - P1 ≤ -0.1 vs. Ha: P2 - P1 > -0.1				
Gart-Nam score	P2 - P1 = -0.03 [(-0.13) - 0.07], width=0.2, p=0.080			
CIS group=high-dose cisatracurium group; ROC group=standard-dose rocuronium group				

no statistically significant difference in the risk of non-excellent conditions between the two groups (risk ratio 1.725, 95% CI 0.394 to 7.555, p=0.469), the non-inferiority of high-dose cisatracurium could

not be established. This was because the lower bound of the 95% CI (-13.0%) exceeded the predefined non-inferiority margin of -10% (p=0.08) (as shown in Table 3).

The secondary outcomes were summarized in Table 4. Anesthesiologist satisfaction (maximum NRS score of 10) did not differ significantly between groups. Regarding neuromuscular monitoring, the CIS group had higher TOF90s at the time of successful intubation compared to the ROC group (p<0.001), reflecting a slower onset. The median TTOF0 was significantly longer in the CIS group [215.5 seconds (IQR 183 to 270) versus 167 seconds (IQR 110 to 220), p=0.024]. No statistically significant difference was found in the duration of action (TTOF1).

Regarding safety, the number of adverse events requiring treatment also showed no significant difference between the two groups. Two patients developed rashes (one in each of the CIS and ROC

Table 4. Comparison of outcomes and adverse events between CIS group and ROC group

	CIS group (n=62)	ROC group (n=62)	p-value
Anesthesiologist's satisfaction (NRS score of 10); n (%)	27 (43.55)	23 (37.10)	0.142
TOF count at 90 seconds; n (%)			<0.001*
4	56 (90.32)	38 (61.29)	
3	5 (8.06)	5 (8.06)	
2	0 (0.00)	1 (1.61)	
1	0 (0.00)	5 (8.06)	
0	1 (1.61)	13 (20.97)	
TOF count at successful intubation; n (%)			<0.001*
4	49 (79.03)	21 (33.87)	
3	5 (8.06)	5 (8.06)	
2	1 (1.61)	4 (6.45)	
1	2 (3.23)	8 (12.90)	
0	5 (8.06)	24 (38.71)	
Time to TOF count of 0 (seconds); median (IQR)	215.5 (183 to 270)	167 (110 to 220)	0.024*
Time to TOF count of 1 (seconds); median (IQR)	4,970.5 (4,510 to 5,605)	4,504 (3,729 to 5,520)	0.489
Adverse events requiring treatment; n (%)			
Rash/flushing/angioedema	1 (1.60)	1 (1.60)	>0.999
Hypotension, number of episodes			
• 3	1 (1.61)	1 (1.61)	
• 2	2 (3.23)	5 (8.06)	
• 1	15 (24.19)	12 (19.35)	
• 0	44 (70.97)	44 (70.97)	
Hypertension	5 (8.06)	2 (3.23)	0.065
Tachycardia	0 (0.00)	0 (0.00)	-
Bradycardia	3 (4.84)	0 (0.00)	>0.999

IQR=interquartile range; CIS group=high-dose cisatracurium group; ROC group=standard-dose rocuronium group; NRS=numeric rating scale; TOF=train-of-four

*p<0.05 is considered statistically significant

groups). The patient in the CIS group developed the rash after administration of the induction agents and NMBA. The rash appeared distal to the blood pressure cuff while the cuff was inflating on the left arm, and the intravenous catheter was placed distal to the cuff (the operative site was at the right shoulder). The inflation of the blood pressure cuff effect might confound this. Additionally, the other medication may confound the results for the other patient in the ROC group, as the rash appeared after the intravenous administration of an antibiotic for the prevention of surgical site infection. Both patients received intravenous chlorpheniramine, after which the rash improved. All patients who developed hypotensive episodes were treated with intravenous ephedrine. The hypertensive episodes in both the CIS group and ROC group were treated with either intravenous nicardipine or esmolol. All three bradycardia episodes that occurred in the CIS group were treated with intravenous atropine. After all the interventions were provided, they had stable hemodynamics without serious complications. Two-way repeated-measures ANOVA with baseline as the covariate using the hemodynamic parameters obtained within the first 60 minutes showed significantly higher heart rate in the ROC group than in the CIS group ($p=0.008$) but no effect on systolic blood pressure ($p=0.611$), diastolic blood pressure ($p=0.558$), or mean arterial pressure ($p=0.664$). However, the authors could not exclude the influence of surgical stimuli or the depth of anesthesia as potential confounders for these hemodynamic changes.

DISCUSSION

Even though the univariable logistic regression analysis of using high-dose cisatracurium as the NMBA in RSI showed no significant increase in the risk of non-excellent intubating conditions, high-dose cisatracurium still did not statistically establish non-inferiority compared to standard-dose rocuronium using the predefined margin of -10% ($p=0.08$). Nevertheless, the anesthesiologist's satisfaction showed no difference between the two groups. High-dose cisatracurium might provide a slower onset time of muscle relaxation than standard-dose rocuronium without significantly increasing the duration of action. This discrepancy may be explained by the TOF count measured at the adductor pollicis (as a peripheral muscle), in contrast to the intubating condition, which involved core muscles such as the vocal cords and diaphragm. This phenomenon has been described in previous studies^(20,26,32-35).

Regarding hemodynamic status, the CIS group might benefit from a lower heart rate than the ROC group during the first 60 minutes.

The protocol was designed to perform classic RSI: no premedication, no assisted ventilation via facemask, and no supplementation with nitrous oxide or volatile agents between the anesthetic induction and intubation gap. This protocol differed from most previous studies, which involved premedication with benzodiazepine and assisted ventilation via facemask with nitrous oxide and volatile agents while calibrating NMT monitoring for baseline. Thus, a key advantage of the present study was the absence of a confounding effect from either premedication or a volatile anesthetic agent interfering with the action of the NMBA. This could apply to the clinical practice outside the operating room. However, the authors used only propofol as the induction agent. However, if patients were anesthetized by the other induction agents rather than propofol (such as etomidate, ketamine, or midazolam), the effect of the NMBA might differ from the present study results because the induction agent also affects the onset of the NMBA and the intensity of blockage. Ko et al.⁽³⁶⁾ demonstrated that etomidate improved intubating conditions and provided a faster onset time for cisatracurium compared to propofol.

A limitation of the present study was that the authors did not calibrate the NMT monitoring to measure the initial baseline values, which differed from those in previous studies. This was because we decided to perform classic RSI to reflect a real-life situation with no delay between administering the intravenous anesthetic agent and NMBA. During the lag period, the authors were affected by how patients responded to the stimulus of intubation and the complexity of the intubation procedure. This could be minimized by randomizing both groups.

The second limitation was determining the precise onset time. The authors measured the first TOF count 90 seconds after anesthetic induction to minimize the potential bias that might have arisen if the anesthesiologist who performed the intubation knew the depth of the NMBA. If the TOF90s count was 0, the onset time might have been earlier than 90 seconds, which the authors did not measure.

Third, the generalizability of the findings was limited, as this study was conducted only in elective surgical patients. The results may not be directly applicable to emergency settings or high-risk patients (e.g., those with anticipated difficult airways or hemodynamic instability), where RSI is most critical.

Lastly, the present study excluded patients with severe hepatic/renal disease and patients aged more than 65 years. Cisatracurium might benefit such patients because of its shorter duration of action compared with rocuronium (cisatracurium exhibits organ-independent elimination). The actual beneficial effects require further investigation in this specific population.

CONCLUSION

Despite achieving a high rate of excellent intubating conditions, high-dose cisatracurium of 0.4 mg/kg fails to meet the predefined non-inferiority margin compared to standard-dose rocuronium of 1.2 mg/kg. Due to its significantly slower onset and the lack of demonstrated non-inferiority, high-dose cisatracurium cannot be recommended as a replacement for rocuronium in routine RSI. However, it remains a viable alternative when standard agents are contraindicated.

WHAT IS ALREADY KNOWN ABOUT THIS TOPIC?

Cisatracurium is a non-depolarizing NMBA used to facilitate endotracheal intubation. A standard dose of cisatracurium is not recommended in RSI due to the slower onset of action compared to rocuronium and succinylcholine.

WHAT DOES THIS STUDY ADD?

The high-dose cisatracurium used to facilitate endotracheal intubation by rapid-sequence induction might be comparable with standard-dose rocuronium.

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AUTHORS' CONTRIBUTIONS

NK helped to design the study, collect the data, revise the manuscript, conduct the analysis, interpret the data, and draft the article. TC helped to create the research and revise the manuscript. Both authors read and approved the publication of the revised version of the manuscript.

DATA AVAILABILITY STATEMENT

The data sets used and analysed during the current study are available from the corresponding author upon reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Ramathibodi Ethics Committee (MURA2021/650, dated August 6, 2021). The researchers informed all enrolled patients about the research methods and provided written informed consent. The first patient was enrolled in the study on August 25, 2021.

CLINICAL TRIAL REGISTRATION

This study was registered at the Thai Clinical Trials Registry (TCTR20210824007, dated August 24, 2021).

USE OF ARTIFICIAL INTELLIGENCE

During the drafting of this paper, Google Gemini 2.5 Pro was employed for linguistic optimization and clarity. The authors have since verified and revised the generated suggestions to ensure accuracy, accepting complete responsibility for the integrity of the published work.

FUNDING DISCLOSURE

This research project had no funding support.

CONFLICTS OF INTEREST

The authors declare no competing interests.

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การศึกษาเปรียบเทียบระหว่างการให้ยา Cisatracurium ขนาดสูงกับยา Rocuronium ในการใส่ท่อช่วยหายใจแบบรวดเร็ว: การทดลองแบบสุ่มที่มีการควบคุม

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ภูมิหลัง: การใส่ท่อช่วยหายใจแบบรวดเร็ว (rapid-sequence intubation, RSI) เกี่ยวข้องกับการบริหารยาสลบทางหลอดเลือดดำและยาคลายกล้ามเนื้อที่ออกฤทธิ์เร็วก่อนที่จะทำการใส่ท่อช่วยหายใจ ซึ่งปัจจุบันยาคลายกล้ามเนื้อที่แนะนำในการใส่ท่อช่วยหายใจแบบรวดเร็ว ได้แก่ succinylcholine และ rocuronium

วัตถุประสงค์: เพื่อศึกษาว่าการให้ยา cisatracurium ขนาดสูง (8ED95) สามารถนำมาเป็นยาทางเลือกในการใส่ท่อช่วยหายใจแบบรวดเร็วโดยเปรียบเทียบกับยา rocuronium ขนาดมาตรฐาน (4ED95) ในการช่วยทำให้เกิดสภาวะที่เหมาะสมในการใส่ท่อช่วยหายใจได้หรือไม่

วัสดุและวิธีการ: การศึกษาแบบสุ่มที่มีการควบคุมที่มีผู้เข้าร่วมทั้งหมด 124 คน แบ่งเป็นสองกลุ่ม กลุ่มละ 62 คน โดยกลุ่มที่ได้รับยา cisatracurium จะได้รับขนาด 0.4 มก./กก. (กลุ่ม CIS) ส่วนกลุ่มที่ได้รับยา rocuronium จะได้รับขนาด 1.2 มก./กก. (กลุ่ม ROC) โดยศึกษาผลลัพธ์หลักคือสภาวะในการใส่ท่อช่วยหายใจแบบรวดเร็ว และผลลัพธ์รอง ได้แก่ ความพึงพอใจของวิสัญญีแพทย์ต่อสภาวะการใส่ท่อช่วยหายใจ การตรวจติดตามระบบประสาทและกล้ามเนื้อผ่าน train-of-four (TOF) ที่เวลา 90 วินาที, TOF ขณะใส่ท่อช่วยหายใจสำเร็จ, ระยะเวลาที่ TOF เท่ากับ 0, ระยะเวลาที่ TOF เท่ากับ 1, ความเปลี่ยนแปลงของสัญญาณชีพ และจำนวนเหตุการณ์ไม่พึงประสงค์ที่ต้องได้รับการรักษา

ผลการศึกษา: พบว่าการใส่ท่อช่วยหายใจชนิดรวดเร็วในกลุ่ม CIS มีผู้เข้าร่วมการศึกษาที่มีสภาวะการใส่ท่อช่วยหายใจระดับดีเยี่ยมอยู่ 91.94% เปรียบเทียบกับในกลุ่ม ROC ที่พบ 95.16% โดยอัตราส่วนความเสี่ยงของสภาวะการใส่ท่อช่วยหายใจให้ได้ระดับดีเยี่ยมในกลุ่ม CIS เมื่อเทียบกับกลุ่ม ROC เท่ากับ 1.725 แต่ไม่มีนัยสำคัญทางสถิติ (95% CI 0.394-7.555, $p=0.469$) อย่างไรก็ตาม การศึกษานี้ยังไม่สามารถแสดงให้เห็นถึงขอบเขตความไม่ด้อยกว่าน้อยกว่า -10% ของการให้ยา cisatracurium ขนาดสูง เมื่อเทียบกับยา rocuronium ขนาดมาตรฐานที่มีนัยสำคัญทางสถิติ ($p=0.08$) และพบว่าการให้ยา cisatracurium ขนาดสูงมีระยะเวลาเริ่มต้นของการออกฤทธิ์ช้ากว่าการให้ยา rocuronium ขนาดมาตรฐาน ส่วนผลลัพธ์รองอื่นๆ รวมถึงความพึงพอใจของวิสัญญีแพทย์ ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างทั้งสองกลุ่ม

สรุป: ยา cisatracurium ขนาดสูงอาจนำมาช่วยในการใส่ท่อช่วยหายใจแบบรวดเร็วได้โดยสภาวะการใส่ท่อช่วยหายใจที่ดีเยี่ยมที่ 90 วินาที สามารถทำได้อย่างปลอดภัย โดยไม่มีความแตกต่างอย่างมีนัยสำคัญจากยา rocuronium ขนาดมาตรฐาน แต่ยังไม่สามารถแสดงให้เห็นถึงขอบเขตความไม่ด้อยกว่าน้อยกว่า -10% เมื่อเทียบกับยา rocuronium ขนาดมาตรฐาน