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## Original Article

# Rocuronium versus Cisatracurium for Rapid Sequence Induction of Anesthesia in Morbidly Obese Patients

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## ABSTRACT

**Introduction and Aim:** Obesity is a challenging problem for anesthetists. Difficult airway with risk of aspiration and regurgitation increases with obesity. Therefore, the need for effective and safe drug for rapid induction of anesthesia is crucial to ensure fast good intubation condition. The aim of this study is to assess Rocuronium versus Cisatracurium for rapid sequence induction of anesthesia in morbidly obese patients.

**Patients and methods:** This study included 60 patients with ASA physical status II, aged 21-40 years, BMI 35-40 kg/m<sup>2</sup> and scheduled for elective surgery under general anesthesia. Patients were classified into two equal groups: Group (R): received Rocuronium bromide (Esmeron) in a dose of 0.9 mg/kg (lean body mass) for intubation; Group (C): received Cisatracurium besylate (Nimbex) in a dose of 0.15 mg/kg (LBM) for intubation. Timing of intubation in seconds, intubation score (excellent, good, poor, or inadequate), and hemodynamic variables before induction (baseline), after induction and before injection of Neuro-muscular blocker (NMB), after injection of NMB and before endotracheal intubation and just after intubation were assessed and measured.

**Results:** There was statistically significant decrease in the timing of intubation in R group (84.0 ± 18.50) as compared to C group (96.0 ± 13.29). However, there was no statistically significant difference in the intubation score among the two groups. There was significant decrease in heart rate and mean arterial blood pressure after the induction of anaesthesia as compared to the baseline in both groups; Heart rate and mean arterial blood pressure changes were comparable among the two groups all of the time.

**Conclusion:** Rocuronium for rapid sequence induction in morbidly obese patients is associated with faster onset compared with cisatracurium, with comparable intubation condition and hemodynamic variables. We recommend further studies to be conducted for evaluation of both drugs with different doses.

**Keywords:** Rocuronium; Cisatracurium; Obese; Anesthesia; Rapid sequence induction.



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## INTRODUCTION

The BMI in clinical practice, it is used to assess the degree of obesity: **Obesity** is defined as having a BMI  $\geq 35$  kg/m<sup>2</sup>. Morbid obesity, defined as a BMI  $\geq 40$  kg/m<sup>2</sup> or BMI  $\geq 35$  kg/m<sup>2</sup> with coexisting medical condition<sup>(1)</sup>. There are several hazards during the intubation of obese patient. One of these hazards is the risk of aspiration that needs effective rapid sequence induction of anesthesia to secure the patient's airway smoothly and quickly, minimizing the chances of regurgitation and aspiration of gastric contents<sup>(2,3)</sup>. Traditionally, suxamethonium has been the neuromuscular blocking drug of choice in these cases owing to its rapid onset of action and relative short duration. The use of suxamethonium can, however, be associated with many side-effects including muscle pains, bradycardia, hyperkalemia, and raised intraocular pressure. It may also act as a trigger for malignant hyperthermia<sup>(4)</sup>.

Rocuronium bromide (Esmeron) is a new aminosteroidal non depolarizing neuromuscular blocker introduced to the clinical use in 1994. It has been proposed for creating intubating conditions similar to those of suxamethonium. The onset time of rocuronium is around 60 seconds. Its duration of action is longer, lasting 37 to 72 minutes with the standard dose<sup>(5,6)</sup>.

Cisatracurium besylate (Nimbex) is a new benzylisoquinoline non depolarizing neuromuscular blocker introduced to clinical application in 1995. It produces good intubating conditions following a dose 0.1 mg/kg within 2 minutes and results in muscle blockade of intermediate duration. However, its relatively long onset time makes it unsuitable for rapid sequence intubation. Many studies were interested in speeding up the onset time of cisatracurium. One of these studies demonstrated that the onset time of cisatracurium is significantly shortened by giving priming dose of it 3 minutes before the induction<sup>(7,8)</sup>.

### AIM OF THE WORK

The aim of this study is to assess Rocuronium versus Cisatracurium for rapid sequence induction of anesthesia in morbidly obese patients.

### PATIENTS AND METHODS

This study was done after approval of the local ethics committee at the department of Anesthesiology and Intensive care Al-Azhar university hospitals (in Damietta and Assiut) from May 2020 to November 2020. The study included 60 patients of both sex with ASA physical status II, Mallampati class I & II, aged 21-40 years, BMI 35-40 kg/m<sup>2</sup> with controlled hypertension or controlled D.M or both and scheduled to undergo elective surgery. Patients were randomized to receive either rocuronium or cisatracurium based on a computer-generated code list (30 patients in each group). This study is a prospective randomized comparative clinical double-blind study. Patients with the following criteria were excluded: refusal to participate in research, had advanced hepatic, renal, cardiovascular, pulmonary and neuromuscular diseases, pregnant patients, patients with known difficult airway intubation Mallampati class III & IV and patient with sleep apnea syndrome.

**Sample size calculation:** Calculation of sample size using EPI-INFO 2002 software package designed by WHO and centers of disease control and prevention revealed that, at least 27 patients were required in each group to find a significant difference of timing of intubation of 30 seconds at a value of 0.05 and power of study 95%. This calculation was based on results of previous study<sup>(9)</sup>.

**The primary** outcome is the intubation characteristics (time to perform, easiness and view). **Secondary** outcomes are the

hemodynamic changes just after intubation.

**Anesthetic techniques:** Patients were randomly classified into two equal groups using computer generated randomization in closed sealed (30 patients in each group). Group I (R): received Rocuronium bromide (Esmeron) (Merck Sharp & Dohme corporation – New Jersey – USA) in a dose of 0.9 mg/kg (lean body mass) for intubation, Group II (C): received Cisatracurium besylate (Nimbex) (GSK co. – London – UK) in a dose of 0.15 mg/kg (LBM) for intubation.

### Intraoperative management:

**Induction of anesthesia:** Following pre-oxygenation through well fitted face mask for 3 minutes, anesthesia was induced with fentanyl 1.5µg/kg iv followed by propofol 1.5 mg/kg IV. Supramaximal stimulation delivered in train-of-four (TOF) every 20 seconds, when twitch height was constant, it was considered as a control and then the intubating dose of the muscle relaxant was injected. Rocuronium bromide 0.9 mg/kg (LBM) IV was given for patient in the first group (R) and Cisatracurium besylate 0.15 mg/kg (LBM) IV was given in the second group (C). Trial of video laryngoscopy was done after suppression 95% of twitch height (Sec), then the intubating conditions was assessed to evaluate the intubation score and this will be done by four-point scale (excellent, good, poor, or inadequate)<sup>(10)</sup>.

The excellent scale showed relaxing jaw, abducting immobile vocal cords, and no diaphragmatic movement, but in the good scale there is relaxing jaw, abducting immobile vocal cords, and some diaphragmatic movement (bucking), in the poor scale there is relaxing jaw, moving vocal cords, coughing on intubation, and in an inadequate scale there isn't relaxing jaw, adducting vocal cords, and impossible intubation<sup>(10)</sup>. When the intubating condition was excellent or good, tracheal intubation was done (Figure: 1) and if it was poor or inadequate (Figure: 2) intubation was postponed and was re-attempted every 30 seconds.



Figure (1): Videolaryngoscopy revealed abducted vocal cords (excellent or good intubation score) and the intubation was performed immediately



Figure (2): Video laryngoscopy revealed adducted vocal cords (poor or inadequate) and the intubation was postponed

**Maintenance of anesthesia:** The maintenance of anesthesia was done by Isoflurane inhalation MAC (1.2) through fresh gas flow and incremental doses of Rocuronium bromide (Esmerone) in a dose of 0.3 mg/kg (LBM) in group R or Cisatracurium besylate (Nimbex) in a dose of 0.03 mg/kg (LBM) in group C when TOF decreased 30%. At the end

of an operation: The isoflurane will be switched off and the residual muscle relaxant was antagonized by neostigmine (0.05mg/kg) with atropine (0.01mg/kg) given by I.V slow injection.

**Measurements:** An anesthetist who is not participating in this research work and was blinded to the groups was used to record the following measurements:

**Timing of intubation in seconds:** Interpretation of the train of four to assess the onset time which was the time from NMB injection to 95% suppression of twitch height. (Sec). Intubation score was done by 4 points scale: (excellent, good, poor, or inadequate) <sup>(10)</sup>. Mean arterial blood pressure (MAP) mmHg, heart rate (HR) bpm and oxygen saturation (SpO<sub>2</sub>) % were recorded at the following intervals: T0, before induction (baseline); T1, after induction and before injection of NMB; T2, after injection of NMB and before endotracheal intubation; T3, just after intubation.

**Statistical Analysis:** Data entry and statistical analyses was completed using SPSS (statistical package of social sciences) version 21 (SPSS Inc., Chicago, IL, USA) (Dean, 2006). Continuous normally distributed data was expressed in mean and standard deviation. The quantitative data was examined by Kolmogorov Smirnov test for normality of data. Independent sample t test (student t test) will be used for continuous normally distributed data. Statistical significance was considered when probability (P) value is less than or equal to 0.05.

**RESULTS**

Seventy-six patients were assessed for eligibility in this study, 16 of them were excluded (12 patients weren't meeting the inclusion criteria and 4 patients refused to join in this study). The remaining 60 patients were selected randomly in two equal groups (30 patients for each). In each of the two groups: All of 30 patients completed the follow up and

their data were analyzed statistically (Figure: 3).

**Demographic data:** Demographic data such as age, sex, body weight and controlled hypertension or controlled D.M or both there was non-significant change between the two groups (p-value > 0.05) as shown in (Table 1).

**Timing of intubation in both studied groups in seconds**

The timing of intubation (time to reach 95% drop in TOF) in R group with mean value of 84.0 ± 18.50 seconds, and in C group with mean value of 96.0 ± 13.29 seconds. Comparison between the two studied groups shows statistically significant decrease in timing of intubation in R group compared to C group (P= 0.005) (Table: 2).

**Intubation score in both studied groups:** The Intubation score in R group was excellent in 15 patients (50%), good in 10 patients (33.3%), poor in 3 patients (10%) and inadequate in two patients (6.7%) and in C group the intubation score was excellent in 14 patients (46.7%), good in 11 patients (36.7%), poor in 3 patients (10%) and inadequate in two patients (6.7%). Comparison between the two studied groups shows no statistically significant difference (P= 0.994) (Table: 3).

**Heart rate (HR) changes (BPM) between the two studied groups:** There was statistically non-significant change in the mean values of heart rate between the two studied groups at all intervals (P= 0.847, 0.859, 0.862, 0.854 at T0, T1, T2 and T3 respectively) (Table: 4).

**Mean arterial blood pressure (MAP) changes (mmHg) between the two studied groups:** There was no significant change in mean arterial blood pressure in two studied groups at all intervals (P= 0.981, 0.187, 0.167, 0.157 at T0, T1, T2 and T3 respectively) (Table: 5).

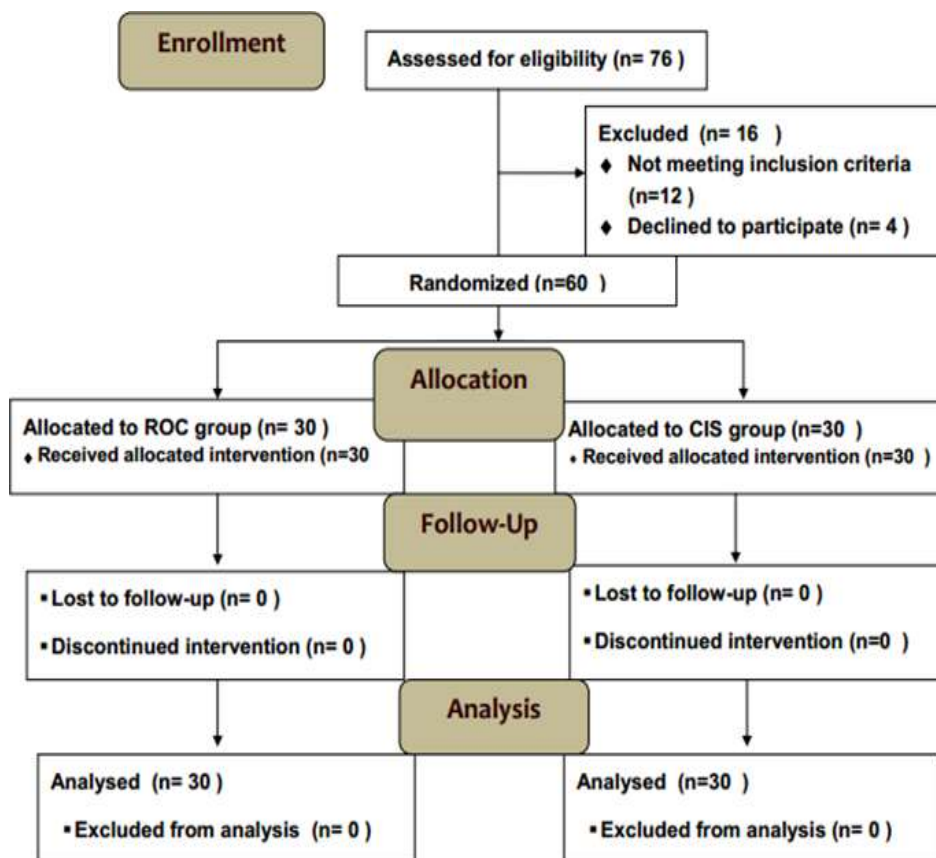


Figure (3): Consort flowchart of the study



Table (1): Demographic data of studied groups

		R	C	Test	P. value
Age (years)	Mean ± SD	28.93 ± 5.94	29.63 ± 5.37	t: 0.229	0.634
BMI (kg/m <sup>2</sup> )	Mean ± SD	37.67 ± 2.07	36.57 ± 3.01	t: 0.016	0.899
Sex (n, %)	Male (%)	11 (36.7%)	12 (40%)	X <sup>2</sup> : 0.071	0.791
	Female (%)	19 (63.3%)	18 (60%)		
Controlled diabetes	n (%)	10 (33.3%)	12 (40%)	X <sup>2</sup> : 0.083	0.65
Controlled hypertension	n (%)	20 (66.6%)	18 (60%)	X <sup>2</sup> : 0.079	0.883

χ<sup>2</sup>: Chi-square test, p: probability t: student "t"-test

Table (2): timing of intubation and intubation score in the two studied groups

		R- group	C-group	Test	P. value
Timing of intubation (seconds)	Mean ± SD	84.0 ± 18.50	96.0 ± 13.29	t: 8.330	<b>0.005*</b>
Intubation Score (n,%)	Excellent	15 (50%)	14 (46.7%)	X <sup>2</sup> : 0.082	<b>0.994</b>
	Good	10 (33.3%)	11 (36.7%)		
	Poor	3 (10%)	3 (10%)		
	Inadequate	<b>2 (6.7%)</b>	<b>2 (6.7%)</b>		

t: student "t"-test and \* indicating significant difference; χ<sup>2</sup>: Chi-square test; p: probability

Table (3): Comparison of the mean values of the heart rate (beat/minute) and mean arterial pressure (MAP (mmHg)) in the two studied groups

		R-group	C- group	t. test	p. value
Heart rate (Beat/minute)	T0	88.97 ± 10.54	89.5 ± 10.76	0.038	<b>0.847</b>
	T1	74.23 ± 9.99	74.70 ± 10.23	0.032	<b>0.859</b>
	T2	70.73 ± 8.12	70.37 ± 8.17	0.030	<b>0.862</b>
	T3	71.27 ± 7.36	71.63 ± 7.99	0.034	<b>0.854</b>
MAP (mmHg)	T0	83.93 ± 10.45	83.93 ± 10.77	0.001	<b>0.981</b>
	T1	76.20 ± 10.05	79.77 ± 10.64	1.782	<b>0.187</b>
	T2	73.70 ± 8.43	77.00 ± 9.79	1.957	<b>0.167</b>
	T3	<b>74.43 ± 6.60</b>	<b>77.43 ± 9.38</b>	<b>2.055</b>	<b>0.157</b>

T0: before induction (baseline). T1: after induction and before injection of NMB. T2: after injection of NMB and before endotracheal intubation. T3: just after intubation.

## DISCUSSION

Suxamethonium has been used for more than 50 years to promote tracheal intubation. For morbidly obese patients, its rapid onset and short period of action makes succinylcholine (Sch) an excellent option since hemoglobin desaturation occurs rapidly after apnea and tracheal intubation must be done quickly<sup>(11)</sup>. Several studies have searched for alternatives to suxamethonium because of its serious complications. One of these studies has compared suxamethonium with rocuronium for rapid sequence induction, and although some have shown good intubating conditions with suxamethonium, others have found that after rocuronium 1.2 mg/kg the speed of onset and intubation conditions are comparable<sup>(12)</sup>. Also, Cisatracurium was one of non-depolarizing neuromuscular agents that included in these studies that looking at the equivalence of suxamethonium and non-depolarizing neuromuscular to achieve effective rapid sequence induction of anesthesia<sup>(7)</sup>.

In our study, both groups were comparable as regard age, sex, body mass index and the time of operation without significant results. There was statistically significant decrease in the timing of intubation in R group as compared to C group. However, there was statistically insignificant difference in the intubation score among the both groups. The hemodynamic variables showed significant decrease in the mean values of both HR and MAP after induction of anesthesia as compared to baseline values. The comparison between the both studied groups revealed insignificant difference of the mean values of HR or MAP. There were no proof of any significant clinical cardiovascular changes in both groups. The heart rates were significantly decreased in both groups (P < 0.05) after induction only and this is consistent with

Jeevarathnam and Solaiappan, who studied the cardiovascular effects, histamine release potential, and pharmacodynamics of rocuronium in adult patients randomized to receive rapid (5s) intravenous (IV) bolus doses of 2.0, 3.0, and 4.0 times the ED with maintenance doses of 150 µg/kg. There were no statistically significant hemodynamic effects after administration of rocuronium<sup>(13)</sup>.

In agreement with our results, the value of rocuronium versus cisatracurium for the intubation in fifty patients were studied on schedule for elective surgery and anaesthetized by propofol 2 mg/kg and remifentanyl 0.5 µg/kg, administered over 60 seconds<sup>(14)</sup>. After induction rocuronium 0.9 mg/kg (3×ED<sub>95</sub>, R group, n=23) or cisatracurium 0.15 mg/kg (3×ED<sub>95</sub>, C group, n = 29) was administered. Laryngoscopy was attempted when suppression 95% occur by TOF after drug administration and adequate time for intubation and the intubation condition was reported and revealed that cisatracurium (197 ± 53 s) onset time was significantly longer compared to rocuronium (102 ± 49 s). During the laryngoscopy, the intubating state and hemodynamic changes after intubation were similar in both groups.

Following a standard anesthesia induction, 0.6 mg/kg rocuronium, 0.1mg/kg vecuronium, and 0.1mg/kg cisatracurium was given to the patients in group R, group V, and group C, respectively and the study suggested that intubation time was found to be shorter in group R than that in groups V and C (P < 0.001)<sup>(15)</sup>.

In all trials performed, succinylcholine results in faster paralysis and a quicker time to intubation when compared with rocuronium. Minimizing the time to enter the safe airway can be clinically important in patients at the highest risk of aspiration. One study found that

succinylcholine was superior to rocuronium in providing both 'excellent' and clinically 'appropriate' intubating conditions, but there was no statistical difference when comparing the recommended rocuronium dose for RSI of 0.9- 1.0mg/kg or 1.2 mg/kg<sup>(16)</sup>.

In agreement with our results, when comparing between atracurium (2×ED95) and different doses of cisatracurium (2×ED95, 4×ED95, 6×ED95) regarding onset time, duration of action, condition of intubation, hemodynamic effects, it was found that the same dose (2×ED95 dose) atracurium is neuromuscular blocking agent that is more effective than cisatracurium, whereas higher doses of cisatracurium 4×ED95 and 6×ED95 provide more powerful, faster neuromuscular blocking with longer period of action and stable hemodynamic status<sup>(17)</sup>. In 2017, Wang et al., studied the onset of action, intubating conditions, efficacy, and safety of rocuronium versus cisatracurium in 40 female patients ASA I&II, 21-50-years-old who underwent elective gynecological outpatient operation under general anesthesia (GA) and were randomly allocated to 2 equal groups. R group, where 0.6mg/kg rocuronium was given and C group, where 0.1mg/kg cisatracurium was given and revealed that acceptable intubating conditions were achieved after 60 sec more frequently after rocuronium (80%) than after cisatracurium (0%). Rocuronium had a significant shorter time of onset than cisatracurium (70.6±18.2 versus 160.4±14.3sec), Rocuronium had a significant shorter time of action than cisatracurium (30.3±5.2 versus 45.7±7.5min)<sup>(18)</sup>.

In 2000, Heier and Caldwell, published a study to establish the rocuronium dose that gives a high probability of achieving ideal conditions for rapid tracheal intubation (within 60s), administering a number of doses of rocuronium, some greater than previously used. Sixty adults, anesthetized with thiopental 4 mg/kg IV and alfentanil 10 µg/kg IV, obtained 0.4 to 2.0 mg/kg IV rocuronium and found that with high doses of rocuronium (up to 2.0 mg/kg) it is possible to have a 90% probability of achieving optimal conditions for rapid tracheal intubation<sup>(19)</sup>.

In conclusion, the use of rocuronium in a dose of 0.9 mg/kg for rapid sequence induction in morbidly obese patients is associated with faster onset compared with cisatracurium in a dose of 0.15 mg/kg, with comparable intubation condition and without hemodynamic affection.

The limitations of our study include the sample size which was relatively small which in turn decrease the power of our findings. However, our findings open a venue for further research.

**Declaration of Financial and Non-Financial Relationships and Activities of Interest:** None

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