



Endotracheal Intubation with Cisatracurium Vs Rocuronium: A Comparative Study

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Abstract

The present study cisatracurium vs rocuronium for endotracheal intubation in adult patients was undertaken to compare the onset of action, intubating conditions, recovery time from neuromuscular blockade, hemodynamic effects of cisatracurium 0.15 mg/kg and rocuronium 0.6mg/kg in 100 adult patients between 20-60 years of age, with ASA physical status I and II of either sex posted for elective surgical procedures after induction with intravenous propofol 2mg/kg and followed by fentanyl 2mcg/kg iv injection. In our study we found that onset of action was quicker and intubating conditions are better and faster with rocuronium (92.02±12.33) compared to cisatracurium(188.45±33.42). There was no statistically significant changes in hemodynamic parameters with both drugs. Intubating conditions were assessed by modified grading given by Cooper et al. It was excellent in 72%, good in 22% and fair in 2% of patients in cisatracurium group, and it was excellent in 78%, good in 14% and fair in 8% of patients in rocuronium group. In all patient the recovery time at TOF>0.9 was between 30–110min. Mean recovery time was 59.33±15.56 and 53±10.23 min in cisatracurium and rocuronium groups respectively. It can be concluded that rocuronium has a rapid onset, time to excellent intubating conditions was significantly faster but both drugs were producing excellent to good intubating conditions with minimal hemodynamic changes and no adverse effects in adult patients of age 20-60 years posted for elective surgery.

Keywords: cisatracurium , rocuronium , endotracheal intubation, on set time, recovery time.

Introduction

Neuromuscular blocking agents are the most commonly used drugs during general anaesthesia^[1]. The introduction of neuromuscular blocking agents [NMBAs] in 1942 into anaesthetic practice was an important development which revolutionized the

practice of anaesthesia^[2]. After the introduction of muscle relaxants, anaesthesia was redefined as a triad of narcosis, analgesia and muscle relaxation, specific drugs being used to produce each of these effects. Neuromuscular blocking agents are muscle relaxants with rapid onset and short duration of action¹. Two current drugs cisatracurium and

rocuronium are non-depolarizing NMBs with an intermediate duration of action. They were introduced into clinical practice in 1992 (rocuronium) and 1995 (cisatracurium), respectively, and currently they are gradually replacing earlier drugs (vecuronium and atracurium). cisatracurium is one of the 10 stereoisomers that constitute the nondepolarizing relaxant atracurium and is frequently used in clinical practice^[3,4]. Although cisatracurium is more potent than the parent mixture its pharmacodynamic profile is similar to that of atracurium, except for a reportedly slower onset. Initial studies of the onset time of cisatracurium, obtained during steady state anaesthesia, reported an onset time of 3.1-5.2 min at 2 times the ED, for neuromuscular blockade^[3,4,5].

Rocuronium bromide is an aminosteroid non-depolarizing neuromuscular blocker or muscle relaxant used in modern anaesthesia to facilitate tracheal intubation by providing skeletal muscle relaxation, most commonly required for surgery or mechanical ventilation. It is used for standard endotracheal intubation, as well as for rapid sequence induction.

The present study was thus planned with the aim of comparing cisatracurium and rocuronium in terms of vocal cord relaxation (intubating conditions), onset time, time to intubation, recovery time from neuromuscular blockade and hemodynamic parameters in patients undergoing general surgical procedures.

Materials & Methods

This study was conducted at Mamatha medical college, Khammam after obtaining approval from the hospital Ethics Committee during the period of January 2017 to December 2018. A total of 100 adult patients, scheduled for elective general surgery under total intravenous anaesthesia with tracheal intubation were included after taking written informed consent. Exclusion criteria were ASA physical status more than III, age under 18 and over 75 years, obesity (BMI over $>30 \text{ kg.m}^{-2}$), patients receiving medication known to interfere with NMBs (anticonvulsants, amino glycosides or

polypeptide antibiotics), patients with anticipated difficult intubation (Mallampati score⁴ III and more), and those with diseases affecting neuromuscular transmission (myopathies).

Patients were randomly allocated into two groups. Patients were premedicated with tab ranitidine 150 mg and tab alprozolam 0.5mg a night before the surgery. In the pre-operative room, a good intravenous (IV) access was secured and baseline parameters were observed and recorded, which included heart rate (HR), Systolic Blood pressure(SBP), Diastolic blood pressure(DBP), mean arterial blood pressure (MAP), electrocardiogram, respiratory rate and pulse oximetry (SpO₂).

All patients were premedicated with glycopyrolate 0.2mg, midazolam 1mg, ondansetron 4mg and fentanyl 2mcg/kg iv. After preoxygenation with 100% oxygen done for 3 minutes and patients were induced with intravenous propofol 2mg/kg.

1. Group C patients received 0.15 mg /kg of cisatracurium (50 patients).

2. Group R patients received 0.6 mg /kg of Rocuronium in (50 patients)

Endotracheal intubation was done after administration of the drug. The onset of action was recorded when the jaw relaxation as assessed by Cooper et al grading was scored as 3 and by using Train of four (TOF). After intubation anaesthesia was maintained with 50% nitrous oxide in oxygen. HR, SBP, DBP, MAP, RR, SPO₂ were measured before induction, and immediately before tracheal intubation, and 1 min, 2 min 5 min after intubation.

At end of the surgical procedure, for each patient residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrolate 0.005 mg/kg intravenously. Recovery time was from neuromuscular blockade assessed by TOF ratios >0.9 , which were recorded at 10 min interval during and after operation. Extubation was done after through suctioning and patient was shifted to post op care for further observation. Intubating conditions were assessed according to Cooper^[6] grading

Table. 1: Cooper grading

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Impossible to open	Closed	Coughing, Bucking
1	Opens with difficulty	Closing	Mild cough
2	Moderate opening	Moving	Slight Diaphragmatic movement
3	Easy opening	Open	None

Individual scores were added to give overall intubation score

8-9-Excellent

6-7-Good

3-5-Fair

1-2-Poor

The mean, standard deviation, mean difference was calculated. Continuous results were analysed using paired ‘t’ test and ANOVA. P value of <0.05 was considered for significant difference.

Results

Hundred patients undergoing various elective surgical procedures between 21- 60 years of age were studied. Fifty patients were given cisatracurium 0.15 mg/kg and the other fifty patients received rocuronium 0.6mg/kg. Onset of action, intubating conditions, hemodynamic changes were observed.

Table 2.Demographic Data

	C- Group	V- Group
No. of Patients	50	50
Males/ Females	27/23	24/26
Age (Yrs)	43.27±10.52	46.23±15.23
Weight (Kgs)	65.33±12.31	66.69±13.65
ASA Grade I/II	19/31	22/28

Table 3: On set of action was assessed by jaw relaxation

Time	C-Group % of patients	R- Group % of patients
90	6%	32%
120	22%	18%
180	30%	0
240	44%	0
Mean time Seconds	188.45±33.42	92.02±12.33

Table 3: Time of intubation

Time	C-Group % of patients	R- Group % of patients
60	6	38
90	14	32
120	14	14
150	42	10
180	10	6
210	4	0
240	6	0
Mean	142.2± 55.23	88.5±33.2

On set of action was assessed by jaw relaxation. In all patients the onset was between 90 – 240 seconds. There exists a significance difference between two groups. After adequate jaw relaxation, laryngoscopy was performed and intubating conditions were graded by modified grading given by Cooper et al grading. The time to excellent intubating conditions was significantly faster with the rocuronium group as compared to the cisatracurium group

Table 4: Intubating Conditions

Cooper et al score	C-Group % of patients	R- Group % of patients
3-5	4	8
6-7	22	14
8-9	74	78

Hemodynamic Effects

There was no significant differences regarding systolic and diastolic blood pressure The rise in mean arterial pressure was maximum post intubation in both the groups and the rise was statistically similar in both groups and not significant.

Recovery time was from neuromuscular blockade assessed by TOF ratios >0.9, which were recorded at 10 min interval during and after operation Some reports suggested that TOF ratio ≥ 0.9 would reflect acceptable neuromuscular recovery and decrease the risk of residual paralysis, postoperative atelectasis, and pneumonia following surgery . In daily clinical practice, the most used neuromuscular monitoring methods are TOF stimulation and clinical tests. TOF ratios >0.9, which were recorded at 10 min intervals starting from 20 min to 120 min range.

Table 5: Recovery time

TOF>0.9 Time (min)	C-Group % of patients	R- Group % of patients
20	0	0
30	6	14
40	8	8
50	10	6
60	24	38
70	16	16
80	18	10
90	14	8
100	2	0
110	2	0
120	0	0
Mean±SD	59.33±15.56	53±10.23

Discussion

Cisatracurium is the most recent iso-quinolone NMB which is 3-4 times more potent than atracurium, it has the same advantage of Hofmann degradation and it does not release histamine. Cisatracurium is the 1R-cis 10R-cis isomer of atracurium. It constitutes 15% of the mixture of atracurium, but cisatracurium has the advantage that it is four times more potent than atracurium and has a slightly longer onset and duration of action. It does not release histamine and has no direct cardiovascular effect. This makes it a choice of NMB agent for anaesthesiologist.

There was no significant difference in the distribution of age, sex and weight between the two groups. In the present study, the onset of action of cisatracurium was assessed by adequate jaw relaxation.

Doenicke AW et al^[7] conducted a study in 60 patients (ASA physical status I or II) compared cisatracurium and vecuronium administration for endotracheal intubation. Onset time of the muscle relaxants was determined by using mechanomyography. Mean (+/- SD) onset times for 0.15 mg/kg cisatracurium group was 105 +/- 41.2 s, 0.25 mg/kg cisatracurium was 68.3 +/- 19.5 s and for 0.15 mg/kg vecuronium was 69.5 +/- 29.2s.

The delayed onset of action of cisatracurium was also documented by Kim et al^[8] who reported 3.9 min at adductor pollicis and 3.0 min at larynx. Ko YK, Kim YH^[9] conducted a study on 46 female patients, undergoing general anesthesia and endotracheal intubation for elective surgery,

compared etomidate and propofol on intubating conditions and the onset time associated with cisatracurium administration. The average onset time of cisatracurium was more rapid in Etomidate group (155.74 ± 32.92 sec) vs. in Propofol group (185.26 ± 38.57 sec); P = 0.008.

In present study all patients were administered propofol for induction. The mean onset time in cisatracurium group was 190±53.29, the results are similar in both the studies.

Paško-Majewska M et al.^[10] compared the onset time, and duration of action of atracurium, cisatracurium, and vecuronium, in 95 ASA I/II patients were randomly allocated to three groups, to receive atracurium (I), cisatracurium (II), or vecuronium (III). Conditions for performing tracheal intubation were noted to be excellent in groups I and III, and good in group II. No significant correlations were found between the duration of neuromuscular blockade and pH, PaCO₂ or palm skin temperature. Vecuronium, besides providing excellent conditions for tracheal intubation, had the fastest onset time and optimal duration of action.

In the present study rocuronium had a mean onset time of 92.02±12.33 sec. Rocuronium has a fast onset of action when recorded by clinical criteria as well as neuromuscular monitoring. Rocuronium has faster onset of action than cisatracurium group which is 188.45±33.42sec.

Adamus M et al^[11] compared the pharmacodynamics of cisatracurium and rocuronium-induced neuromuscular block following single dose in 120 patients scheduled for elective surgery randomized into 4 groups with different cisatracurium or rocuronium doses administered. The onset times were 277 (SD58), 220 (46), 91 (16) and 77 (16) s for the CIS 0.10, CIS 0.15, ROC 0.60 and ROC 0.90 groups (p < 0.05), respectively, with lower variability in both ROC groups (p < 0.05). The clinical durations were 42 (7), 52 (7), 35 (11) and 52 (12) min, respectively (p < 0.05 for lower doses). During spontaneous recovery, the variability of DUR 25-TOF90 was twice as great for ROC than CIS groups (p < 0.05), while after neostigmine

administration it was uniform in all groups. For equipotent doses, the onset times for CIS were approximately three times longer than for ROC. The average clinical duration for both relaxants ranged from 35 to 52 min with acceptable variability.

Melloni C et al.^[12] compared the time course characteristics of cisatracurium (C) and vecuronium (V) induced neuromuscular block (NMB) following multiple doses, allowing spontaneous complete recovery (SCRT) and evaluated the influence of age in 177 adult ASA 1-2 patients in a randomized, double-blind, multicenter study. Both drugs offered good/excellent intubating conditions.

The intubating conditions were assessed by Cooper et al^[6] grading. Parasa M et al^[13] compared intubating conditions of rocuronium and vecuronium in 60 adult American Society of Anesthesiologists physical status 1–2 patients of age 20–60 years. They concluded that intubating conditions were excellent in 100% of patients in Group R as compared to 70% in Group V. They utilised the cooper et al grading for assessment of intubating conditions.

Misra MN et al^[14] compared rocuronium, vecuronium and succinylcholine in their study. Succinyl choline and rocuronium had statistically comparable duration of onset of muscle relaxation while vecuronium took significantly longer time. Succinylcholine and rocuronium produced good to excellent intubating conditions in all patients at 90 seconds whereas that of vecuronium was acceptable in only 83.3% of cases.

The time to intubating conditions by clinical criteria were assessed by SmithJ and Saad^[15] after rocuronium 0.6mg/kg and vecuronium 0.1mg/kg in 52 adult patients. intubating conditions with Rocuronium were excellent in 19 (63.3%) and good in 9(30%) patients while in the Vecuronium group, intubating condition were excellent in 18(60%) and good in 11(36.7%) patients.

Lee H et al.^[16] examined intubating conditions after administering rocuronium or cisatracurium in a rapid sequence induction with remifentanyl propofol and reported that best time to laryngoscopy was predicted by measuring TOF and was found to be

significantly longer in the C group (197 ± 53 s) than in the R group (102 ± 49 s) (P value < 0.05). However, time to laryngoscopy, intubating condition during the laryngoscopy, and hemodynamic changes after intubation was similar in both groups. Despite fundamentally slower onset time, cisatracurium provided quite good intubating conditions, which were comparable to those achieved with equipotent doses of rocuronium. The results in both studies shows cisatracurium has slower time to excellent intubating conditions compared to rocuronium.

Sagir O et al.^[17] investigated effects of the rocuronium, vecuronium, and cisatracurium in adult patients, Intubation time was found to be shorter in Group R than that in Groups V and C ($P < 0.001$). Times to positive visual disturbances and grip strength tests were shorter in Group C than that in Group V. In Group R and group C, time to TOF ≥ 0.9 was significantly longer than all positive clinical test times except grip strength ($P < 0.05$).

The timing of intubation was based on ease of jaw opening and vocal cord visualization and the time to intubation was 134 ± 50 sec in the cisatracurium group and 93 ± 38 sec in vecuronium group. here intubation times was found to be shorter in vecuronium group than cisatracurium group.

In our study inhalational anesthetics were not used. cisatracurium and rocuronium group had no significant effect on systolic and diastolic blood pressure. The fall in systolic blood pressure after induction could be due to propofol. In our study there was no significant changes in Heart rate and systolic blood pressure, diastolic blood pressure, mean arterial pressures after administration of cisatracurium which are similar to post induction values. In a study conducted by Shaik Mira Shareef et al conducted a comparative study of rocuronium produces intubating conditions which are satisfactory in comparison to Succinylcholine. Rocuronium is haemodynamically stable except for slight tachycardia and has no adverse effects.

Recovery time from neuromuscular blockade assessed by TOF ratios >0.9 , which were recorded at 10 min interval during and after operation. Duration of TOF >0.9 was defined as the interval

time between the extubation time and a TOF ratio of 0.9. The trachea was extubated when 4 responses to TOF stimulation were present the recovered the consciousness and the anaesthetist judged that the neuromuscular function recovered adequately for airway protection and spontaneous ventilation. TOF was similar to Sagir O et al.^[17] study.

In present study TOF>9 was used for assessing recovery time, which were recorded at 10 min interval starting from 20 min to 120 min range. The mean recovery time is 69.33 min (SD 19.31 min) in cisatracium group and 63 min in the 56 Vecuronium group which is correlating with the above study. Recovery time is more cisatracium group than vecuronium group.

Neuromuscular blocking agents represent the most frequently involved Anaphylactic substances¹⁰, with a range of 50 % to 70 %. Rocuronium (43.1 %) and succinylcholine (22.6 %) are the most frequently incriminated NMBs¹⁰⁻¹⁶. Compared to atracurium, the risk of histamine release following cisatracurium is markedly reduced but sporadic reports on anaphylactic reactions are available¹⁷. In our study, there were no signs of anaphylaxis during anaesthesia. However, the number of patients studied was too small to draw conclusions.

Conclusion

It can be concluded that rocuronium has a rapid onset, produces excellent to good intubating conditions in 50-90 seconds with a dose of 0.6 mg/kg in adults with minimal hemodynamic changes and no adverse effects.

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