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Clinical profile comparison of cisatracurium and rocuronium in elective surgery

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ABSTRACT

Background: Most surgeries are carried out with ease using neuromuscular blocking agents. This study was aimed to compare the intubating dose of cisatracurium and rocuronium regarding the onset of action, clinical duration, recovery index, intubating conditions, efficacy, and safety in elective surgery.

Method: 60 adult patients of American Society Anesthesiology (ASA) grade I & II, underwent elective laparoscopic surgery were randomized to receive either cisatracurium 0.1 mg/kg (Group C) or rocuronium 0.6 mg/kg (Group R). Neuromuscular monitoring was done using STIMPOD Xavant NMS450. Relaxogram interpretation was carried out for the onset of action, clinical duration, and recovery index.

Results: Cisatracurium had significant longer onset (233.33±62.31 vs. 86.66±28.62 seconds, p <0.001) and significant longer clinical duration (40±3.56 vs. 27.46±2.14 minutes, p <0.001) than rocuronium. Recovery index was significantly longer in the cisatracurium group (12.23±1.54 vs. 8.30±1.80 minutes, p <0.001). Clinically acceptable intubating conditions were achieved in 180 seconds (C group) compared to 60 seconds in the R group. No untoward or adverse response and complications were distinguished in either group.

Conclusion: Cisatracurium 0.1 mg/kg exhibited a slower onset of action than rocuronium 0.6 mg/kg and provided excellent intubating conditions in the majority of patients after 180 seconds. The clinical duration and recovery index were significantly longer in cisatracurium compared to rocuronium. Both are potent and safe agents with excellent cardiovascular stability.

Keywords: neuromuscular relaxants, cisatracurium, rocuronium, monitoring, train of four.

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INTRODUCTION

In modern anesthesia practice, most general surgeries are carried out with ease using neuromuscular blocking agents. A neuromuscular blocker agent should ideally have high potency, rapid onset, and short clinical duration. It should evade any hemodynamic changes due to histamine release, ganglion block, and anti-muscarinic actions.[1,2]

Cisatracurium is a recent benzylisoquinoline introduced in 1989 by Hill and Turner. It lacks histamine-releasing properties and undergoes Hoffmann elimination.[3] Rocuronium is a steroidal non-depolarising muscle relaxant (NDMR). Its potency is 1/6 of vecuronium. Its principal route of elimination is by the liver and, to a little extent, the kidneys.[4]

This study was aimed to see if twice the dose of ED95 of cisatracurium and rocuronium differ in regards to their onset of action, clinical duration, recovery index, intubating conditions, efficacy, and safety in elective surgery.

PATIENTS AND METHODS

This was a hospital-based, prospective, randomized, interventional, and double-blind study. After achieving permission from our institutional review board and ethical committee, we obtained written informed consent from 60 subjects. Inclusion criteria were American Society of Anesthesiologists (ASA) physical status I & II, nonobese patients, aged 20-50 years, Mallampati class I & II upon pre-anesthesia evaluation, and undergoing elective surgery of 45 minutes duration under general anesthesia.

The minimal sample size was calculated based on the results of a previous study.[5] Patients were randomized by computer-generated sequence, and allotment was done by sealed envelope method. Patients with major hepatic, renal, cardiovascular, pulmonary and neuromuscular disease, on any preoperative medication interfering with neuromuscular transmission, and patients requiring more than three attempts at intubation were excluded from the study.

Standard ASA monitoring was applied in the operating theatre: electrocardiography, pulse oximetry (SpO_2), heart rate, blood pressure (NIBP), body temperature, and end-tidal carbon dioxide concentration ($EtCO_2$). Acceleromyography method of the evoked response by STIMPOD Xavant NMS450 was used for neuromuscular monitoring. It includes features like accurate and real-time neuromuscular transmission (NMT) monitoring, nerve mapping and location, and reusable 3D acceleromyography (AMG) sensor. The electrodes were applied at the

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volar side of the wrist. The distal electrode was placed 1 cm proximal to the proximal flexion crease of the wrist, and the other electrode was placed 4 cm proximal to the distal electrode.

All patients were given intravenous (IV) ranitidine 50 mg, metoclopramide 10 mg, glycopyrrolate (0.005 mg/kg), and midazolam (0.02 mg/kg) as premedication. We induced anesthesia by 2 mcg/kg fentanyl and 2 mg/kg propofol. Before neuromuscular drug administration, the accelerometer was calibrated using 0.2 ms supramaximal square wave impulse at 2 Hz. The ulnar nerve was stimulated at the wrist with the supramaximal stimulus of 0.2 ms duration, in a TOF (train of four) mode at 2 Hz every 20 seconds.

Patients were randomized using a sealed envelope technique to receive either cisatracurium 0.1 mg/kg (Group C) or rocuronium 0.6 mg/kg (Group R), both diluted to 10 mL. The first intubation attempt was made by the anesthesiologist when the TOF ratio was 0/4, indicating the onset of action. Intubating conditions were assessed using a four-point scale: (1) Excellent – easy passage of the tracheal tube without coughing, vocal cords relaxed; (2) Good – light coughing, vocal cords relaxed; (3) Poor – passage of tracheal tube with moderate coughing or bucking , some movement of the vocal cords; and (4) impossible.[6]

Anesthesia was maintained with 60% nitrous oxide (N2O) in oxygen (O2) and isoflurane to total MAC of 1.5. Mechanical ventilation was adjusted to maintain EtCO2 between 35-40mmHg. Hemodynamics parameters were recorded every five minutes throughout the study. After 15 minutes of an intubating dose of muscle relaxant in both the groups, TOF stimulation repeated every 3 minutes until 25% of twitch height achieved, which indicated the clinical duration.

After the surgery, we used 50 mcg/kg neostigmine and 0.4 mg glycopyrrolate to antagonize the neuromuscular blockade. Then, TOF stimulation was repeated every 20 seconds, and recovery index was recorded, which defined as achieving 75% of twitch height. We extubated the patient when the patients regained consciousness with adequate muscle power.

The following parameters were logged in both groups: onset time, clinical duration, and recovery index. The onset time was defined as the duration from neuromuscular blocker (NMB) administration to TOF ratio 0/4. The clinical duration was defined as the duration from NMB injection to 25% recovery of twitch height (recorded in minutes). And the recovery index was defined as the duration from 25% to 75% recovery of twitch height (recorded in minutes).

We used Statistical Packages for Social Sciences (SPSS) version 21 for the statistical analysis. Chi-square test was utilized for comparison of categorical data. Quantitative data were presented as mean and standard deviation and were compared by student t-test. A p value of <0.05 was considered statistically significant.

RESULTS

Demographics variables and the results of the study are presented in Table 1. There was no significant difference regarding the distribution of age between the two groups. Transient diastolic and mean blood pressure after induction and transient tachycardia after intubation were recorded, as shown in Figures 1 and 2. The excellent intubating conditions in this study were achieved in 22 patients in group C and 23 patients in group R. The good intubating conditions were seen in 8 patients in group C and 7 patients in group R.

The mean onset of action in group C was 233.33±62.31 seconds compared to 86.66±28.62 seconds in group B ($p < 0.001$). The mean duration of cisatracurium was 40±3.56 minutes compared to rocuronium's 27.46±2.14 minutes ($p < 0.001$). The mean recovery index in group C was 12.23±1.54 minutes, and in group R was 8.30±1.80 minutes ($p < 0.001$). No untoward or adverse reaction and complications were noted.

DISCUSSION

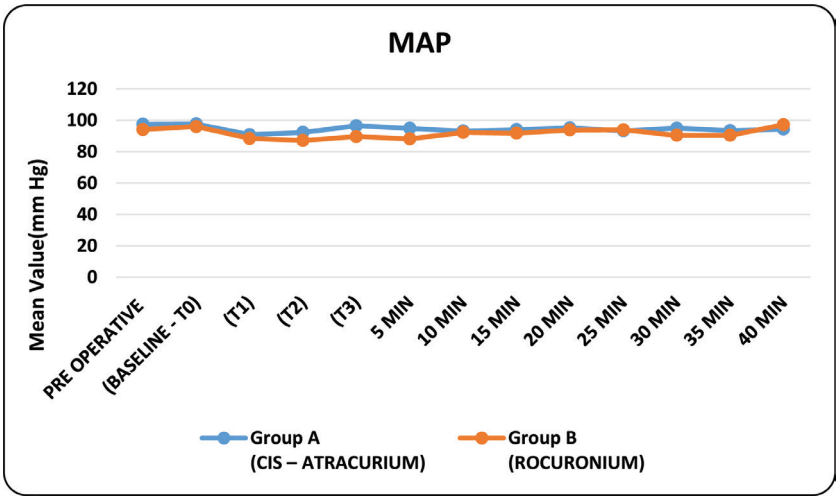
In our study, both groups were comparable in terms of age, weight, and Mallampati class, ensuring that there was no confounding bias (Table 1). As shown in figures 1&2, the hemodynamic variables were comparable in both the groups. There was a transient fall in systolic, diastolic, and mean arterial blood pressure after induction in both the groups, which was statistically insignificant.

The mean onset of action of cisatracurium 0.1 mg/kg was 233.33±81.71 seconds, and with rocuronium 0.6 mg/kg was 86.66±28.41 seconds ($p < 0.001$), which showed that the onset of action was significantly longer with cisatracurium group as compared to the rocuronium group. Other studies reported that the faster onset of action of rocuronium could be attributed to the fact that low potency neuromuscular blockers like rocuronium have more molecules to diffuse from the central compartment into the effect compartment, where they act promptly.[6-8] Weaker binding of low potency drugs to receptors prevent buffered diffusion, and more molecules occupy receptors causing rapid onset. Potent drugs like cisatracurium undergo

Table 1 Study variables and observation results

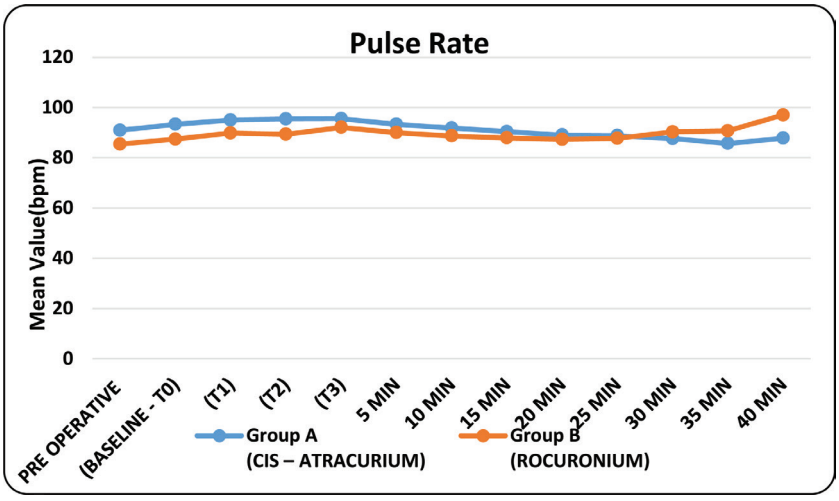
Variables	Group C	Group R	p
Age, mean±SD	39.50±8.06	35.90±7.29	
Body weight (kg), mean±SD	59.07±6.08	61.60±9.16	
Mallampati class, mean±SD	1.27±0.45	1.27±0.45	
Intubating condition at TOF 0/4:			
Excellent, n(%)	22 (73.3)	23 (76.7)	
Good, n(%)	8 (26.7)	7 (23.3)	
Poor, n(%)	0	0	
Impossible, n(%)	0	0	
Onset of action (seconds), mean±SD	233.33±62.31	86.66±28.62	<0.001[a]
Clinical duration (minutes), mean±SD	40.00±3.56	27.46±2.14	<0.001[a]
Recovery index (minutes), mean±SD	12.23±1.54	8.30±1.80	<0.001[a]

C: cisatracurium; R: rocuronium; SD: standard deviation; TOF: train of four; [a]Chi-square



T1: after induction and before injection of NMB
T2: after injection of NMB and before endotracheal intubation
T3: just after intubation

Figure 1 Comparison of the mean arterial pressure (MAP)



T1: after induction and before injection of NMB
T2: after injection of NMB and before endotracheal intubation
T3: just after intubation

Figure 2 Comparison of the pulse rate

buffered diffusion causing repetitive binding and unbinding to receptors, so onset is prolonged.

Our study is in agreement to results documented by Carroll *et al.*[9] who observed median onset time as 3.4 minutes for cisatracurium and 1 minute for rocuronium. Kim *et al.*[10] also reported median onset time with cisatracurium group as 3.9 minutes, which is similar to our study. However, few authors have reported a slight difference in onset time with cisatracurium and rocuronium as compared to our study, which could be attributed to methodological differences in recording the onset time. In our study, the onset of action was recorded when the TOF ratio was 0/4.[5]

The mean duration of action in our study was 40±3.56 minutes for cisatracurium and 27.46±2.14 minutes for rocuronium. It is in agreement with Carroll *et al.*[9] who observed the median duration of action for cisatracurium at 0.1mg/kg was 41 minutes and rocuronium at 0.6mg/kg was 33 minutes. Hofmockel *et al.*[11] studied endotracheal intubation with 0.6 mg/kg rocuronium using mechanomyographic and electromyographic neuromuscular monitoring and reported the duration of action as 28.4±8 minutes. Puhringer *et al.*[12] observed the duration of action for rocuronium was 25.3±5 minutes, which is similar to our study.

The mean recovery index in our study for cisatracurium (12.23±1.54 minutes) was significantly longer than rocuronium (8.30±1.80 minutes). Lepage *et al.*[13] reported recovery index for cisatracurium was 15 minutes, while Puhringer *et al.*[12] observed recovery index with rocuronium as 7.8±2.1 minutes, which is similar to our study. Another study recorded that recovery index after a single dose of rocuronium was 12±5 minutes with isoflurane and 26±11.7 minutes with sevoflurane.[14] The reported recovery index with isoflurane is comparable to our study. The prolonged recovery index with sevoflurane is probably due to faster and more complete equilibrium among the end-tidal, blood, and muscle concentrations of sevoflurane because of its smaller muscle-gas partition coefficient resulting in slow recovery.

The excellent intubating conditions in our study were seen in 22 patients in group A and 23 patients in group B. The good intubating conditions were seen in 8 patients in group A and 7 patients in group B. We attempted intubation in both groups for the first time only when we found TOF to be 0/4 at adductor pollicis. Since vocal cords and other laryngeal muscles are affected more rapidly than the adductor pollicis muscle, we obtained excellent and good intubating conditions in all our patients in both groups. It is in contrast to previous studies that attempted intubation at 60 seconds irrespective of the twitch height.[6,12]

The intubating conditions after cisatracurium in our study were only acceptable after 180 seconds, and this is similar to a previous study.[5] Chetty *et al.*[15] found that the percentage of good or excellent intubating conditions at 60 seconds was 80% for rocuronium but only 12.5% for atracurium. Inconsistent with our results, Zhou *et al.*[8] reported 84% clinically accepted intubating conditions with rocuronium after 60 seconds.

No adverse effects in terms of cardiovascular instability, bronchospasm, or cutaneous flushing due to histamine release were observed in any patient in either group in our study. Various studies have also reported a safe clinical profile with no adverse events with the use of cisatracurium and rocuronium.[5,13,16]

CONCLUSION

Cisatracurium 0.1mg/kg exhibited a slower onset of action compared to rocuronium 0.6 mg/kg but provided acceptable intubating conditions in the majority of patients after 180 seconds. The clinical duration and recovery index were significantly longer in cisatracurium compared to rocuronium.

Both agents are potent and safe with excellent cardiovascular stability. These data suggest that cisatracurium is a useful addition to the armamentarium of currently available non-depolarizing neuromuscular blocking drugs for patients undergoing long duration surgical procedures.

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