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Comparison between rocuronium and cisatracurium: Efficacy and safety, in patients requiring general anesthesia: A randomized prospective study

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Abstract

Background: Neuromuscular blockers (NMB) are very important adjuvant to general anesthesia. Rocuronium bromide (aminosteroidal NMB) and cisatracurium besylate (benzyl isoquinoline NMB) are intermediate acting non-depolarizing muscle relaxants. In a prospective randomized study we had compared both drug at a dose of 3xED95 for Rocuronium and 6xED95 for Cisatracurium as regard the onset of action, intubating conditions, clinical duration, hemodynamic changes, and adverse effects.

Method: 60 patients, ASA I&II, 20-60 year old underwent elective surgical procedure under general anesthesia (GA) were randomly assigned into 2 equal groups. ROC group, where 1mg/kg rocuronium was given and CIS group, where 0.3mg/kg cisatracurium was given. Neuromuscular monitoring was done by stimulating ulnar nerve and recording the action potential of adductor pollicis using TOF count. Standardized GA was given to all patients as follows, fentanyl 2mcg/kg, propofol 2mg/kg, followed by NMB agent of corresponding group at designated dose, patient will be ventilated till TOF count reaches 0, intubation was tried by the anaesthesiologist who was blind to the given NMB, intubation was done if the intubating condition was acceptable (excellent or good), and it was re-attempted every 30 sec if it was poor or inadequate. Anesthesia was maintained by N₂O, O₂ and sevoflurane to a total MAC 1, controlled ventilation was adjusted to normocarbida. Mean arterial blood pressure (MAP), heart rate, and intubating conditions were recorded. Interpretation of TOF count for the onset of action, clinical duration, recovery index was done.

Results: Clinically acceptable intubating conditions were achieved after 60 sec more frequently after rocuronium (80%) than after cisatracurium(0%) and after 90 sec rocuronium (98%) and Cisatracurium(60%). Rocuronium had a significant shorter onset time than cisatracurium (90±30 versus 120±30sec), Rocuronium had a significant shorter duration of action than cisatracurium (35±5 versus 45±5min). There were no evidences of any significant clinical cardiovascular changes in both groups. There were no clinical signs of histamine release in both groups.

Conclusion: Rocuronium has a rapid onset of action with good intubating conditions, cisatracurium has an intermediate duration of action, both are potent and safe with excellent cardiovascular stability and without apparent histamine release.

Keywords: rocuronium, cisatracurium, muscle relaxant and TOF ratio

Introduction

Neuromuscular blockers (NMB) have become essential parts of the anaesthetist armamentarium. They aid in endotracheal intubation, mechanical ventilation, reduce anaesthetic requirements, facilitate surgery for long hours and decrease oxygen consumption. An ideal neuromuscular blocking agent should have rapid onset of action, produce good intubating condition rapidly, intermediate to short duration of action, provide rapid airway control, lack of side effects, should provide cardiovascular stability and adequate recovery [1]. In the development of new neuromuscular blocking drugs, the anaesthesiologist is now provided with drugs that are almost free of unwanted effects, have a time course of action that allows great control of their activity and in most cases, allows the anaesthesiologist to substitute them for succinylcholine. In selecting a neuromuscular blocking agent, an anaesthetist strives to achieve three competing goals: rapid adequate muscle relaxation, hemodynamic stability, and predictable complete return of skeletal muscle function. Succinylcholine [2] reliably produces muscle relaxation within 60 seconds of its administration but it produces side effects such as bradycardia, hyperkalemia [3],

masseter spasm [4], malignant hyperthermia and increase in intra ocular pressure [5].

To replace Succinylcholine, newer non-depolarizing muscle relaxants with intermediate action like rocuronium and cisatracurium are being used. Rocuronium bromide [6] is a non-depolarizing muscle relaxant introduced to the clinical use in the year 1994. It is a mono quaternary analogue of vecuronium with a short onset time, an intermediate duration of action and rapid recovery characteristics coupled with cardiovascular stability, with no histamine release or other side effects.

It produces clinically acceptable intubating condition in 60-90 seconds [7]. However, because rocuronium is mostly metabolized in the liver and excreted through bile, the duration of neuromuscular blockade of rocuronium may be prolonged in patients with liver and renal failure.

Cisatracurium is a new benzylisoquinoline neuromuscular blocker. The generic name cisatracurium was conceived by scientists at Burroughs Wellcome [8] Co. by combining the name "atracurium" with "cis" because the molecule is one of the three cis-cis isomers comprising the ten isomers of the parent atracurium. It has an intermediate duration non-depolarizing neuromuscular blocking drug that has recently been introduced into clinical practice and has a potency approximately three to four times at higher doses than atracurium. Cisatracurium besylate undergoes Hofmann elimination, a process dependent on pH and Temperature. Cisatracurium unlike atracurium is devoid of histamine induced cardiovascular effects.

Materials and Methods

This present study was designed as a prospective double blind randomized comparative study on 60 ASA I & II patients undergoing elective surgical procedures under general anaesthesia. After obtaining prior institutional ethical committee clearance, the patients were visited pre operatively, full pre anaesthetic check-up were done. An informed written consent was taken from all the patients under this study.

Patients between 20 to 60 age group who are ASA I & II and elective surgeries under general anaesthesia were included in this study. Patient who are ASA III and above, pregnant females, patients with any hepatic or renal disease, history of any neuromuscular disorder and BMI >30 kg/m² were excluded in this study.

All the patients were kept nil by mouth for 6 to 8 hrs. On arrival in the operation room, Standard monitors were attached and baseline heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (spo₂) were recorded. Neuromuscular monitors (TOF) were attached. Intravenous access was obtained with an intravenous cannula 18 G in the left upper limb.

All patients were preloaded with crystalloid Ringer lactate 8ml/kg. Patients were premedicated with Inj. Glycopyrolate 0.004mg/kg, Inj. Ondansetron 0.08 mg/kg, Inj. Midazolam 0.02mg/kg, Inj. Fentanyl 2 mcg/kg, and baseline TOF readings were taken. Patients were induced with standard dose of Inj. Propofol 2mg/kg. After confirming adequacy of ventilation, group C and group R received designated dose of their muscle relaxant. Both intubator and the patients were blind to this study. Patients were ventilated till the TOF count reached 0 in neuromuscular monitor. Intubation was attempted once the TOF reached 0 and intubating

conditions were assessed using a four point scale during direct laryngoscopy (CL grade) [9] [excellent, good, poor, or inadequate]. If the intubating condition was excellent or good, tracheal intubation was performed with appropriate size cuffed endotracheal tube, and if it was poor or inadequate, intubation was postponed and re-attempted every 30 second. The time taken from induction dose of muscle relaxant to ideal condition for laryngoscopy was noted.

Conditions for intubation are graded as follows [10]

Excellent: Relaxed jaw, abducted immobile vocal cords, and no diaphragmatic movement.

Good: Relaxed jaw, abducted immo-bile vocal cords, and some diaphragmatic movement (bucking).

Poor: Relaxed jaw, moving vocal cords, coughing on intubation.

Inadequate: Jaw is not relaxed, add-ucted vocal cords, and impossible intubation.

Anaesthesia was maintained with O₂ (1L/min), N₂O (1L/min), Sevoflurane @ 1.0 MAC, maintenance dose of muscle relaxant based on TOF response, to maintain TOF % less than 30%.

Intra operative monitoring included hemodynamic monitoring i.e, heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure oxygen saturation and neuromuscular monitoring i.e, TRAIN OF FOUR (TOF) [11]. At the end of surgery, administration of all anaesthetic agents were stopped and reversal attempted with Inj. Neostigmine 0.05mg/kg and Inj. Glycopyrolate 0.008mg/kg. Reversal was given after TOF count raised to 4 and TOF % >90%. Extubation was done after full reversal of muscle relaxation.

Observation and Results

Statistical Analysis

The statistical analysis was done by using SPSS-2. The statistical analysis was done by calculating mean and standard deviation. For detail analysis, Chi-square test, Unpaired t test and Mann-Whitney test were used to calculate the P value and to establish correlation between study groups. A p value < 0.001 was considered highly significant statistically, a p value <0.05 was considered significant, whereas a p value > 0.05 was considered insignificant.

Results

60 patients were recruited in the study, the patients were randomly divided in two groups of 30 patients. The current study showed no significant differences in demographic data that included age, gender and also with regards to ASA and mallampati classification.

ASA and mallampati classification

	Group R (n=30)	Group C (n=30)
Age (year)	38.8 ± 8.39	43.43 ± 11.32
Gender (M/F)	8/22	7/23
Body Weight (kg)	54.9 ± 5.14	53.96 ± 5.46
ASA (I/II)	17/13	20/10
Mallampati score (I/II)	22/8	21/9

Values are expressed in terms of mean±SD. No significant differences were found between the two groups. (P>0.05), SD= Standard deviation With regards to vital signs and hemodynamic stability pre operatively and intra operatively the recorded HR, MAP showed no statistically significant

difference between both the groups.

Mean value for baseline HR for group C and group R were 78.26 ± 5.42 and 79.46 ± 5.55 respectively which were not statistically significant.

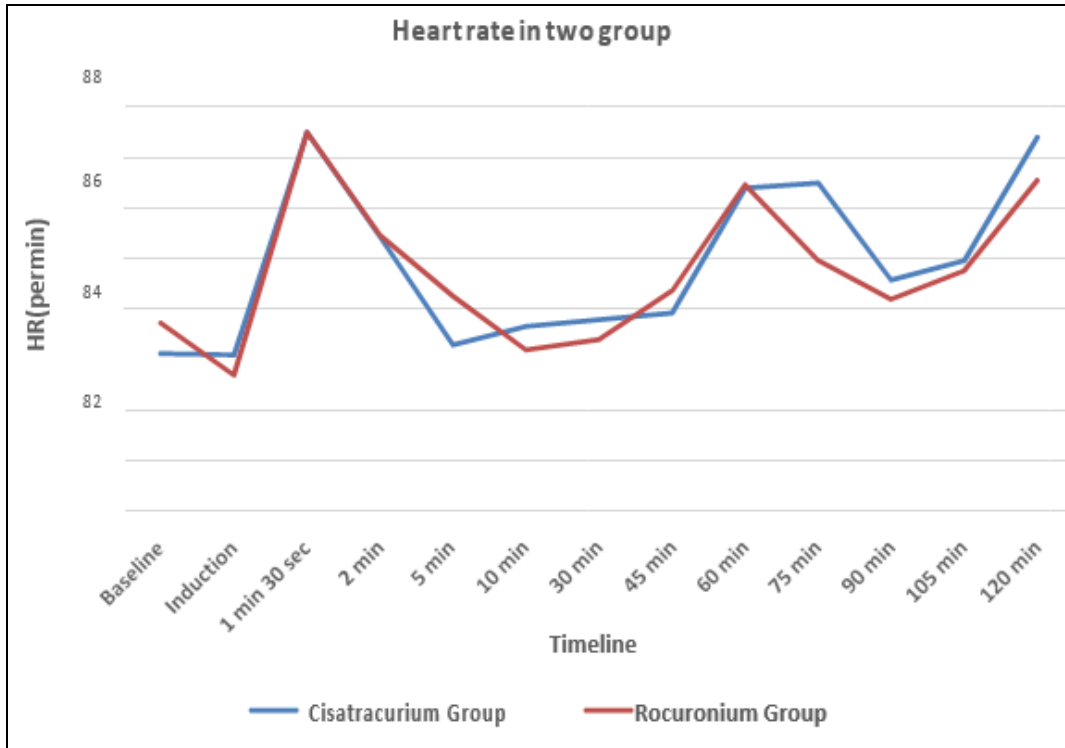


Fig 1: shows distribution of heart rate among two groups ie, baseline, induction, starting from 0 min of administration of imuscle relaxant till end of surgery.

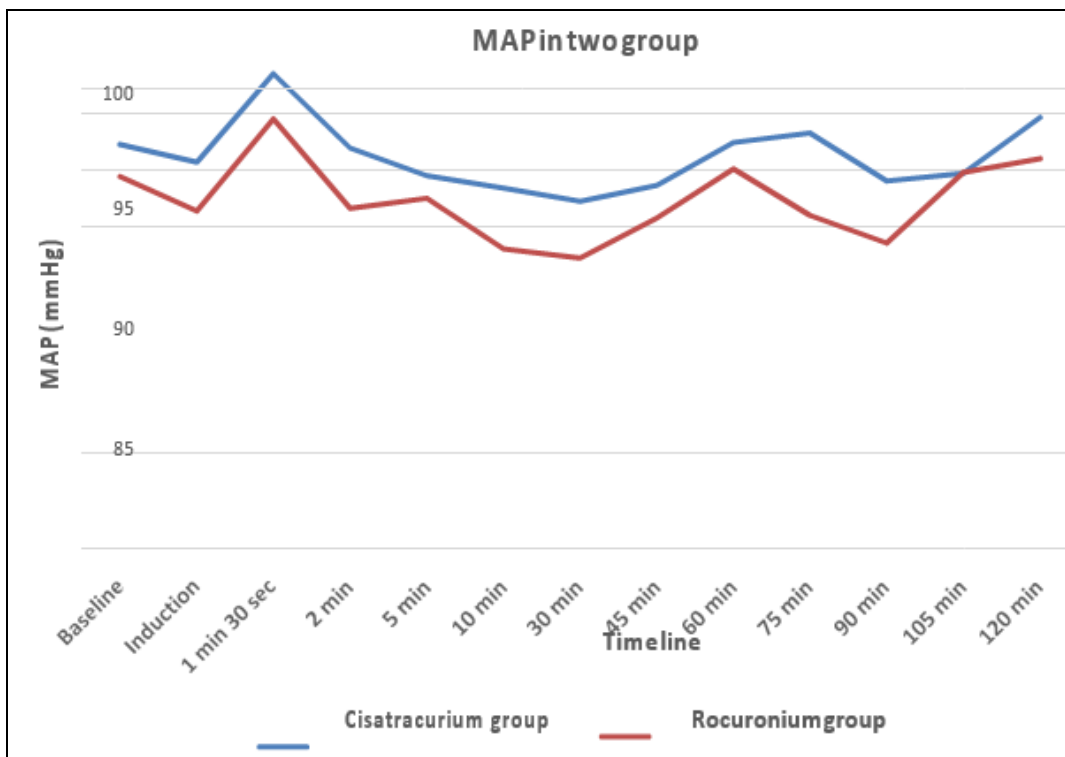


Fig 2: Shows distribution of mean arterial blood pressure among two groups ie, baseline, induction, starting from 0 min of administration of muscle relaxant

After administration of muscle relaxant the mean value of mean arterial blood pressure for group C 98.53 ± 9.82 and for group R 94.53 ± 1 . This trend continued every min

thereafter till end of surgery. On applying Mann Whitney test none of the p value showed any significant difference between the two groups.

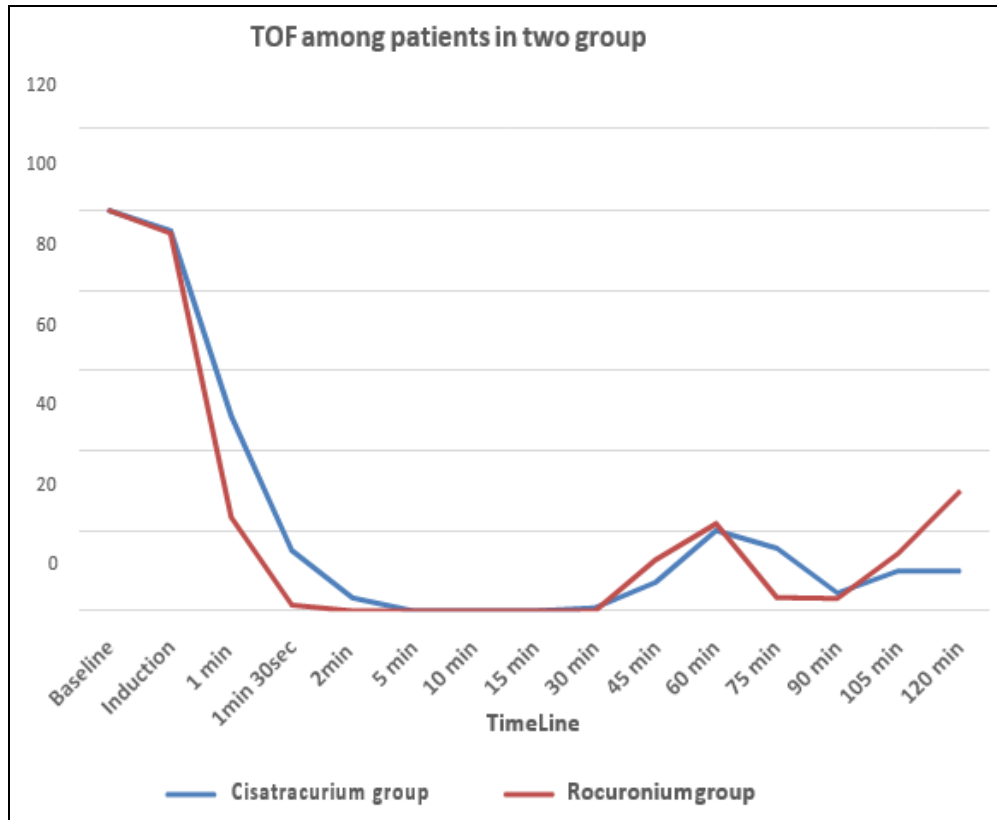


Fig 3: shows distribution of TOF score among two groups ie, baseline, induction, starting from 0 min of administration of muscle relaxant till end of surgery.

After administration of muscle relaxant the mean value of TOF score at 1min 30 sec for group C 15.1 ± 16.10 , group R 1.5 ± 4.5 . On applying Mann whitney test showed a p value

< 0.0001 (< 0.001) and the observed difference was highly significant.

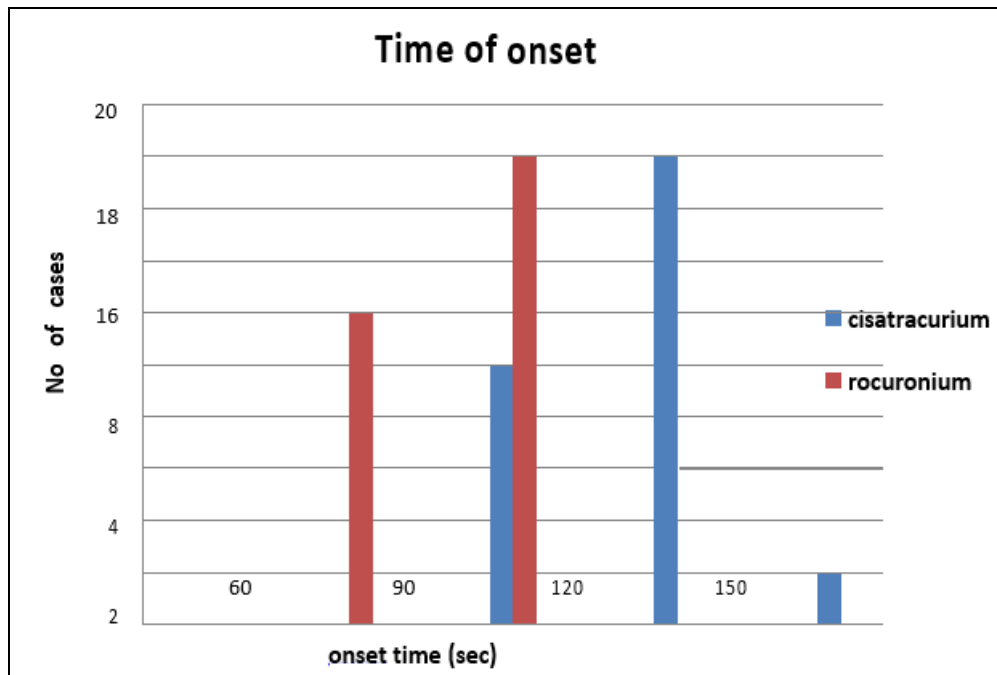


Fig 4: Shows comparison of onset of action between two groups with TOF score.

Group C showed TOF 0 at 90 sec for 10 cases and at 120 sec for 18 cases and at 150 sec 2 cases, whereas group R showed TOF 0 at 60 sec for 12 cases and 90 sec for 18

cases. On applying Mann Whitney test p value 0.0003 (<0.001) showed highly significant difference between the two groups.

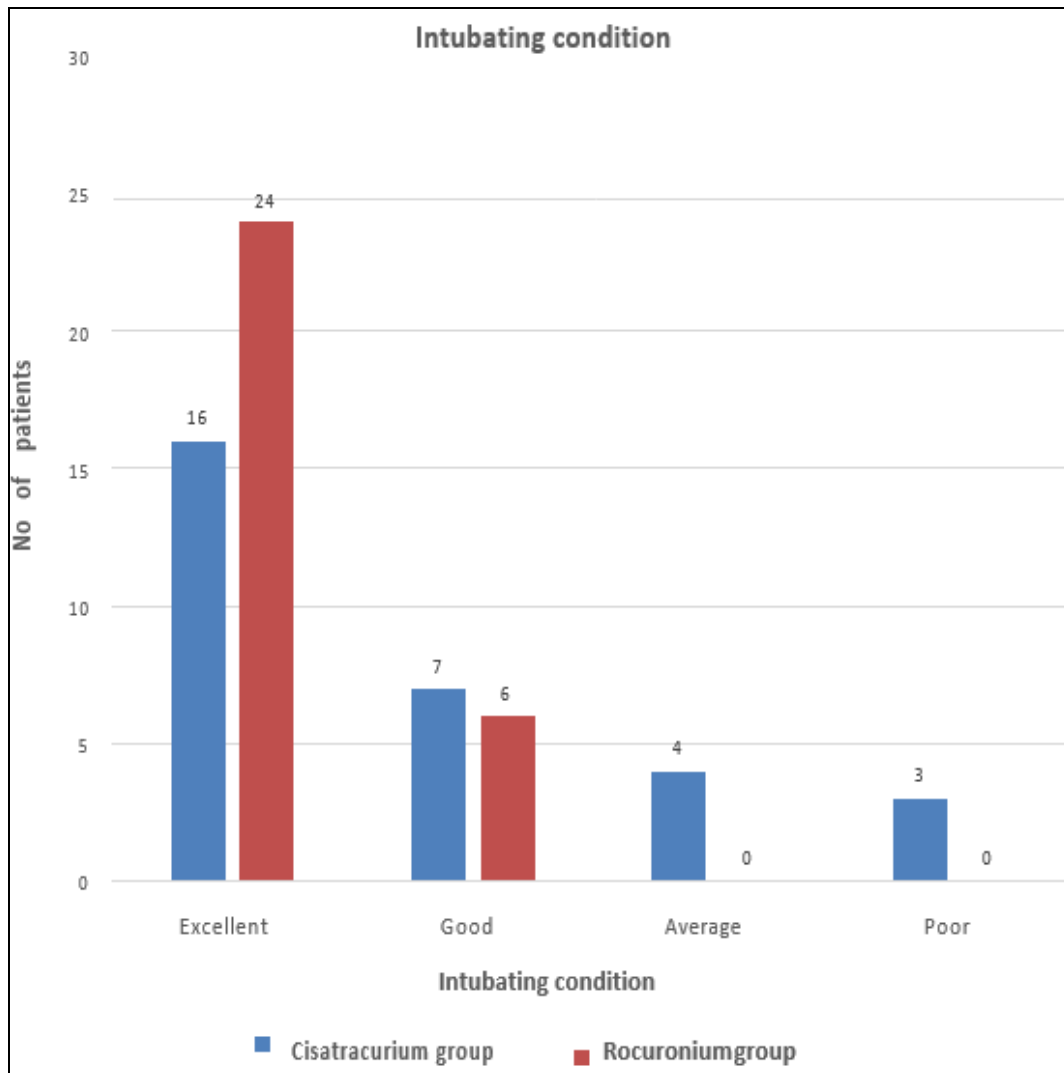


Fig 5: Shows comparison between intubating condition among the two groups.

Group C showed excellent intubating conditions in 16 cases, good intubating conditions in 7 cases, average intubating conditions in 4 cases and poor intubating conditions in 3 cases whereas in group R showed excellent intubating conditions in 24 cases, good intubating conditions in 6 cases and no cases showed average or poor intubating conditions. On applying chi square test which showed a p value 0.03 (<0.05) and the difference between two groups were statistically significant.

Neuromuscular blockers (NMB) are very important adjuvant to general anesthesia. During general anaesthesia, after induction endotracheal intubation is facilitated by either depolarizing or non-depolarizing neuromuscular blocking agent. Succinylcholine is undoubtedly the ultra-short acting muscle relaxant with rapid onset but it has many side effects such as increase in IOP, intragastric pressure, myalgia, bradycardia and cardiac arrest. Hence globally there was search for an alternative for succinylcholine which has rapid onset and less side effects. Rocuronium is an amino steroidal non-depolarizing

neuromuscular blocking drug and represents a major step forward in meeting the requirements of an ideal muscle relaxant. It has a rapid onset and excellent intubating condition. It is used in different doses: 0.6 mg/kg, 0.9mg/kg, 1.2 mg/kg for rapid intubation [12]. Cisatracurium is a new benzyl isoquinoline neuromuscular blocker which has intermediate action. It is one of the 10 stereoisomers of atracurium and has a potency approximately three to four times at higher doses than atracurium.. It is used in different doses 0.1 mg/kg, 0.2mg/kg, 0.3 mg/kg. It has longer onset of action which makes it less suitable for rapid sequence intubation. In the current study we decided to compare Rocuronium and Cisatracurium for onset of action, intubating condition and hemodynamic changes in patients posted for elective surgeries under general anaesthesia.

Heart rate, systolic BP, Diastolic BP, Mean arterial pressure were measured at baseline, induction, 1 min, 2 min, 5 min till 15 min after administration of NMB till end of surgery for both the groups. There were no significant hemodynamic parameter changes observed between these two groups on

administration of NMB. These findings correlate with the study conducted by Magdy Omera, Yasser M. Hammad [13] in 2005 to compare onset of action, intubating condition and safety between rocuronium and cisatracurium. On observation there were no evidence of any significant clinical cardiovascular changes in both the groups and our results were consistent with this study.

Ashraf Mounir Amin, Mohammad Yosry [14] in 2009 also conducted a study to compare neuromuscular blocking and hemodynamic effects of rocuronium and cisatracurium under sevoflurane or TIVA. On observation hemodynamically rocuronium and cisatracurium did not exert significant changes and our result was consistent with this study.

Onset of action for group C was 120 ± 30 sec and group R was 90 ± 30 sec with a p value $0.0003 (<0.001)$ which showed statistically high significance. These findings correlates with study conducted by Magdy Omera, Yasser M. Hammad in 2005 [13] to compare the onset of action, intubating condition and safety between rocuronium. On conclusion of this study rocuronium showed significant shorter onset time than cisatracurium (70.6 ± 18.2 sec vs 160.4 ± 14.3 sec) which is consistent with our study.

There was another study conducted by Geoffrey K. lighthall, Mark A Jamieson [15]. in 1999 to compare onset of action and duration of high dose cisatracurium and rocuronium. 40 patients of ASA I and II, 10 in each group where randomly assigned and group 1 received rocuronium 0.9 mg/kg, group 2 received rocuronium 1.2 mg/kg, group 3 received 0.15 mg/kg cisatracurium and group 4 received 0.2 mg/kg cisatracurium. On conclusion of this study equipotent dose of rocuronium had faster onset compared to cisatracurium 3 x ED95 (134 sec vs 220 sec) and 4 x ED 95 (95 sec vs 162 sec) The mean difference between cisatracurium and rocuronium at 3 and 4 times the ED95 were 86 seconds and 67 seconds (p value <0.05) showed significant shorter onset time for rocuronium which was consistent with our study.

Milan Adamusa, Radim belohlavekb [16] in 2006 also conducted a study with 120 patients scheduled for elective surgery randomly assigned into 4 groups with group 1 received cisatracurium 0.1mg/kg, group 2 cisatracurium 0.15 mg /kg, group 3 rocuronium 0.6 mg/kg and group 4 rocuronium 0.9 mg /kg. On conclusion the study revealed onset time were 277 sec, 220 sec, 92 sec and 77 sec for cisatracurium and rocuronium respectively which showed shorter onset of action for rocuronium at higher dose and it was consistent with our study.

In our study intubating condition for group C showed excellent intubating condition in 16 cases, good intubating condition in 7 cases, average intubating condition in 4 cases and poor intubating condition in 3 cases whereas in group R showed excellent intubating condition in 24 cases and good intubating condition in 6 cases (p value 0.03) statistically which showed rocuronium had better intubating condition than cisatracurium.

These findings correlate with the study conducted by Magdy Omera, Yasser M. Hammad [13] in 2005 to compare onset of action, intubating condition and safety between rocuronium and cisatracurium. Intubation was attempted at 60 sec after administration of NMB. Clinically acceptable intubating condition were achieved more frequently after rocuronium (80%) than cisatracurium (0%). On conclusion rocuronium provided better intubating condition than cisatracurium and

it was consistent with our study M. El-Kasaby, H. M. Atef [17] in 2010 also conducted a study to compare between atracurium (2 x ED95) and different doses of cisatracurium (2 x ED95, 4 x ED95, 6 x ED95) for onset of action, duration of action and intubating condition. On conclusion $6 \times ED95$ dose of cisatracurium showed statistically significant difference versus the atracurium dose with higher percentages of patients with excellent condition of intubation. $4 \times ED95$ and $6 \times ED95$ doses of cisatracurium were significantly better than $2 \times ED95$ dose of cisatracurium.

Conclusion

From the present study we concluded that Rocuronium had shorter onset of action (90 ± 30 sec) than Cisatracurium (120 ± 30 sec). Rocuronium at a dose of 1mg/kg (3 x ED95) provided excellent intubating conditions with a TOF score at 90 sec and Cisatracurium at a dose of 0.3 mg/kg (6 x ED95) provided better intubating conditions with TOF 0 at 120 sec. Rocuronium provided excellent intubating condition than Cisatracurium at a shorter onset of time. There were no hemodynamic changes and adverse reactions noted during the study between these two drugs.

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