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Comparative evaluation of the effect of rocuronium and cisatracurium on intubating conditions

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Abstract

Introduction: A study was undertaken in 60 patients to evaluate the effect of rocuronium and cisatracurium on intubating conditions, who were scheduled for various surgical procedures under general anaesthesia. The aim of the study was to compare the onset of action, intubating conditions, clinical duration, and side effects of the rocuronium and cisatracurium.

Methods: After the institutional ethics committee approval and informed consent, 60 patients scheduled for elective surgery under general anaesthesia, were randomized into 2 groups to receive rocuronium 0.90 mg.kg^{-1} (3×ED95) and cisatracurium 0.15 mg.kg^{-1}(3×ED95) doses to facilitate tracheal intubation. For each patient, the onset time for 95% depression of T1, clinical duration until 25% recovery from T1 were recorded.

Results: Rocuronium bromide 0.9 mg.kg^{-1} body weight produces excellent intubating conditions in 100% of patients at 90 seconds with a mean onset of action 87 ± 6.51 sec and average clinical duration of action of 63.1 ± 4.50 minutes. Cisatracurium 0.15 mg.kg^{-1} body weight produces excellent intubating conditions in 56.67% of patients and good intubating conditions in 43.4% of patients at 90 seconds with an average onset of action 122.8 ± 8.03 sec and average clinical duration of action of 50.83 ± 3.77 minutes. Recovery time in both groups was statistically insignificant. None of the patient in both groups had any side effect.

Conclusion: Rocuronium bromide appeared to be a safe alternative to cisatracurium for intubation in adult patients with same 3×ED_{95} dose as rocuronium provides shorter duration of action and better intubating conditions with same recovery profile.

Keywords: rocuronium, cisatracurium, tracheal intubation

Introduction

The introduction of muscle relaxants, more appropriately called neuromuscular blocking agents, into clinical practice in 1942 was an important milestone in the history of anaesthesia. Neuromuscular blocking agents are used to improve conditions for tracheal intubation, to provide immobility during surgery, and to facilitate mechanical ventilation. Neuromuscular blockers (NMBs) become an essential part of the anaes thesiologists armamentarium. They aid endotracheal intubations, mechanical ventilation, decrease anaesthetic requirement, prevent patient movement, facilitate surgery and decrease oxygen consumption.

For several decades, suxamethonium was the gold standard relaxant for rapid sequence intubation. However, the side effects such as muscle fasciculations, hyperkalaemia, rise in intracranial and intraocular pressure led to search of newer muscle relaxants. Therefore search for an ideal neuromuscular blocking agent continued for rapid and safe endotracheal intubation. Rocuronium has an intermediate duration of action and produces its maximum effect within two minutes which is much more rapid than any other non-depolarizing relaxant and this is probably a result of its poor potency [1].

Cisatracurium, the isomer of atracurium, is another kind of non-depolarizing neuromuscular blocking agent introduced in clinical practice in 1995. It belongs to benzylisoquinolinium class and have intermediate duration of action. A Good to excellent conditions for tracheal intubation occur within 1.5–2 or 1.5 minutes following IV dose of 0.15 or 0.2 mg/kg, respectively.

Thus the present study was undertaken with the aim to evaluate and compare the effect of rocuronium and cisatracurium on the onset of action and intubating conditions in patients undergoing general anaesthesia.

Material and Methods

After obtaining institutional ethical committee's approval and a written informed consent, a prospective, randomized, double blind study was done in 60 patients, aged 18-60 years, of ASA status 1 & 2 who were undergoing elective surgeries under GA. Exclusion criteria were: increased risk of pulmonary aspiration, neuromuscular disease, Mallampatti grade III and IV, medications known to influence neuromuscular function, anticipated difficulty with airway management, and contraindications to succinylcholine. Patients were randomly allocated into two groups of 30 patients each. Group 1 patients received rocuronium (0.9mg/kg) (ED_{95}×3) and Group 2 patients received cisatracurium (0.15mg/kg) (ED_{95}×3) to facilitate tracheal intubation.

All patients underwent a thorough preanaesthetic checkup

which included complete medical history, physical examination including vital signs and airway assessment. All routine investigations including complete blood count, fasting blood sugar, chest x-ray, ECG, BT, CT for all patients were done. Patients were kept fasting for 6-8 hrs preoperatively. All patients received injection metoclopramide 10 mg, 1 hour before anaesthesia. Standard monitoring, including noninvasive arterial blood pressure, electrocardiography and pulse oximetry were applied and assessed continuously. Baseline pulse rate, mean arterial pressure were recorded. Before induction of anaesthesia, surface electrodes were placed over the ulnar nerve at the wrist for neuromascular monitoring. Neuromascular monitoring were done by using the NMT module of Mindray anaesthesia work station (BeneViewT9).

In operative room patients were premedicated with inj. glycopyrrolate 0.004 mg/kg, midazolam 0.04 mg/kg and inj. fentanyl 2 mcg/kg intravenously. After preoxygenation with 100% oxygen, anaesthesia was induced with propofol 2.0 mg/kg slow intravenously. After the loss of consciousness, the ulnar nerve was stimulated at the wrist with a square wave stimulus set at a current of 50 mA and duration of 0.2 ms. Each stimulus was delivered in a train-of-four (TOF) sequence and repeated every 12 seconds using NMT module of Mindray anaesthesia work station (BeneViewT9). After induction of anaesthesia and loss of eye lashes reflex, the group 1 (n = 30) received 0.9 mg/kg of rocuronium (3 × ED95), and the group 2 (n = 30) received 0.15 mg/kg of cisatracurium (3× ED95). Rocuronium and cisatracurium syringes were prepared by an independent anaesthesiologist in a total volume of 10 ml with normal saline. Endotracheal intubation was performed after 90 seconds of the study drug administration that supposed to be appropriate time for intubation. The anaesthesiologist who performed intubation, was not involved in the anaesthesia technique, and he was blinded to the neuromuscular blocking agent's type. Intubating conditions were assessed using the four point scoring scale described by Goldberg ME *et al*[2] (Table-1). Another anaesthesiologist, who was not involved in preparing and administering the study drug, recorded the time to intubation and suppression of maximal T1 on TOF. To avoid vocal cord injury, endotracheal intubation was not be attempted if the vocal cords were fully closed. After endotracheal intubation, anaesthesia was maintained with sevoflurane inhalation in oxygen. Mechanical ventilation was adjusted to maintain end tidal CO_2 between 35 and 40 mmHg. Subsequent neuromascular blockade was maintained to a depth of no response to TOF using repeated doses of rocuronium 0.1mg/kg and cisatracurium 0.02mg/kg according to group allocated. At the end of the surgery, neuromascular blockade was reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.008mg/kg, when two response to TOF stimulation and twitch height recovery above 25% was appeared. The trachea was extubated when four response to TOF stimulation was present, the patient regained consciousness and attained adequate muscle power and normal respiration with adequate tidal excursion.

Haemodynamic status was monitored by observing changes in pulse rate, mean arterial pressure at different time intervals. The onset time and duration of action of drug was determined by using NMT module of Mindray anaesthesia work station (BeneViewT9). The onset time of muscle relaxant is defined as the time from the injection of drug to its peak effect. Hence, onset time was taken as the time interval from the end of neuromuscular blocking agent administration to the maximal suppression of T1. The time between the administration of neuromuscular blocking drug and return to 25% of twitch response (by train of four) was taken as the clinical duration of action.

The observed results were compiled and analyzed statistically by using Chi Square test for qualitative data and Student "t" test for quantitative data. Difference between the groups were considered significant when p value was <0.05.

Table 1: Gldberg's scale for evaluation of Intubation

S. No.	Grade	Intubating conditions
1	Excellent	Easy passage of the tube without coughing. Vocal cords relaxed and abducted
2	Good	Easy passage of the tube, slight coughing and/or buckling. Vocal cords relaxed and abducted
3	Poor	Easy passage of the tube, moderate coughing and/or buckling. Vocal cords relaxed and abducted.
4	Impossible	Vocal cords not relaxed. Tightly abducted.

Results

Patient's demographic variables were comparable in both groups (Table-2). Both groups were comparable with regard to haemodynamic changes during the study period (Fig. 1 & 2) All patients had excellent intubating condition in group 1 which was significantly better than group 2 where only 17 patients (56.6%) had excellent intubating condition and 13 patients (43.4%) had good intubating conditions. None of the patient had poor intubating conditions in either of the group. The mean onset time was found to be significantly longer in group 2 than group 1 while mean duration of action of intubating dose of muscle relaxant (clinical duration) was found to be significantly longer in group 1 than group 2 (Table-2). Recovery time in both groups was statistically insignificant. None of the patient in both the groups had any side effects intraoperatively and postoperatively up to 24 hrs.

Table 2: Patient Characteristics

Group Parameters	Group 1	Group 2	P-Value
Age (Years)	46.46±8.21	43.26±9.84	Insignificant
Weight (Kg)	53.8 ± 7.27	52.9±6.37	Insignificant
Sex M:F	14:15	16:15	Insignificant
Mean Onset time (sec)	87±6.51	122.8±8.03	0.001
Duration of action of intubating dose (min)	63.1±4.50	50.83±3.77	0.001

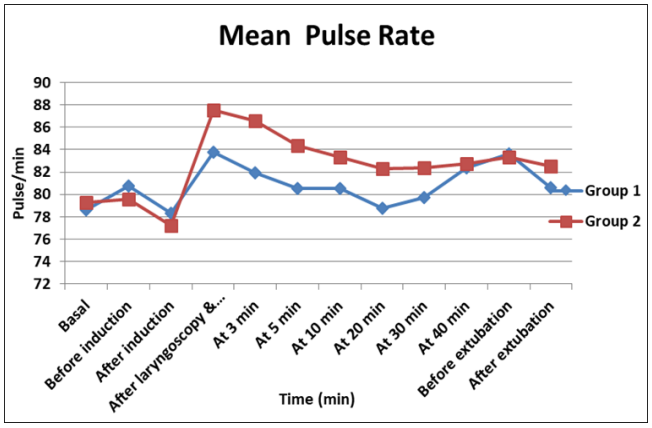

Fig 1: Changes in Pulse rate

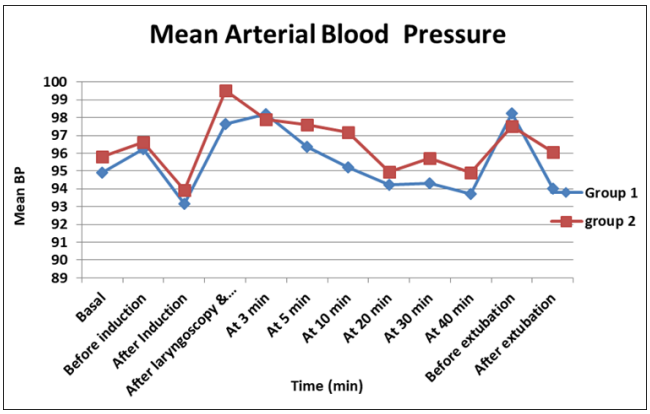

Fig 2: Changes in Mean arterial blood pressure

Discussion

The ideal neuromuscular blocking drug should be competitive and nondepolarizing in nature, having rapid onset of action with relatively short duration of action, cessation of neuromuscular blockade, should not depend on renal and hepatic functions, should also be highly specific so that no harmful side effects would occur on other systems and last but not least, the neuromuscular blockade should be antagonized by acetylcholine esterase inhibitors.

Though it is true that suxamethonium chloride, the synthetic quaternary ammonium compound is fairly satisfactory muscle relaxant, it is not free from side effects like postanaesthetic myalgia, hyperkalaemia, an increase in intragastric pressure and intraocular pressure. Therefore, there has been a continuing search for a nondepolarising muscle relaxant with rapid onset of action suitable for early intubation to provide an alternative to suxamethomiun chloride.

Rocuronium bromide is a monoquaternary aminosteroidal nondepolarizing neuromuscular blocking agent. It may provide an alternative to succinylcholine for intubation and especially for rapid sequence induction whenever suxamethonium chloride is contraindicated such as in patients susceptible to malignant hyperthermia, hyperkalaemia or in patients with abnormal cholinesterase genotype. This agent is also free from cardiovascular side effects. Rocuronium appears to be drug permitting early intubation of the trachea with nearly all properties of an ideal non-depolarizing muscle relaxant. The drug seems to have sufficient versatility to be used in routine clinical anaesthesia. Cisatracurium is the most recent iso-quinolone NMB which is 3-4 times more potent than atracurium, has the same advantage of Hoffmann degradation and it does not seem to release histamine [3].

This study was performed to compare rocuronium and cisatracurium with regard to onset of action, intubating conditions, clinical duration, haemodynamic changes and adverse effects in patients undergoing elective surgery under general anaesthesia in sixty patients.

In our study rocuronium had a significant shorter onset time than cisatracurium and this early onset of rocuronium correlate with previous studies done by Trekova *et al* [4], Adamus M *et al* [5] and Lee H *et al* [6] who also found significant shorter onset time of rocuronium than cisatracurium. Similarly Toni Magorian *et al* [7] also observed shorter onset time of rocuronium which was 75±28 seconds. In contrast to our study, Lighthall G *et al* [8] found delayed onset of rocuronium (134 sec).

The rapid onset of rocuronium observed in our study has been attributed to its low potency [3, 8], different buffering mechanism (i.e., the repetitive binding of relaxant molecules), or both. Because of the rapid onset of rocuronium and the acceptable intubating conditions after 60 sec, rocuronium was used for rapid sequence intubation [9, 10, 11]. Hence rocuronium offers the fastest onset time of all currently available nondepolarizing neuromuscular blockers [12].

In our study clinical duration of action of rocuronium found to be significantly longer as compared to cisatracurium as evident in Table-1. Similar results were observed by Trekova N *et al* [4], Cooper RA *et al* [13] and Melloni C *et al* [14]. However, Naguib M. *et al* [15] noted a very short clinical duration of action of rocuronium which was 36.4 ± 7.4min.

England AJ *et al* [16] suggested that rocuronium has higher affinity for presynaptic sites than the other NMBDs, which means that rocuronium has a relatively long duration of action compared to short onset time, atypically. Thus, they hypothesized that clinical duration will be prolonged in rocuronium group because of high affinity for the prejunctional nicotinic acetylcholine receptor of rocuronium and recovery characteristics would also be affected by rocuronium.

In present study, we did not observed any change in haemodynamic variables following the administration of rocuronium bromide. Similar trends were seen following the administration of cisatracurium, 0.15 mg kg^{-1} body weight.

The intubating conditions were excellent in 100% patients in rocuronium group as compared to 56.67% patients in cisatracurium group. In our study, recovery time in both groups was statistically insignificant. None of the patient in both groups had any side effect.

Conclusion

Thus we concluded that rocuronium bromide appeared to be a safe alternative to cisatracurium for intubation in adult patients with same $3\times ED_{95}$ dose as rocuronium provided shorter onset of action and better intubating conditions with similar recovery profile.

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