NEUROMUSCULAR BLOCKADE AND INTUBATION CONDITIONS OF THE SINGLE BOLUS DOSE (2xED₉₀) OF ROCURONIUM BROMIDE

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ABSTRACT

Rocuronium bromide (2xED₉₀), a new non depolarising neuromuscular blocking drug with rapid onset, intermediate duration of action and cardiostability was studied in open randomised trial in 30 patients. Neuromuscular block was monitored using a Train of Four stimulus by stimulator electrodes placed on the ulnar nerve close to the wrist. Intubation conditions were assessed subjectively by scoring the jaw relaxation, vocal cord and the response to intubation with same technique of anaesthesia. Clinical recovery (Dur₂₅) of neuromuscular blockade was monitored. Haemodynamic changes were recorded. Intubation conditions were clinically acceptable in 99.6% of patients, (excellent 73%; good 26.6%) at 90s. Time to onset (Lag time) of neuromuscular block was 22.5 ± 12.6 sec and average time for the onset of block (maximum effect) was 90.9 ± 10.6 sec. The duration of clinical muscular relaxation (25% recovery of twitch height) was 22.4 ± 8.30 min. Stability of cardiocirculatory system was seen.

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KEY WORDS: Anaesthesia; Intubation conditions; Muscular relaxants; Rocuronium bromide.

Introduction

Rocuronium bromide is a structural analogue (2-Morpholine 3-hydroxy 16 N-allylpyrrolidine derivative) of vecuronium with a neuromuscular block potency 6-7 times less than that of vecuronium [1,2]. It has intermediate duration of action, cardiovascular stability and more rapid onset than other non-depolarising muscle relaxants. Therefore, it has been suggested to accomplish rapid tracheal intubation [3,4]. This study was designed to determine onset time, intubation conditions, clinical duration and cardiovascular changes of 600 µg kg⁻¹ (2 x ED₉₀) dose of Rocuronium bromide, a new non-depolarising neuromuscular blocking agent recently released commercially in India.

Material and Methods

Thirty patients in American Society of Anaesthesiologists grade I or II of either sex (Male:4, Female:26) between 20-60 years of age gave informed consent to participate in this study. Permission from Institutional Ethics Committee was obtained. Investigators were registered with the Drug Controller of India for this trial at Command Hospital (WC) Chandimandir. Patients with potential airway problems, renal, hepatic, metabolic and neuromuscular disorder were excluded.

Rocuronium bromide, a clear colourless aqueous solution buffered to pH 4 with acetic acid and sodium acetate adjusted to isotonicity with sodium chloride, ampoules containing 50 mg/ 5ml were used. Patients were administered injections atropine 0.6 mg and pethidine 2 mg kg⁻¹ intramuscularly one hour prior to surgery in the operating suite. Anaesthesia was induced with thiopentone

5-6 mg kg⁻¹ intravenously and maintained with N₂O: O₂ (60:40 ratio) and halothane 0.5 -1.0%. Haemodynamics, ECG, Pulse oximetry, capnograph and ambient temperature (32°C) were monitored throughout the study period. Neuromuscular block was monitored using a train of four-Guard, by stimulator electrodes placed on the ulnar nerve close to the wrist. Prior to the administration of the muscle relaxant, a stable control response was obtained by supramaximal stimuli at a frequency of 0.1 Hz recording the force of contraction of the adductor pollicis. Further neuromuscular response of rocuronium bromide was recorded with single twitch stimulation till spontaneous recovery of the TI response to 25% when the effect of neuromuscular block was reversed with atropine neostigmine mixture or further block was maintained with pancuronium bromide. Same stimulation mode was used in all patients.

At loss of eyelash rocuronium bromide 600 µg kg⁻¹ was administered as a bolus dose within 5s in a rapidly running IV infusion. Patients were intubated when maximum neuromuscular block was achieved. Time lag (from end of administration of neuromuscular blocking agent to first measurable effect) and time to onset (Time of maximum block) were recorded. The recovery to twitch height to 25% of control was recorded as (Dur₂₅) clinical duration of action.

Cardiovascular status, systolic, diastolic and mean arterial pressure; and heart rate were recorded every 5 min after the administration of muscle relaxant.

Intubating conditions: Intubation conditions were assessed using the standard scoring of intubation conditions (Table 1).

Scoring of Intubation may be clinically defined as the criteria of intubation conditions, excellent (Score 3): easy passage of the endotracheal tube without coughing; good (score 2): passage of the tube with slight cough, vocal cords relaxed; poor (score 1): passage of the tube with moderate coughing or bucking; Impossible (Score 0): vocal cords adducted or not visualised, jaw not

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TABLE 1
Scoring of intubation conditions

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Poor	Closed	Severe coughing or bucking
1	Minimal	Closing	Mild coughing
2	Moderate	Moving	Slight diaphragmatic movement
3	Good	Open	None

relaxed. Good and excellent (Score 2 or 3) intubating conditions will be clinically acceptable where as poor and impossible (Score 1 or 0) will be clinically unacceptable.

Statistical analysis of the data was carried out as sample size, mean standard deviation and chi square test.

Results

Thirty adults, male 4; female 26 with average age 37.9 ± 4.2 yr, weight 59.2 ± 8.13 kg, height 165.4 ± 15.0 cm were administered $600 \mu\text{g kg}^{-1}$ rocuronium bromide with thiopentone: $\text{N}_2\text{O} : \text{O}_2$ halothane anaesthesia to assess single bolus dose neuromuscular blockade of the drug. Intubation conditions were clinically acceptable in 99.6% of patients (excellent, 73%; good 26.6%) at 90s based on scoring of intubation conditions. The first demonstrable effect of neuromuscular block (Lag time) was 22.53 ± 10.66 s and an average for the onset of block was 90.96 ± 10.66 s. The duration of clinical muscular relaxation (25% recovery of twitch height) was 22.43 ± 8.30 min. No significant changes were observed in arterial pressure and heart rate.

Discussion

Rocuronium, 1- [(2, 3, 5, 16, 17)-17-(acetyloxy) -3 hydroxy-2 (4 morpholinyl) - androstan-16-YL]-1-(2-propenyl) pyrrolidinium bromide is a new muscle relaxant, 5-10 and 6-7 times less potent in animals [5] and man [6] than vecuronium. Fast onset of action to block peripheral muscle twitches may be the outstanding property of this drug to facilitate its release in clinical anaesthesia. Its onset is 3-5 times more rapid in animals [5] and 2-3 times in man [6]. ED₉₀ dose of rocuronium [7] ranges between $0.27\text{--}0.41 \text{ mg kg}^{-1}$, less potent than other non-depolarising muscle relaxants (Table-2).

TABLE 2
Potency of nondepolarising muscles relaxants

Drug	ED ₉₀ ($\mu\text{g kg}^{-1}$)
Doxacurium	30
Pipecuronium	40
Vecuronium	50
Pancuronium	60
Mivacurium	100
Atracurium	250
Rocuronium	300
D-tubocurarine	400

Mogensen [7] concluded that ED₅₀ is around $200 \mu\text{g kg}^{-1}$ and ED₉₀ around $300 \mu\text{g kg}^{-1}$. ED₉₀ ($300 \mu\text{g}$

kg^{-1}) dose of rocuronium has onset time between 1.5-4.0 min in man. Increasing the dose to $2 \times \text{ED}_{90}$ ($600 \mu\text{g kg}^{-1}$) reduced the time to onset between 1.0-1.7 min. Present study showed time to onset 90.96 ± 10.66 s comparable with other workers [8-10]. Rocuronium, ED₉₀ dose produces [6] clinical duration of neuromuscular block between 11.0 ± 4 to 14.0 ± 3 min. Time course of action of rocuronium $2 \times \text{ED}_{90}$ during nitrous oxide oxygen opioid anaesthesia produces >85% neuromuscular block in <90 secs for 14-47 mins [11]. Meistelman et al [12] demonstrated that rocuronium bromide produces more rapid but less intense vocal cord neuromuscular block than at the adductor pollicis. Therefore, good to excellent intubation conditions can be achieved in <90 secs because the paralysis of the vocal cords precedes that of the adductor pollicis. Short duration and low intensity neuromuscular blockade at the larynx reduces the incidence of post operative respiratory distress due to laryngeal paresis.

In the present study, rocuronium $2 \times \text{ED}_{90}$ produced neuromuscular blockade within 90 secs with good to excellent intubation conditions. This time frame of neuromuscular blockade is acceptable in clinical anaesthesia without compromising cardiovascular stability and duration of action of the muscular relaxation. Speed of onset is built onto the structure activity relationship of this new drug. Retaining the rapid time to onset action, rocuronium has intermediate duration of action similar to that of vecuronium and atracurium. Residual neuromuscular blockade of rocuronium could be easily antagonised by neostigmine as seen by us in this study.

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