Comparative Study of Two Different Doses of Rocuronium Bromide with Suxamethonium Chloride for Endotracheal Intubation

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INTRODUCTION

The introduction of muscle relaxant (d-tubocurarine) into clinical practice in 1942 by Griffith HR and Johnson GE) has refined and improved the anesthetic practice and was an important milestone in the history of anesthesia.¹ Before the introduction of muscle relaxants, inhalational agents had to be used for endotracheal (ET) intubation which was associated with inadequate depth of anesthesia. Further to achieve adequate intubating conditions, higher concentrations were needed to be used and were associated with hemodynamic disturbances.²

Succinylcholine (also known as suxamethonium chloride—introduced by Thesleff and Foldes in 1952) with its ultrarapid onset and short duration of action has been

Abstract

Introduction: Suxamethonium chloride was a time-tested depolarizing muscle relaxant with quick onset of action and produced excellent intubating conditions but it is contraindicated and hazardous in certain situations. Rocuronium bromide had the most rapid onset, intermediate duration of action, minimal cardiovascular side effects, and no histamine release emerged as a good alternative.

Purpose of the Study: To evaluate the efficacy of two different doses of rocuronium bromide in comparison to suxamethonium chloride on the intubating conditions, with emphasis on the duration of action, hemodynamic changes after intubation, and occurrence of any untoward side effects with either drug.

Methods: This was a randomized clinical study conducted at a tertiary care center. 90 patients posted for elective surgeries were divided into groups of 30 each. Depending on the dose of the muscle relaxant Group S received succinylcholine 1.5 mg/kg, Group R6 and R8 received rocuronium bromide 0.6 mg/kg and 0.8 mg/kg, respectively. Laryngoscopy and intubation were done with an appropriate size oral endotracheal tube at 60 s. Relaxation of jaw, vocal cords, and response to intubation were assessed at 60 s and scored using a standard intubation scoring system after injection of the study drug. Results were tabulated and analyzed using mean, standard deviation, and Chi-square test.

Results: We observed excellent intubating conditions in 100% of Group S, 86.66% and 93.33% in Group R6 and R8, respectively. The duration of action of rocuronium 0.6 mg/kg was shorter than 0.8 mg/kg. Thus, increasing the dose led to a longer duration of action. Hemodynamic changes returned to preinduction baseline values by the end of 10 min in all three groups.

Conclusion: Rocuronium at both doses of 0.6 mg/kg and 0.8 mg/kg produced clinically acceptable intubating conditions and can be used as a safer alternative to succinylcholine in situations where it is contraindicated.

Key words: Endotracheal intubation, Intubating conditions, Intubation scoring system, Rocuronium bromide, Suxamethonium chloride
the drug of choice to obtain excellent intubating conditions in less than 60 s for both elective and emergency surgeries. However, the undesired side effects of succinylcholine led to a search for ideal neuromuscular blocking agent among the nondepolarizing type. Rocuronium bromide introduced into clinical practice by Dr. Sleigh and late Dr. Savage in 1990, was the first drug to challenge the onset time of succinylcholine facilitating rapid and safe ET intubation devoid of its side effects.

In this context, the present study was undertaken to compare the intubating conditions of rocuronium bromide with that of succinylcholine along with the clinical duration of action, the hemodynamic changes, and the occurrence of any untoward side effects with either drug.

**METHODS**

This was a randomized clinical study conducted in the Department of Anesthesiology in the operating rooms of Rajah Muthiah Medical College and Hospital, Chidambaram, during 2014-2016. After getting approval from the Institutional Ethical Committee, the study was conducted on a total of 90 adult patients of either sex, aged between 18 and 60 years, belonging to either ASA Class I or II, posted for elective surgery. Patients were excluded from this study when they refused or if they were on medication that might interact with the study drugs. Those with potential airway problems and suspected difficult intubations were also excluded. Furthermore, those with hyperkalemia, neuromuscular, renal, hepatic, and allergic disorders were excluded. A detailed preanesthetic checkup was done for all patients, and informed consent was taken and procedure of the study was explained to them.

Patients were randomly assigned to any one of the following three groups with 30 patients in each group. Group S patients received intravenous (IV) succinylcholine 1.5 mg/kg, Group R6 and Group R8 patients received IV rocuronium 0.6 mg/kg and 0.8 mg/kg, respectively.

In the operation theater, an IV line was secured with appropriate size IV cannula and IV fluid connected. Monitors including noninvasive blood pressure (BP), electrocardiogram, pulse oximeter, and end-tidal carbon dioxide were connected, and pre-operative data such as baseline heart rate, oxygen saturation, and systolic and diastolic BPs were recorded. Patients were premedicated with injection glycopyrrolate 0.2 mg IV, injection ranitidine 50 mg IV, injection midazolam 0.05 mg/kg IV, and injection fentanyl 1.5 µg/kg IV 5-10 min before surgery.

All patients were preoxygenated with 100% oxygen for 5 min through Bain’s circuit followed by standard anesthetic induction with injection thiopentone sodium 5 mg/kg body weight till there was loss of eyelash reflex. The IV line was flushed with running IV fluid, and a bolus dose of the study drug was given. Atraumatic laryngoscopy was done with Macintosh blade, and intubation with oral cuffed ET tube of appropriate size was done at 60 s. The anesthetist who performed laryngoscopy and intubation was blinded by covering the patient with a drape sheet while another anesthetist loaded the muscle relaxant and administered it. The time taken for laryngoscopy was kept within 15 s relaxation of jaw, vocal cords, and response to intubation was assessed and scored by the grading criteria given by Cooper *et al.* 1992 (Table 1).

Vital parameters were recorded and monitored immediately after the study drug administration, immediately after intubation, and at 3, 5, 10, and 30 min intervals. If laryngoscopy and intubation failed at 60 s, it was repeated at 90 s and intubating conditions were assessed again. Any side effects such as electrocardiography (ECG) changes, muscle fasciculations, or any untoward effects due to histamine release such as skin flushing and erythema were also recorded if they occurred.

Bilateral air entry was confirmed and ET tube was firmly secured. After connecting the ET tube to Bain’s circuit, controlled ventilation was started. Anesthesia was maintained with 33% oxygen, 66% nitrous oxide and sevoflurane. The clinical duration of action of initial bolus doses (from the time of administration of the study drug to the first respiratory attempt) was noted, and subsequently, all groups were maintained with injection vecuronium bromide 0.04 mg/kg till the end of the surgery.

At the end of the surgery, all patients were reversed with after adequate reversal with injection neostigmine 0.05 mg/kg IV and injection glycopyrrolate 0.01 mg/kg IV and were extubated after ascertaining the adequacy of reversal of neuromuscular blockade.

**Table 1: Cooper et al. Scale (1992)**

<table>
<thead>
<tr>
<th>Score</th>
<th>Jaw relaxation</th>
<th>Vocal cords</th>
<th>Response to intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Poor (impossible)</td>
<td>Closed</td>
<td>Severe coughing</td>
</tr>
<tr>
<td>1</td>
<td>Minimal (difficult)</td>
<td>Closing</td>
<td>Mild coughing</td>
</tr>
<tr>
<td>2</td>
<td>Moderate (fair)</td>
<td>Moving</td>
<td>Slight diaphragmatic</td>
</tr>
<tr>
<td>3</td>
<td>Good (easy)</td>
<td>Open</td>
<td>movement</td>
</tr>
<tr>
<td></td>
<td>Total score: Excellent 8-9, Good 6-7, Fair 3-5, Poor 0-2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
RESULTS

The results were analyzed using SPSS software version 16 and Epi Info 6th version was used for trend analysis. The mean and standard deviation were calculated and used for calculating the significance of the difference. Qualitative data were analyzed using Chi-square test. \( P > 0.05, P < 0.05, \) and \( P < 0.001 \) were considered statistically nonsignificant, significant, and highly significant, respectively.

All the three groups did not differ with respect to age weight or gender distribution and were comparable with each other (Table 2). In Group S, all the 30 patients who received had excellent intubating conditions. In Group R6, 26 (86.66\%) patients out of 30 had excellent intubating conditions with 4 (13.33\%) patients showing good intubating conditions. In Group R8, 28 (93.33\%) patients out of 30 had excellent intubating conditions with 2 (6.67\%) patients showing good intubating conditions. None of the patients in all three groups had fair or poor intubating conditions. There were no cases of failed intubation at 60 s in any of the groups. Thus, the intubating conditions were comparable and statistically nonsignificant \( (P = 0.389) \) (Table 3 and Figure 1).

The jaw relaxation in Group S was good compared with Groups R6 and R8 and was statistically significant \( (P = 0.0526) \) (Table 4). There was no significant difference in the state of vocal cords at intubation between S, R6, and R8 groups \( (P = 0.338) \) (Table 5). Diaphragmatic movements were seen more in number in Group R6 (33.3\%) and were statistically highly significant \( (P = 0.0016) \) (Table 6).

The duration of action of rocuronium 0.6 mg/kg was shorter than rocuronium 0.8 mg/kg. Thus, increasing the dose led to a longer duration of action. Succinylcholine had the shortest duration of action among the drugs (Figure 2).

There was no significant rise in the mean heart rate after intubation \( (P = 0.390) \) which declined to the baseline preinduction values by the end of 10 min (Figure 3). The mean systolic BP was found to be more in Group S when compared to Groups R6 and R8, immediately after intubation up to 3 min which was statistically significant \( (P = 0.074) \). This returned to baseline values by the end of 5 min and became statistically nonsignificant \( (P = 0.682) \) (Figure 4). It was found that mean diastolic BP was higher in Group S when compared with R6 and R8, immediately after intubation up to 5 min which was statistically significant \( (P = 0.097) \) (Figure 5). This returned to baseline values by the end of 10 min and became statistically nonsignificant \( (P = 0.129) \). The rise in mean arterial pressure was more with succinylcholine than with rocuronium and declined to preinduction baseline values by the end of 10 min (Figure 6).

<table>
<thead>
<tr>
<th>Intubating conditions and scores</th>
<th>n (%)</th>
<th>Chi-square value</th>
<th>P value and significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent (8-9)</td>
<td>30 (100)</td>
<td>26 (86.66)</td>
<td>28 (93.33)</td>
</tr>
<tr>
<td>Good (6-7)</td>
<td>0 (0)</td>
<td>4 (13.33)</td>
<td>2 (6.67)</td>
</tr>
<tr>
<td>Fair (3-5)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Poor (0-2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>30 (100)</td>
<td>30 (100)</td>
<td>30 (100)</td>
</tr>
</tbody>
</table>

Table 2: Demographic data

<table>
<thead>
<tr>
<th>Group</th>
<th>Group S</th>
<th>Group R6</th>
<th>Group R8</th>
<th>P value with significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>32±12 (SD)</td>
<td>29±10 (SD)</td>
<td>32±11 (SD)</td>
<td>0.101 (NS)</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>58±11 (SD)</td>
<td>54±9 (SD)</td>
<td>54±9 (SD)</td>
<td>0.667 (NS)</td>
</tr>
<tr>
<td>Gender ratio (male/female)</td>
<td>16/14</td>
<td>16/14</td>
<td>14/16</td>
<td>(NS)</td>
</tr>
</tbody>
</table>
DISCUSSION

Succinylcholine is the most commonly used muscle relaxant for intubation in both elective and emergency settings but with some adverse effects such as bradycardia, rise in intraocular and intracranial pressures, muscle fasciculations, and post-operative myalgia. It is also not suitable in certain circumstances such as hyperkalemia, musculoskeletal disorders, burns, and central nervous system disorders.

Rocuronium bromide is a low potency, intermediate-acting derivative of vecuronium devoid of cardiovascular side effects\(^4\) and also devoid of histamine release.\(^5\) It was found to have a shorter onset time compared to vecuronium,\(^6\) cisatracurium,\(^7\) and mivacurium.\(^8\) Hence, this study was intended to test the efficacy of rocuronium bromide as a safer alternative to suxamethonium chloride for rapid ET intubation.

Selection of Drug Dose\(^9,10\)

The dosage of the neuromuscular blocking drug is usually selected based on the ED95 value. The dose required for ET intubation is employed in multiples of ED95 dose. The ED95 dose of succinylcholine is 0.3 mg/kg body weight. Three times the ED95 that is 1 mg/kg administration results in complete suppression of neuromuscular stimulation in approximately 60 s. Furthermore, there were no advantages when succinylcholine was used in doses larger than 1.5 mg/kg even in a rapid sequence intubation.

Rocuronium has been used in doses two to three times the ED95 dose to obtain clinically acceptable intubating...
conditions. The ED95 dose of rocuronium bromide is 0.305 mg/kg body weight. Two times the ED95 dose of rocuronium bromide is 0.6 mg/kg body weight. Three times the ED95 dose of rocuronium bromide is 0.9 mg/kg body weight has also been shown to provide excellent intubating conditions comparable to...
succinylcholine. However, the duration of action was longer.

In our study, succinylcholine and rocuronium bromide has been employed at a dose of 1.5, 0.6 and 0.8 mg/kg body weight to assess the intubating conditions at 60 s.

Selection of Intubation Criteria

In most studies, the appropriate timing of ET intubation has been determined by 3 ways.

1. Clinical criteria such as jaw relaxation, vocal cord movement, and response to intubation were assessed according to a scale or a scoring system
2. Neuromuscular monitoring by twitch suppression (maximum blockade) or train of four (TOF) ratio
3. Predetermined time after administration of neuromuscular blockers, e.g., 60 s, 90 s, and 120 s.

In our study, we have relied on two of the parameters, namely, predetermined time after muscle relaxant administration at 60 s and the clinical criteria given by Cooper et al., which most of the authors followed. We did not use neuromuscular monitoring at adductor pollicis because it was found that the onset of paralysis at the vocal cords and laryngeal muscles were rapid and preceded that of adductor pollicis. Hence, the TOF may give an incorrect picture of the intubating conditions with neuromuscular monitoring as there was significant difference in the onset times and the rate at which the neuromuscular block occurred between the two groups of muscles.

Assessment of Intubating Conditions

In the present study, succinylcholine 1.5 mg/kg produced excellent intubating conditions in 100% of patients. The results were comparable to those studies conducted by Bhati and Parmar (2008),13 Gupta and Kirbahar (2010),14 Feroz et al (2011),15 Bhale et al. (2013),16 and Parikh et al. (2014).17

Rocuronium 0.6 mg/kg produced excellent intubating conditions in 86.67% of patients and good intubating conditions in 13.33% of patients. The results were comparable to those studies conducted by Bhati and Parmar (2008),13 Gupta and Kirbahar (2010),14 and Belekare and Khamankar (2013).18

Rocuronium 0.8 mg/kg produced excellent intubating conditions in 96.67% of patients and good intubating conditions in 3.33% of patients. The results were comparable to the study conducted by Kurshid et al. (2015).19

Thus, increasing the dose of rocuronium bromide from 0.6 mg/kg to 0.8 mg/kg body weight not only increased the incidence of excellent intubating conditions but also increased the duration of action.

The reason for the rapid onset time for a neuromuscular block with rocuronium was suggested to be the relative low potency of the drug. This ensured the presence of more relaxant molecular load in the blood stream and neuromuscular junction resulting in the larger concentration gradient toward the biophase. Another explanation could be the earlier occurrence of the block at the adductor muscle of the larynx and intubation can be performed before complete block is obtained at the adductor pollicis muscle.20

Although the jaw relaxation was best with succinylcholine (100%), rocuronium was able to provide relatively good relaxation (83.33-93.33%) required for easy atraumatic laryngoscopy which is useful in emergent situations. There was no significant difference in the state of the vocal cords at intubation between the three groups. Open vocal cords without any movement were seen with succinylcholine in 96.66% and rocuronium bromide 86.66-93.33%. Diaphragmatic movements were seen more in those patients who received rocuronium bromide 0.6 mg/kg (33.33%) which was highly significant and may not be acceptable in the patients with a full stomach who are at increased risk of pulmonary aspiration of gastric contents as in emergency.

Clinical Duration of Action

In the present study, the time between the administration of the neuromuscular blocking drug and the first attempt at respiration clinically was taken as the clinical duration of action.

With succinylcholine 1.5 mg/kg, the clinical duration of action in this study was found to be a mean duration of 4.968 min. The minimum duration was 3.33 min, and the maximum was 7.00 min. The results were comparable with the following studies: Shukla et al. (2004), 21 Parikh et al. (2014),17 and Kurshid et al. (2015).19

The clinical duration of action of rocuronium 0.6 mg/kg in the present study was found to be with a minimum duration of 14.03 min and a maximum duration of 25.16 min. The mean duration of action was 18.21 min. This concurred with those studies by Verma et al. (2006)21 and Kurshid et al. (2015).19

In the present study, we used rocuronium at a dose of 0.8 mg/kg. The minimum duration of action was observed as 16.10 min, and the maximum duration of action was 33.80 min. The mean duration of action was 25.81 min. This was comparable to the study done by Kurshid et al. (2015).19
Hemodynamic Changes

In our study, there was an increase in heart rate from baseline values by 24.49%, 12.26%, and 24.99% with succinylcholine 1.5 mg/kg, rocuronium 0.6 mg/kg, and 0.8 mg/kg respectively, immediately after intubation. This gradually decreased to 7.5%, 4.92%, and 7.10% at the end of 5 min and returned to preinduction values by the end of 10 min.

The rise in systolic BP was 15.17%, 11.70%, and 13.83% in Group S, R6, and R8, respectively immediately after intubation. This declined to 2.13%, 4.42%, and 0.59%, respectively, among the three groups by the end of 5 min and was statistically nonsignificant. Furthermore, there was increase in diastolic BP from preinduction values by 14.50%, 13.65%, and 12.74% in group S, R6, and R8, respectively, postintubation. The diastolic pressures dropped to 2.08%, 2.76%, and 2.33%, respectively, by the end of 5 min.

The increase in mean arterial pressures after intubation was 15.57%, 13.98%, and 13.21% in Group S, R6, and R8, respectively. This gradually declined to 2.62%, 3.51%, and 2.57%, respectively, among the three groups by the end of 5 min and was seen by the end of 10 min in all groups.

These changes concurred with the studies by Bhale et al. (2013), Parikh et al. (2014), and Kurshid et al. (2015). Thus, greater hemodynamic stability was seen with rocuronium than with succinylcholine. The rise in heart rate and mean arterial pressure could be due to the sympathetic stimulation and stress produced by laryngoscopy and intubation. However, succinylcholine caused a greater stimulation of autonomic ganglion than rocuronium which explained the more significant hemodynamic variability in this group.

In our study, no adverse changes in ECG and oxygen saturation were observed. No other untoward side effects such as bradycardia, tachycardia, hypotension, hypertension, bronchospasm, cutaneous flushing, erythema, urticaria, or rashes. Only muscle fasciculations after the administration of suxamethonium chloride were noticed as predicted.

CONCLUSION

Rocuronium bromide at both doses of 0.6 mg/kg and 0.8 mg/kg produced clinically acceptable intubating conditions and can be used as a safer alternative to suxamethonium chloride in situations where suxamethonium chloride is contraindicated.

However, increasing the dose of rocuronium to 0.8 mg/kg produced excellent intubating conditions at 60 s itself, which was comparable with suxamethonium chloride and with lesser diaphragmatic movements that were found to be more useful in emergency situations, although it resulted in a longer duration of action.

ACKNOWLEDGMENTS

We express our sincere thanks to Professor Dr. M. Dhakshinamoorthy, Professor Dr. C. Dhanasekaran, Professor Dr. S. K. Srinivasan, and Professor Dr. R. Gowthaman from the Department of Anaesthesiology, R.M.M.C.H., Annamalai University, Chidambaram, for their timely help and constant encouragement while conducting this study.

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Source of Support: Nil, Conflict of Interest: None declared.