Rapid Sequence Induction using Rocuronium in Adult Patients


ABSTRACT:
BACKGROUND:
Several studies using rocuronium as an alternative to suxamethonium for endotracheal intubating conditions in rapid sequence induction are available in literature, all claiming obvious advantages, but intubating conditions after suxamethonium and rocuronium have not been assessed in our hospitals yet.

OBJECTIVE:
The aim of this study was to assess the efficacy of rocuronium for rapid sequence induction by comparing the endotracheal intubating conditions with suxamethonium, following induction with sodium thiopentone as the sole induction agent in elective, otherwise healthy, adult patients.

MATERIALS AND METHODS:
The patients were divided into two groups, each consisting of 40 patients: group A patients received rocuronium bromide 0.6 mg/kg IV, and group B patients received suxamethonium chloride 1.5 mg/kg IV. In both groups, jaw relaxation and vocal cord relaxation were considered for atraumatic laryngoscopy at 60 seconds. Induction of anesthesia achieved with thiopentone as a sleeping dose for all patients.

RESULTS:
All the patients in the suxamethonium group have excellent intubating conditions, while in the rocuronium group, 90% of the patients were excellent and 10% were good regarding the intubating conditions.

CONCLUSION:
It is concluded from this study that intubation can be performed under good to excellent conditions at 60 seconds after a bolus dose of rocuronium of 0.6 mg/kg. The result of this study indicates that this nondepolarizing neuromuscular blocking agent may be considered as a valuable alternative to suxamethonium for rapid sequence induction, i.e., within 60 seconds, even after induction with thiopentone as the sole anesthetic agent.

KEY WORDS: rapid sequence induction, intubating conditions, rocuronium, suxamethonium.

INTRODUCTION:
The RSI technique involves the rapid sequential administration of medications (including a sedative, induction anesthetic and a muscle relaxant, with or without narcotic) followed by endotracheal intubation within one minute of administering the muscle relaxant (1). In emergency situations, intubation is often required in unstable situations with the potential of hemodynamic instability. This frequently requires modification of the rapid sequence induction for the individual patient, with the goal of securing a patent airway as safely and quickly as possible (2). The concept of RSI evolved after the introduction of suxamethonium in 1951 and the description of cricoid pressure in 1961 (2). The traditional components of the technique as outlined in the original description include oxygen administration, injection of a predetermined dose of thiopental immediately followed by suxamethonium, application of cricoid pressure, and avoidance of positive pressure ventilation before tracheal intubation with a cuffed endotracheal tube (3). Currently, RSI is the standard of care for anesthesia induction in patients with an increased risk for gastric aspiration. However, in practice, there is considerable variation and not a little controversy regarding some elements of the technique (4).
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Two important uses of muscle relaxants are to facilitate endotracheal intubation and to provide surgical relaxation. Suxamethonium is the only depolarizing muscle relaxant used clinically. Furthermore, it is the only muscle relaxant with both a rapid onset and ultrashort duration of action (5). Typically, doses of 0.5 to 1.5 mg/kg intravenously are administered and produce a rapid onset of skeletal muscle paralysis (30 to 60 seconds) that lasts 5 to 10 minutes because of its unique breakdown (5).

These characteristics make suxamethonium ideal for providing rapid skeletal muscle paralysis to facilitate tracheal intubation. However, it falls short of the ideal muscle relaxant due to its potentially hazardous side effects, such as hyperkalemia, cardiac arrest and malignant hyperthermia, which are more frequently reported in children when suxamethonium is administered to facilitate rapid sequence endotracheal intubation (13-15).

Suxamethonium has been used clinically for more than 50 years. Despite consistent industrial efforts, no drug has been developed that is better than suxamethonium for tracheal intubation (16). The idea was to replace suxamethonium with a drug that provides good intubating conditions for the rapid tracheal intubations with short duration of action, and at the same time is devoid from the adverse effects of suxamethonium which are mainly the result of the depolarization of the muscles, i.e., a nondepolarizing muscle relaxant.

Among the nondepolarizing muscle relaxants vecuronium and atracurium were presented as an attractive alternative to suxamethonium. However, neither of these agents had the onset time as short as needed for endotracheal intubation. The various methods like using higher bolus dose, priming principle, timing principle were used to reduce their onset time, but, at the cost of a prolonged duration of action or hazardous side effects (11). Therefore quest for an ideal nondepolarizing agent continued for rapid and safe endotracheal intubation until rocuronium was introduced into clinical practice.

Rocuronium bromide, a newer amino-steroidal compound, is a derivative of vecuronium. Rocuronium has a rapid onset time, an intermediate duration of action and rapid recovery with cardiovascular stability (12). It has no significant histamine release (13). Onset time of a 0.6 mg/kg IV dose of rocuronium ranges from 1 to 1.5 minutes under nitrous oxide opioid anesthesia (14-15). Nevertheless, with this dose of rocuronium, the intubating conditions at 60 seconds are similar to those observed with suxamethonium (16-17).

This might persuade many clinicians to use rocuronium to facilitate endotracheal intubation not only in elective cases under adequate anesthesia but also in emergency situations requiring rapid sequence intubation.

The aim of this study was to assess the efficacy of rocuronium in comparison to suxamethonium for endotracheal intubating conditions following induction with sodium thiopentone as a sole anesthetic agent in elective, otherwise healthy, adult population.

MATERIALS AND METHODS:

80 patients aged between 22 and 60 years, were selected randomly from routine operative lists, with ASA physical status I or II, to make a comparison of intubating conditions after rocuronium with those after suxamethonium. The patients were divided into two groups according to the neuromuscular blocking agents received. Each group consists of 40 patients. The two groups were as follows:

- **Group A:** received rocuronium bromide 0.6 mg/kg IV
- **Group B:** received suxamethonium chloride 1.5 mg/kg IV

All the patients were free from neuromuscular disease and do not receive any medications known to influence the neuromuscular function, burns, family history of malignant hyperthermia, difficult airway (known or anticipated), known or anticipated difficult endotracheal intubation warranting awake fiberoptic intubation, cesarean delivery, complications during birth before delivery, contraindication against propofol, and allergy to rocuronium.

After informed consents were taken, all the patients were evaluated and investigated preoperatively, and then premedicated with atropine 0.6 mg IV, metoclopramide 0.15 mg/kg IV and tramadol 1 mg/kg IV. Then, before induction of anesthesia, pulse rate, blood pressure, SpO2, and ECG were recorded. All patients were preoxygenated with 100% O2 for three minutes using face mask. In group A, anesthesia was induced with thiopentone 5 mg/kg IV, slowly, followed by rocuronium 0.6 mg/kg IV. In group B, anesthesia was induced with thiopentone 5 mg/kg IV, slowly, followed by suxamethonium 1.5 mg/kg IV.
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In both groups, jaw relaxation and vocal cord relaxation were considered for a traumatic laryngoscopy at 60 seconds. Intubating conditions were assessed using the criteria of Cooper et al. The three items of this score: jaw relaxation, position of vocal cords during laryngoscopy and response to endotracheal intubation were noted and a score from 0 to 3 was given as shown in Table 1.

Table 1: Cooper’s criteria for intubating conditions.

<table>
<thead>
<tr>
<th>Jaw relaxation</th>
<th>Vocal Cords</th>
<th>Response to intubation</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor (impossible)</td>
<td>Closed</td>
<td>Server coughing</td>
<td>0</td>
</tr>
<tr>
<td>Minimal (difficult)</td>
<td>Closing</td>
<td>Mild coughing</td>
<td>1</td>
</tr>
<tr>
<td>Moderate (fair)</td>
<td>Moving</td>
<td>Slight diaphragmatic</td>
<td>2</td>
</tr>
<tr>
<td>Good (easy)</td>
<td>Open</td>
<td>None</td>
<td>3</td>
</tr>
</tbody>
</table>

Intubating conditions in all patients were graded as follows: Excellent 8-9, Good 6-7, Fair 3-5, Poor 0-2. Good and excellent intubating conditions were taken to be “clinically acceptable” by Cooper et al.

RESULTS:
A total of 80 patients were included in this study with 40 patients in each group. The two groups were comparable with regards to the demographic data (Table 2).

Table 2: Demographic data.

<table>
<thead>
<tr>
<th>GROUP A [n=40]</th>
<th>GROUP B [n=40]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Mean</td>
</tr>
<tr>
<td>Age [years]</td>
<td>33.06 ± 3.233</td>
</tr>
<tr>
<td>Weight [kg]</td>
<td>78.375 ± 9.101</td>
</tr>
<tr>
<td>Gender [m/f]</td>
<td>18:22</td>
</tr>
<tr>
<td>ASA physical status I/II</td>
<td>27/13</td>
</tr>
<tr>
<td>Mallampatti grade I/II</td>
<td>16/24</td>
</tr>
</tbody>
</table>

Ease of laryngoscopy was different in both groups. Jaw relaxation was good in 30 patients of rocuronium group and in 33 patients of suxamethonium group, while the other patients in both groups had moderate jaw relaxation. Vocal cords were open and immobile at 60 seconds in 35 patients after administration of rocuronium, while they were open and immobile at 60 seconds in 38 patients after administration of suxamethonium. But the vocal cords were found to be moving in 5 patients given rocuronium and in 2 patients given suxamethonium. “No diaphragmatic movement” and “slight diaphragmatic movement” were observed in 34 and 6 patients, respectively, given rocuronium (group A) and “no diaphragmatic movement” was observed in all the patients given suxamethonium (group B).

Reaction of diaphragm to intubation was more pronounced at 60 seconds after the administration of rocuronium. Intubating conditions were rated as excellent in 90% and good in 10% of the patients who received rocuronium and excellent in 100% of the patients who received suxamethonium (Tables 3 and 4).

Table 3: Intubating conditions at 60 seconds.

<table>
<thead>
<tr>
<th></th>
<th>Group A no. of patients (%)</th>
<th>Group B no. of patients (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>36(90)</td>
<td>40(100)</td>
<td>0.2373</td>
</tr>
<tr>
<td>Good</td>
<td>04(10)</td>
<td>00</td>
<td>0.2373</td>
</tr>
<tr>
<td>Fair</td>
<td>00</td>
<td>00</td>
<td>0.00</td>
</tr>
<tr>
<td>Poor</td>
<td>00</td>
<td>00</td>
<td>0.00</td>
</tr>
</tbody>
</table>
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Figure 1: Intubating conditions at 60 seconds

Intubating scoring system (at 60 seconds)

Table 4: Jaw relaxation (ease of laryngoscopy).

<table>
<thead>
<tr>
<th></th>
<th>Group A no. of patients (%)</th>
<th>Group B no. of patients (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good (Easy)</td>
<td>30(75)</td>
<td>33(82.5)</td>
<td>0.748</td>
</tr>
<tr>
<td>Moderate (Fair)</td>
<td>10(25)</td>
<td>07(17.5)</td>
<td>0.748</td>
</tr>
<tr>
<td>Minimal (Difficult)</td>
<td>00</td>
<td>00</td>
<td>--</td>
</tr>
<tr>
<td>Poor (Impossible)</td>
<td>00</td>
<td>00</td>
<td>--</td>
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</tbody>
</table>

Table 5: Conditions of vocal cords.

<table>
<thead>
<tr>
<th></th>
<th>Group A no. of patients (%)</th>
<th>Group B no. of patients (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open</td>
<td>35(87.5)</td>
<td>38(95)</td>
<td>0.3533</td>
</tr>
<tr>
<td>Moving</td>
<td>05(12.5)</td>
<td>02(5)</td>
<td>0.3533</td>
</tr>
<tr>
<td>Closing</td>
<td>00</td>
<td>00</td>
<td>--</td>
</tr>
<tr>
<td>Closed</td>
<td>00</td>
<td>00</td>
<td>--</td>
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</tbody>
</table>

Table 6: Response to intubation.

<table>
<thead>
<tr>
<th></th>
<th>Group A no. of patients (%)</th>
<th>Group B no. of patients (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>34(85)</td>
<td>40(100)</td>
<td>0.0522</td>
</tr>
<tr>
<td>Slight diaphragmatic movement</td>
<td>06(15)</td>
<td>00</td>
<td>0.0522</td>
</tr>
<tr>
<td>Mild coughing</td>
<td>00</td>
<td>00</td>
<td>--</td>
</tr>
<tr>
<td>Severe coughing</td>
<td>00</td>
<td>00</td>
<td>--</td>
</tr>
</tbody>
</table>

Figure 2: Jaw relaxation at 60 seconds.
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**Figure 3:** Conditions of the vocal cords at 60 seconds.

**Figure 4:** Response to intubation at 60 seconds

In group A, the time required for cessation of respiration was 60-70 seconds in 30 patients (75%), 71-80 seconds in 7 patients (17.5%) and 81-90 seconds in 3 patients (7.5%) patients, while in group B, it was 60-70 seconds in all the patients (Table 8, Figure 4).

**Table 7:** Time required for cessation of respiration.

<table>
<thead>
<tr>
<th>Time (seconds)</th>
<th>Group A no. of patients</th>
<th>Group B no. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-70</td>
<td>30 (75)</td>
<td>40 (100)</td>
</tr>
<tr>
<td>71-80</td>
<td>07 (17.50)</td>
<td>00</td>
</tr>
<tr>
<td>81-90</td>
<td>03 (7.50)</td>
<td>00</td>
</tr>
</tbody>
</table>

**Figure 5:** Cessation of respiration.

**DISCUSSION:**
Patients often require a rapid sequence induction (RSI) endotracheal intubation technique during emergencies or electively to protect against aspiration, increased intracranial pressure, or to facilitate intubation\(^{19}\). Suxamethonium has been a mainstay of RSI for more than 50 years, primarily because of the drug’s rapid onset time. This property facilitates that fundamental axiom of RSI, which is that the time from induction of anesthesia to endotracheal
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intubation with a cuffed endotracheal tube, the airway’s period of vulnerability to aspiration risk, should be as short as possible (30).

For more than 30 years, questions over suxamethonium use in RSI have been raised (10). Suxamethonium possesses the fastest onset (45 seconds) and produces the shortest period of muscle relaxation (6 to 10 minutes) compared with all other agents. However, it is a ‘pharmacologically dangerous drug’ with the potential to result in acute lethal hyperkalemia (10). Several commonly encountered conditions in the ICU predispose patients to dangerous elevations in serum potassium with suxamethonium, including upper or lower motor neuron defects (for example, spinal cord injury and critical illness polyneuropathy), prolonged chemical denervation (for example, muscle relaxants), direct muscle trauma or inflammation, thermal trauma, disuse atrophy, and severe infection. In each, there is an upregulation of muscle nicotinic acetylcholine receptors, which when depolarized with suxamethonium lead to efflux of intracellular potassium into the plasma, leading to acute hyperkalemia leading to dysrhythmias and potentially, cardiac arrest (21).

Owing to its severe adverse effects, several investigators had tried to search for alternative drugs that might provide acceptable intubating conditions for rapid tracheal intubation. As the vast majority of these adverse effects are the results of depolarization of the skeletal muscles caused by suxamethonium, the investigators tested some nondepolarizing muscle relaxants, but all their efforts failed to solve the problem because of their adverse effects and their slow onset of action.

These issues have increased the interest in the use of rocuronium, an aminosteroid non-depolarizing neuromuscular blocking drug, in place of suxamethonium for RSI in surgical (22), obstetric (23), and, now, critically ill (24) populations, as it is a relatively safe drug with rapid onset of action.

This clinical study was undertaken to evaluate whether rocuronium onset time was sufficiently short to permit its use for rapid sequence induction of anesthesia and whether intubating conditions achieved by rocuronium were similar to those achieved by suxamethonium.

The endotracheal intubation was commenced at 60 seconds with cessation of breathing in the majority of patients (75% of rocuronium group and all the suxamethonium group). Similar clinically acceptable (excellent or good) intubating conditions were found in both rocuronium 0.6mg/kg and suxamethonium 1.5 mg/kg.

After rocuronium administration, the response of diaphragm to intubation was more pronounced than that after administration of suxamethonium, but the overall intubating conditions were similar to those after suxamethonium administration.

Similar results about the onset time and the intubating conditions were found in other studies of Dubios et al (25), and Huizinga et al (26). In these studies, no difference was observed in the frequency distribution of clinically acceptable intubating conditions at 60 and 90 seconds after the administration of suxamethonium or rocuronium.

These findings are also supported by other authors who concluded that the onset time of rocuronium and suxamethonium were comparable, and that rocuronium is a suitable alternative for suxamethonium for rapid intubation in rapid sequence induction (27-32).

CONCLUSION:
It is concluded from this study that rocuronium was as safe and effective as suxamethonium in facilitating laryngoscopy and intubation during RSI in this study intubation can be performed under good to excellent conditions at 60-90 seconds after a bolus dose rocuronium of 0.6 mg/kg.

Recommendations
The result of this study indicates that rocuronium may be considered as a valuable alternative to suxamethonium for rapid tracheal intubation, i.e., within 60 seconds after induction, even when thiopentone was used as the sole anesthetic agent. Rocuronium can serve as a good alternative to suxamethonium for tracheal intubation in conditions where suxamethonium is contraindicated or where its use is hazardous.

REFERENCES:
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