RAPID SEQUENCE INDUCTION WITH ROCURONIUM AT 0.45 MG/KG: COMPARISON OF INTUBATING CONDITIONS BETWEEN KETAMINE AND PROPOFOL INDUCTION

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Abstract

Introduction  Rocuronium is an alternative neuromuscular blocking agent used during rapid sequence induction (RSI) when suxamethonium is contraindicated. However, the optimal intubating dose of rocuronium is 1 mg/kg, which is associated with a long duration of action. The aim of this study was to compare the intubating conditions after a relatively low-dose of rocuronium (0.45 mg/kg) in simulated RSI between ketamine and propofol induction.

Methods  Eighty ASA 1-2 adult patients, who required tracheal intubation during anesthesia for elective surgery, were randomly assigned to receive either ketamine at 2.5 mg/kg (group K) or propofol at 2.5 mg/kg (group P) followed by rocuronium 0.45 mg/kg. Tracheal intubation was performed at 75 seconds after administration of rocuronium. The intubating conditions, twitch suppression of the adductor pollicis and hemodynamic responses were evaluated.

Results  All patients in both groups were successfully intubated at the first attempt. Clinically acceptable intubating conditions (good or excellent) were obtained in 90% of group K compared to 85% of group P (p=0.499). Fraction of excellent intubating conditions was 67.5% and 57.5% in group K and group P, respectively (p=0.356). No difference in the twitch suppression at the time of intubation or the onset time of rocuronium was observed. After induction, group K presented significantly increased blood pressure, which was higher than in group P (p=0.000).

Discussion and conclusion  When compared with propofol, ketamine is likely to produce better intubating conditions, due to its analgesic and hemodynamic effects, but this was not confirmed in this study. Ketamine or propofol at 2.5 mg/kg and rocuronium at 0.45 mg/kg provided clinically acceptable intubating conditions at 75 seconds after rocuronium in the majority of patients studied. This technique may be applied in RSI, when suxamethonium is contraindicated and a short duration of neuromuscular blockade is needed. The choice of either induction agent therefore depends mainly on its hemodynamic effects.

Keywords: rapid sequence induction, rocuronium, ketamine, propofol

Rapid sequence induction (RSI) usually applies when tracheal intubation must be performed in patients suspected of having a full stomach and at risk for pulmonary aspiration of gastric contents. The main goal is to minimize the time between induction and tracheal intubation in order to reduce the chance of pulmonary aspiration, while preventing hypoxia during the
the induction-intubation sequence. Poor muscle relaxation at the time of intubation has been identified as a major factor for pulmonary aspiration in emergency cases. To achieve the best possible intubating conditions, succinylcholine remains the neuromuscular blocking agent of choice, and should be administered unless there are contraindications to its use. Rocuronium provides the fastest onset of action in clinically available non-depolarizing neuromuscular blocking agents, and is currently referred to as an alternative to succinylcholine. However, the dose of rocuronium required to match the intubating conditions of succinylcholine at 60 seconds appears to be 0.6-1 mg/kg (2-3 xED95)\(^{(1-3)}\) and is associated with a long duration of action, thus making it unsuitable for short operations.

The choice of an intravenous anesthetic induction agent also has potential impact on intubating conditions. Apart from its different capacity to attenuate the reactions to intubation, its hemodynamic effects may play substantial roles in the onset of a neuromuscular blocking agent. The onset time of rocuronium was found to increase in patients receiving esmolol and decrease in those receiving ephedrine.\(^{(4)}\) In this context, induction agents such as etomidate and ketamine, which maintain cardiac output and blood pressure, have been shown to accelerate the onset of block and improve the intubating conditions when rocuronium at 0.6 mg/kg was used.\(^{(5,6)}\)

We hypothesized that induction of anesthesia with ketamine at 2.5 mg/kg may improve rocuronium intubating conditions at 75 seconds. The aim of this study was to compare the intubating conditions after rocuronium at 0.45 mg/kg (1.5xED95) in simulated RSI between 2 intravenous anesthetic induction agents, ketamine and propofol.

### Methods

After obtaining approval from the Faculty Ethics Committee and informed consent, 80 ASA 1-2 Thai patients, aged 18-60 years and undergoing elective surgery under general anesthesia, were enrolled in this prospective, double blind, randomized controlled trial study. The exclusion criteria were patients with obesity (body mass index, BMI > 28 kg/m\(^2\)), risk of aspiration, potentially difficult airway, evidence of neuromuscular, cardiovascular, hepatic or renal diseases, or medication known to influence neuromuscular function.

Patients were randomly allocated to receive either ketamine at 2.5 mg/kg (group K, n=40) or propofol at 2.5 mg/kg (group P, n=40) as the intravenous induction agent. Random allocation sequence was computer-generated and the random numbers were kept in sealed envelopes. Upon arrival in the operating room, an ECG, a NIBP and pulse oximeter were applied to all patients. A crystalloid solution was infused into a vein on the back of the patient’s hand, on the same side as the NIBP and pulse oximeter application. Neuromuscular monitoring (an accelerograph) was applied to the ulnar nerve at the wrist on the other side.

After injection of either intravenous anesthetic agent over 10 seconds, supramaximal currents were applied and a calibration done, pursued by 1 Hz single twitch stimulation. Rocuronium at 0.45 mg/kg was then injected over 5 seconds. All drugs were followed by rapid injection of normal saline at 10 mL. Seventy-five seconds after the injection of rocuronium, tracheal intubation was performed by an experienced anesthesiologist, who was blind to the drugs used. Intubating conditions were assessed and rated as excellent, good, fair or poor, using the criteria of Cooper, et al\(^{(2)}\):

<table>
<thead>
<tr>
<th>Jaw relaxation</th>
<th>Vocal cords</th>
<th>Response to intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor</td>
<td>Closed</td>
<td>Severe coughing/bucking</td>
</tr>
<tr>
<td>Minimal</td>
<td>Closing</td>
<td>Mild coughing</td>
</tr>
<tr>
<td>Moderate</td>
<td>Moving</td>
<td>Slightly diaphragmatic movement</td>
</tr>
<tr>
<td>Good</td>
<td>Open</td>
<td>None</td>
</tr>
</tbody>
</table>

Score 8-9 = Excellent, 6-7 = Good, 3-5 = Fair, 0-2 = Poor
components were added together to give an overall intubation score for each patient. A score of 8-9 was considered excellent, 6-7 good, 3-5 fair and 0-2 poor. Excellent and good conditions were considered clinically acceptable.

Apart from the intubating conditions, the intubation time, twitch height at intubation (T75 sec) and onset to 100% twitch suppression were recorded. Blood pressure and heart rate were also recorded at preinduction (baseline) and 30 seconds after induction.

Age, BMI, intubation time, blood pressure and heart rate were compared using the student’s t-test. Sex and ASA class distribution and intubating conditions were analyzed with the Chi-squared test. T75sec and onset time of rocuronium were compared using the Mann-Whitney U-test. A p value of < 0.05 was considered statistically significant.

### Results
The two groups were comparable with respect to sex and ASA class ratios, age, BMI and baseline blood pressure and heart rate (Table 2). All patients in both groups were successfully intubated at the first attempt with no difference in intubation time (32.03±14.71 in group K, 30.9±12.66 in group P, p=0.715). The T75sec was 0% (0, 4.75) and 0% (0, 4.75), whereas the onset time of rocuronium was 71 seconds (60.5, 85) and 62.5 seconds (52, 83.75) in group K and P, respectively and was not significantly different between groups (p=0.46 and 0.11, respectively). Intubating conditions were clinically acceptable in 90% of group K compared to 85% of group P, and not significantly different (p=0.5). The proportion of excellent intubating conditions was 67.5% in group K and 57.5% in group P, with no statistical difference (p=0.36) (Fig. 1).

In group K, when compared with baseline, the mean arterial pressure (MAP) and heart rate significantly increased after induction (p=0.000), whereas in group P, only heart rate significantly rose (p=0.009). When comparing between groups after induction, group K had significantly higher MAP than group P (p=0.000), while group P had a significantly higher heart rate than group K (p=0.04).

### Discussion
There have been very few studies in which RSI was applied to patients scheduled for emergency surgery in the wake of patient safety and ethical concern. Hence, almost all studies including this one dealt with the problem of neuromuscular blockade, and intubating conditions during the course of RSI, by using elective patients in whom RSI was simulated.

With the introduction of propofol and the rapidly acting opioids, alfentanil and remifentanil, tracheal intubation could be accomplished without a neuromuscular blocking agent. However, the quality of intubating conditions was less predictable and tracheal intubation frequently impossible. Heavy doses of alfentanil (60 μg/kg)
or remifentanil (4 μg/kg) are required to produce conditions that approach those produced by succinylycholine.(7) These doses are likely to be associated with hypotension, even in elective patients. It is therefore logical to include a neuromuscular blocking agent in RSI when successful rapid intubation is crucial at the first attempt. Intense neuromuscular blockade can increase the chance of successful tracheal intubation. Moreover, pulmonary aspiration is less likely,(8) as is the incidence of laryngeal injuries.(9)

Succinylcholine, with its rapid onset and short duration of action, remains the neuromuscular blocking agent of choice in RSI and should be administered unless there are contraindications to its use. Since rapacuronium was withdrawn from market in 2001, rocuronium, with its relatively fast onset, has remained the most interesting alternative neuromuscular blocking agent recommended in RSI. Still, the dose required to match the intubating conditions of succinylcholine appears to be 1 mg/kg (3xED95)(3) and is certainly associated with a long duration of action, thus making it unsuitable for short operations.

Apart from the dose of a neuromuscular blocking agent, the onset speed of neuromuscular blockade depends in part on physiological factors such as cardiac output, circulation time and muscle perfusion. In an elective situation, the onset time of rocuronium was found to increase in patients receiving esmolol and decrease in those receiving ephedrine.(4) Although the peak plasma concentration of a neuromuscular agent is increased when the cardiac output is decreased, as may happen in emergency patients, the net effect is a longer onset time. The onset time can be lengthened by the induction effect of anesthesia, which produces changes of its own, usually by depressing cardiac output and peripheral vascular resistance. Induction agents such as etomidate and ketamine, which maintain cardiac output and blood pressure, have been shown to accelerate the onset of block and improve intubating conditions when used in association with 0.6 mg/kg of rocuronium.(5,6) In addition, ketamine possesses potent analgesic property and capacity to blunt the airway reflexes. These may decrease the dose of rocuronium used to achieve the same intubating conditions. On the contrary, propofol causes hypotension, as well as bradycardia, which should result in a longer onset time of neuromuscular block. The addition of ephedrine to propofol can help maintain a normal heart rate and obtund the hypotensive effect of propofol, resulting in

Figure 1. Intubating conditions 75 seconds after 0.45 mg/kg of rocuronium; comparison between ketamine and propofol induction.
better intubating conditions. However, one should consider the fact that, if neuromuscular blocking agents are omitted, propofol is associated with better intubating conditions than either thiopentone or etomidate, which may be due to its capacity to blunt the pharyngeal reflexes and central effects. The good intubating conditions from propofol may be obtained before the onset of neuromuscular blockade.

Barclay, et al, found that during induction of anesthesia with propofol at 2.5 mg/kg and alfentanyl at 10 μg/kg, rocuronium at 0.3 mg/kg provided optimal intubating conditions in 90% of patients at 120 seconds. However, the time between induction and tracheal intubation was too long and might not be appropriately applied in RSI. In this study, tracheal intubation was performed at 75 seconds after administration of rocuronium at 0.45 mg/kg. This study could not demonstrate the difference in either twitch suppression of the adductor pollicis muscle at the time of tracheal intubation or the onset time of rocuronium between groups. After induction, it was not surprising that blood pressure significantly increased in group K, was maintained in group P, and significantly differed between groups (p=0.000). The blood pressure in group P did not drop drastically, and had little effect on the onset time of rocuronium. While the increased blood pressure from ketamine might not always be associated with the increase in cardiac output, it rather is connected to the increase in peripheral vascular resistance at the dose given in this study (2.5 mg/kg). This might, to some extent, prolong the onset time of rocuronium from decreased muscle perfusion. It was also noteworthy that the onset times for both groups (71 and 62.5 seconds in group K and P, respectively) were faster when compared with other studies. Rocuronium, as well as other non-depolarizing neuromuscular blocking agents, has a great interindividual variability in its neuromuscular blocking effects. As all the patients in this study were Asian (Thai), they might be an example of ethnic variability in the effects of rocuronium. Almost every patient in both groups was intubated at the point of complete twitch suppression of the adductor pollicis muscle (median twitch height=0), hence, the fractions of optimal intubating conditions were comparable in both groups (0.9 in group K, 0.85 in group P). However, the action onset of rocuronium is slower at the diaphragm, but faster at the laryngeal muscles than at the adductor pollicis muscles. While jaw relaxation was good and the vocal cords were wide open, some incidents of straining and diaphragmatic movement after intubation could still occur, hence, rendering the intubating conditions only fair in a few patients from both groups. Some crucial measures to prevent regurgitation and pulmonary aspiration should include applying cricoid pressure and inflating the endotracheal tube cuff as soon as it passes the vocal cords. In order to ensure optimal intubating conditions with a low dose of rocuronium during RSI, some interventions have been proposed, for example, the priming technique, or the administration of rapidly acting opioids, ephedrine or lidocaine, along with the induction agent.

In summary, ketamine or propofol at 2.5 mg/kg and rocuronium at 0.45 mg/kg provided clinically acceptable intubating conditions at 75 seconds after administration of rocuronium in the majority of the patients studied (90% and 85% in group K and P, respectively). This technique may be an alternative in RSI, when succinylcholine is contraindicated, and especially when surgery is of a short duration. The choice of either induction agent therefore depends mainly on its hemodynamic effects and the patient’s cardiovascular status. However, some interventions may be needed to ensure optimal intubating conditions during RSI.

References


การใส่ท่อช่วยหายใจอย่างรวดเร็วด้วย rocuronium ขนาด 0.45 มิลลิกรัม / กิโลกรัม เมื่อนำสลบด้วย ketamine เปรียบเทียบกับ propofol

วิวัฒนาการที่แม่พยัคฆ์, นพ. สุทธิ จันท์ชัย, นพ. นิสิต ชัยพิทักษ์

การใส่ท่อช่วยหายใจอย่างรวดเร็วด้วย rocuronium ขนาด 0.45 มิลลิกรัม / กิโลกรัม เมื่อนำสลบด้วย ketamine เปรียบเทียบกับ propofol

บทคัดย่อ

Rocuronium เป็นยาหย่อนกล้ามเนื้อชนิดที่สามารถใช้ในการใส่ท่อช่วยหายใจอย่างรวดเร็ว (rapid sequence induction: RSI) โดยเฉพาะอย่างยิ่งในผู้ป่วยที่มีข้อจำกัดในการใช้ succinylcholine แต่อย่างไรก็ตามนอกจากrocuronium ยังมีประโยชน์ในการใส่ท่อช่วยหายใจโดยใช้ 1 มก./กิโลกรัม. อย่างไรก็ตาม rocuronium ขนาด 0.45 มก./กิโลกรัม เมื่อนำสลบด้วย ketamine เปรียบเทียบกับ propofol ในแง่ของสภาพขณะใส่ท่อช่วยหายใจ (Intubating condition) โดยจำลองสถานการณ์ RSI ไม่ได้การกระตุ้นคีโคไรด์

รูปแบบการศึกษา

ผู้ป่วยทั้งหมด 80 คน ได้รับการบันทึกรายละเอียดเกี่ยวกับการใส่ท่อช่วยหายใจจำนวน 80 คน. ที่มี ASA physical status ระดับ 1-2 จะถูกสุ่มแบ่งเป็นสองกลุ่ม กลุ่ม A 40 คน โดยกลุ่ม K คือกลุ่มที่ได้รับ ketamine 2.5 มก./กิโลกรัม และกลุ่ม P ได้รับ propofol 2.5 มก./กิโลกรัม. ทั้งสองกลุ่มได้รับ rocuronium 0.45 มก./กิโลกรัม. ศาสตราจารย์เชียงใหม่ ประณัยสวัสดิ์วงศ์ ผู้ศึกษาที่_media , คมตาลกิจ ผู้ช่วยศาสตราจารย์, ภิรมย์ นิยม, พ.บ.

ผลการศึกษา

สามารถใส่ท่อช่วยหายใจสำเร็จในผู้ป่วยทุกคนของทั้งสองกลุ่มในการใส่ครั้งแรก สามารถใส่ท่อช่วยหายใจที่ยอมรับได้ในกลุ่ม K (good หรือ excellent) พบในกลุ่ม K 90 เปอร์เซ็นต์เปรียบเทียบกับกลุ่ม P ซึ่งมีค่า p = 0.000 ซึ่งดีกว่าระดับ 0.05. ตัวแปรที่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติและเพิ่มสูงกว่ากลุ่ม P ในค่าทั้งหมด (p=0.000)

วิเคราะห์สรุป

โดยที่ ketamine จะมีฤทธิ์ที่มีความสำคัญในการระบายไขมันและกระตุ้นระบบไหลเวียนเลือด แต่การศึกษาพบว่าผู้ป่วยที่ได้รับ ketamine มีสภาพขณะใส่ท่อช่วยหายใจไม่แตกต่างจากกลุ่ม propofol โดยสามารถทำให้ต้องการกระตุ้นของยาหย่อนกล้ามเนื้อด้วย propofol ซึ่งมีการล่าช้าก่อนการหย่อนกล้ามเนื้อจะทำให้ระยะเวลาการออกฤทธิ์ของ rocuronium คืบหน้ากว่า propofol. จึงทำให้การใช้ propofol ในการใช้ rocuronium สำเร็จได้ในการศึกษา 2553;49(1):11-17.

คำสำคัญ: การใส่ท่อช่วยหายใจอย่างรวดเร็วด้วย rocuronium, ketamine, propofol