The Effect of Ephedrine on the Onset Time of Rocuronium in Thai Patients

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Abstract

The aim of this study was to determine the effect of ephedrine on the onset time of rocuronium. The study population was 60 ASA physical status 1 and 2 patients, aged 15-60 years scheduled for elective surgery under general anesthesia at Ramathibodi Hospital. The patients were randomly assigned into 2 groups. Group I (ephedrine group), ephedrine 70 μg/kg was given 1 minute before induction and group II (control group), saline was given instead of ephedrine and midazolam 7.5 mg was given orally 30-60 minutes before the induction. Anesthesia was induced with fentanyl 1 μg/kg and sodium thiopentone 3-5 mg/kg. The patient was intubated with 0.9 mg/kg of rocuronium. The intubation time (from rocuronium administration to the time of intubation) was predetermined by the Dixon's up and down method (with 5 seconds as a step size) for each patient and started at 60 seconds for the first patient in each group. The intubation time in the ephedrine group (39.41 ± 4.64 seconds) was significantly different from the control group (59.17 ± 9.00 seconds); p-value < 0.01. The hemodynamics were similar in both groups.

Conclusion : Intravenous ephedrine shortened the onset time of rocuronium with no significant adverse hemodynamic effects. As an alternative to suxamethonium for rapid intubation, the authors recommend the use of ephedrine 70 μg/kg at one minute before induction followed by 0.9 mg/kg of rocuronium intravenously in healthy patients. The intubation could be achieved at 40 seconds after the administration.

Key word : Intubation Time, Rocuronium, Ephedrine

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At the present time, a muscle relaxant with short onset time is usually desired for use in anesthetic induction-intubation. Rocuronium is a nondepolarizing muscle relaxant (NDMR) of choice for this purpose (1-4). When the dose of NDMR is increased, the intubation time is usually decreased. The onset time of the NDMR is also determined by the speed of these drugs reaching the neuromuscular junction. In the previous study by Munoz et al(5), 70 μg/kg of ephedrine was administered prior to 0.6 mg/kg of rocuronium in order to reduce the onset time of neuromuscular blockade. They found that the onset time of rocuronium was reduced by 26 per cent. It is considered that rocuronium rapidly reaches the neuromuscular junction by the increasing cardiac output from the effect of ephedrine. This is beneficial to patients since the prolonged time of loss of consciousness with tracheal intubation increases risks of hypoxia and pulmonary aspiration. The authors questioned the benefit of ephedrine in reducing the onset time of rocuronium as the dose of rocuronium was increased to 0.9 mg/kg. The aim of this study was to determine the effect of 70 μg/kg of ephedrine on the onset time of 0.9 mg/kg of rocuronium and on heart rate, blood pressure during the induction of anesthesia.

METHOD

With the approval of ethics committee and patients' consent, 60 patients aged between 15 to 60 years, ASA physical status I and II scheduled for elective surgery under general anesthesia at Ramathibodi Hospital were double blind randomly assigned to receive either 70 μg/kg of ephedrine (Ephedrine group; n = 30) or a 5 ml of normal saline (Control group; n = 30). Exclusion criteria were patients with cardiovascular diseases, neuromuscular disease, risk of gastric content aspiration and predicted difficult intubation. Midazolam 7.5 mg was given orally at 60-90 minutes before induction as premedication. Vital signs, including blood pressure, heart rate, were measured for baseline. 1-2 μg/kg of fentanyl was given at 4 minutes before induction. Ephedrine 70 μg/kg diluted up to 5 ml with saline was given at one minute before the induction of anesthesia for the study group and 5 ml of normal saline for the control group were given. Sodium thiopentone 3-5 mg/kg was subsequently given for the induction in both groups. After loss of eyelash reflex, rocuronium 0.9 mg/kg was administered in 5 seconds and the patient was ventilated *via* facemask. In the first case of the study, the intubation time was determined at 60 seconds after rocuronium was administered. In the next case, Dixon's up and down method(6) was used to set the intubation time. The intubation time would be either increased or decreased by 5 seconds each time, depending on the clinical standard (Table 1)(7). For example, if the intubation status of the first case was grade 3 to 4, no cough and a little diaphragm movement up to no reflex, the intubation time of the next case would be reduced to 55 seconds. Otherwise, if the intubation status was below grade 3, it meant that the patient still coughed and had a severe reflex, the intubation time would be increased 5 seconds to 65 seconds. Usual vital signs were immediately measured after tracheal intubation and 3 minutes later. The record of the onset of intubation time, hemodynamic variables were compared with unpaired two-tailed Student's *t*-test. A p-value less than 0.05 was considered significant. Values are mean ± SD unless otherwise stated.

RESULTS

No difference in demographic data in age, sex, weight and ASA physical status, was found in both groups (Table 2). The onset of intubation time in the ephedrine-rocuronium group was 39.41 ± 4.64 seconds, which was statistically significantly less than the rocuronium group only, 59.17 ± 9.00 seconds. The hemodynamic profiles, at post intubation and 3 minutes

Table 1. The intubation status.

Intubation status	Reflex during intubating
Not good (grade 1)	Cough, severe reflex
Fair (grade 2)	Still has little cough
Good (grade 3)	No cough, little movement of the diaphragm
Excellent (grade 4)	No reflex

Table 2. Demographic data.

	Ephedrine-rocuronium	Rocuronium
Age (year)	34.2 ± 8.2	34.4 ± 6.6
Weight (kg)	55.4 ± 7.5	53.2 ± 8.5
Male/female	3/27	7/23
ASA I/II	23/7	25/5

post intubation, were similar in both groups (Fig. 1 and Fig. 2).

DISCUSSION

The small dose of ephedrine administered at the moment of induction reduced the onset time of rocuronium. A previous study by Munoz et al[5] demonstrated that the onset time of ephedrine 70 μg/kg with 0.6 mg/kg of rocuronium (70 ± 19 seconds) was significantly less than the saline with 0.6 mg/kg rocuronium group (98 ± 31 seconds). Szmuk et al[8] also found that the ephedrine group (coadministration of 70 μg/kg of ephedrine with rocuronium 0.6 mg/kg) the onset time was significantly less than the control group. The onset time was 64 ± 6.7 seconds and 93 ± 6 seconds respectively. In the present study, the authors also found that the onset time of ephedrine 70 μg/kg with 0.9 mg/kg of rocuronium was 39.41 ± 4.64 seconds and was significantly less than the onset time of the saline and rocuronium 0.9 mg/kg group. (59.17 ± 9.00). The systolic, diastolic blood pressures and the heart rates were similar in both groups.

The fast reliable onset time and short duration of suxamethonium make it the muscle relaxant of choice for tracheal intubation. Rocuronium is the NDMR that has a rapid onset of action. It is an alternative to suxamethonium for rapid intubation especially when suxamethonium is contraindicated[9,10]. To improve the intubation condition of rocuronium, a high dose such as 0.9 mg/kg rocuronium is recommended instead of 0.3-0.6 mg/kg rocuronium[11]. But clinical duration of action was also significantly longer. Priming principle is another technique to hasten the onset of paralysis[12,13]. But this technique is associated with an unacceptably high incidence of unpleasant (weakness associated with priming) and potentially dangerous side effects such as pulmonary aspiration [13,14]. From the present study, a coadministration of ephedrine 70 μg/kg with rocuronium 0.9 mg/kg had

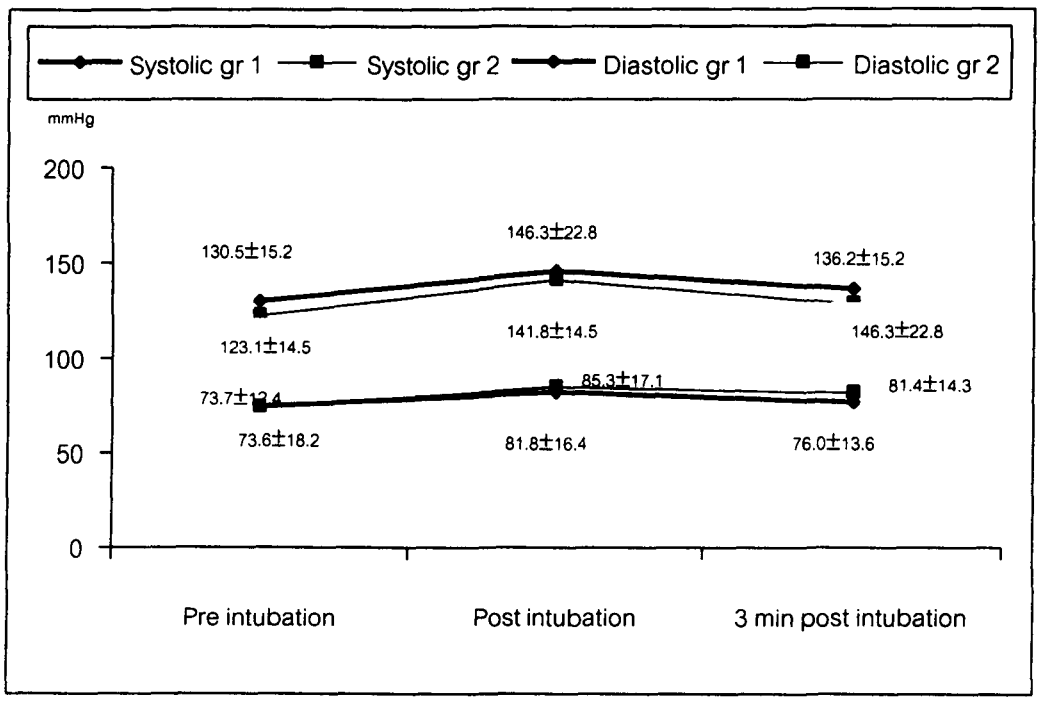

Fig. 1. Comparison of systolic blood pressure, and diastolic blood pressure between ephedrine-rocuronium (group I) and rocuronium (group II).

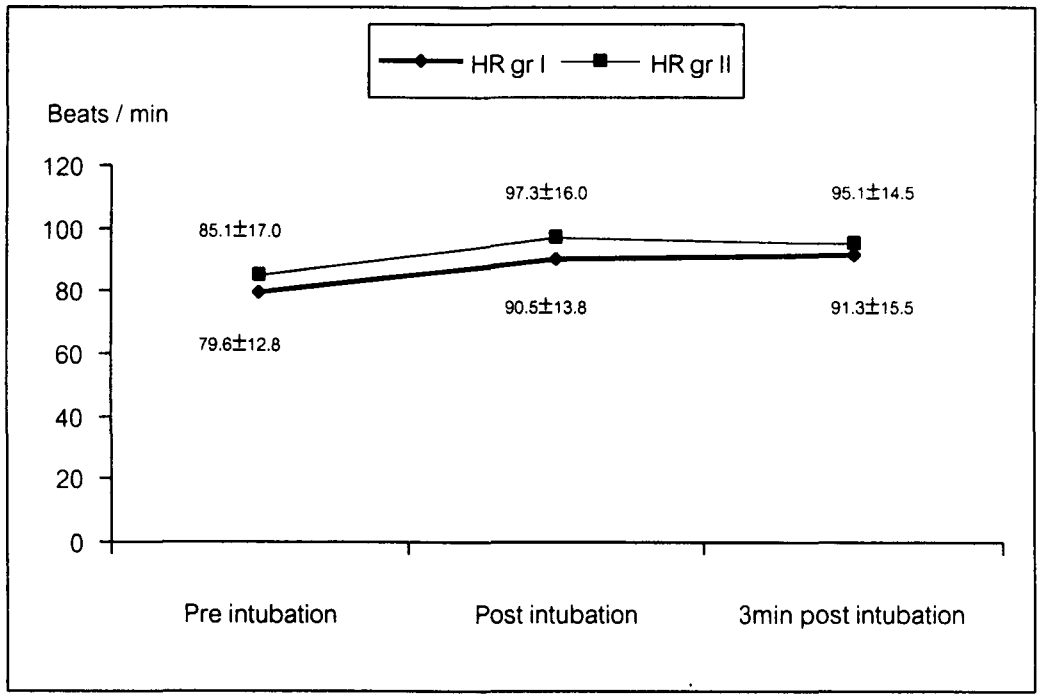

Fig. 2. Comparison of heart rate between ephedrine-rocuronium (group I) and rocuronium (group II).

a fast and reliable onset time with no significant side effects. However, the duration of action was prolonged. If the patient has a difficult airway such as difficulty in facemask ventilation or intubation after administration of rocuronium, the risk of hypoxia, hypercarbia and aspiration is greater in rocuronium when compared to suxamethonium. In conclusion, intravenous ephedrine 70 μg/kg reduced the onset time of high dose rocuronium 0.9 mg/kg with no significant side effects in healthy patients. The authors recommend the use of ephedrine 70 μg/kg at one minute before induction followed by 0.9 mg/kg of rocuronium as an alternative to suxamethonium in healthy patients who have no difficult intubation conditions.

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REFERENCES

1. Cooper RA, Mirakhur RK, Maddineni VR. Neuromuscular effects of rocuronium bromide (ORG 9426) during fentanyl and halothane anaesthesia. Anaesthesia 1993; 48: 103-5.
2. Huizinga ACT, Vandenbrom RHG, Wierda JMKH, Hommes FDM, Hennis PJ. Intubating condition and onset of neuromuscular block of rocuronium (ORG 9426): A comparison with suxamethonium. Acta Anaesthesiol Scand 1992; 36: 463-8.
3. Cooper R, Mirakhor RK, Clarke RSK, Bules Z. Comparison of intubating condition after administration of ORG 9426 (rocuronium) and suxamethonium. Br J Anaesth 1992; 69: 269-73.
4. McCourt KC, Salmela L, Mirakhur RK. Comparison of rocuronium and suxamethonium for use during rapid sequence induction of anaesthesia. Anaesthesia 1998; 53: 867-71.
5. Munoz HR, Gonazalez AG, Dagniono JA, Gonzalez JA, Perez AE. The effect of ephedrine on the onset time of rocuronium. Anesth Analg 1997; 85: 437-40.
6. Dixon WJ. Quantal response variable experimentation : The up and down method. In: Mc Arthur JW, Colton T. eds. Statistics in endocrinology, proceedings. Cambridge: MIT Press; 1970: 251-67.
7. Foldes FF. Rapid tracheal intubation with non depolarizing neuromuscular blocking drugs. Anesthesiology 1985; 62: 392-5.
8. Szmuk P, Ezri T, Chelly JE, Katz J. The onset time of rocuronium is slowed by esmolol and accelerated by ephedrine. Anesth Analg 2000; 90: 1217-9.
9. Puhringer FK, Khuen-Brady KS, Koller J. Evaluation of the endotracheal intubating conditions of rocuronium (ORG 9426) and succinylcholine in outpatient surgery. Anesth Analg 1992; 75: 37-40.
10. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anaesthesia in adult patients. Anesthesiology 1993; 79: 913-8.
11. Somboonviboon W, Bunburaphong P, Whanna O. Intubating conditions after three different doses of rocuronium. J Med Assoc Thai 2000; 83: 850-5.
12. Mehta MP, Choi WW, Gergis SD, Sokoll MD. Facilitation of rapid endotracheal intubations with divided doses of nondepolarizing neuromuscular blocking drugs. Anesthesiology 1985; 62: 392-5.
13. Jones RM. The priming principle: How does it work and should we be using it? Br J Anaesth 1989; 63: 1-3.
14. Musich J, Walts LF. Pulmonary aspiration after a priming dose of vecuronium. Anesthesiology 1986; 64: 517:9.

ผลของการให้ยา Ephedrine ต่อระยะเวลาการเริ่มออกฤทธิ์ของ Rocuronium ในผู้ป่วยไทย

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ได้ทำการศึกษาโดยวิธีการสุ่มตัวอย่างประชากร ในผู้ป่วย 60 ราย ASA physical status 1–2 อายุ 15–60 ปี แบ่งผู้ป่วยออกเป็น 2 กลุ่ม กลุ่มละ 30 ราย กลุ่มที่ 1 ได้รับ ephedrine 70 มคก/กก จำนวน 5 มล และกลุ่มที่ 2 ได้รับสารน้ำเกลือนอร์มอล จำนวน 5 มล ผู้ป่วยทุกรายได้รับประทาน midazolam 7.5 มก ก่อนนำสลบเป็นเวลา 60–90 นาที เริ่มนำสลบด้วย fentanyl 1 มคก/กก หลังจากนั้น 4 นาที ให้ ephedrine หรือสารน้ำเกลือนอร์มอล ตามที่แบ่งกลุ่มไว้ จากนั้นให้ sodium thiopentone 3–5 มก/กก เมื่อผู้ป่วยสลบแล้ว (loss of eyelash reflex) จึงให้ rocuronium 0.9 มก/กก ใน 5 วินาที และช่วยหายใจโดย face mask ventilation เมื่อครบตามกำหนดเวลาจึงใส่ท่อหายใจ ซึ่งผู้ป่วยแต่ละรายจะได้รับการกำหนดระยะเวลาสำหรับใส่ท่อหายใจไว้ก่อน โดยระยะเวลาที่กำหนดในผู้ป่วยรายแรกของแต่ละกลุ่มเท่ากับ 60 วินาที ระยะเวลาในผู้ป่วยลำดับต่อไปใช้วิธี Dixon's up and down method (เพิ่มหรือลดครั้งละ 5 วินาที) ถ้าใส่ท่อหายใจทำได้ดี การใส่ท่อหายใจในผู้ป่วยรายต่อไปจะลดระยะเวลาลงจากเดิม 5 วินาที แต่ถ้าการใส่ท่อหายใจทำได้ไม่ดี การใส่ท่อหายใจในผู้ป่วยรายต่อไปจะเพิ่มระยะเวลาจากเดิมอีก 5 วินาที

ผลการศึกษาพบว่าไม่มีความแตกต่างระหว่างอายุ, น้ำหนัก, เพศ และ ASA physical status ในผู้ป่วยทั้งสองกลุ่ม ส่วนระยะเวลาที่ใช้ใส่ท่อหายใจในกลุ่ม ephedrine เท่ากับ 39.41 $\pm$ 4.64 วินาที น้อยกว่าในกลุ่ม สารน้ำเกลือนอร์มอล ซึ่งเท่ากับ 59.17 $\pm$ 9.00 วินาที อย่างมีนัยสำคัญทางสถิติ เมื่อเปรียบเทียบความดันเลือด systolic ความดันเลือด diastolic และอัตราการเต้นของหัวใจของ ทั้งสองกลุ่มพบว่าไม่แตกต่างกันทั้งค่าพื้นฐาน, หลังใส่ท่อหายใจทันทีและหลังใส่ท่อหายใจเป็นเวลา 3 นาที

สรุปได้ว่า Ephedrine ขนาด 70 มคก/กก สามารถลดระยะเวลาการเริ่มออกฤทธิ์ของ rocuronium ขนาด 0.9 มก/กก และสามารถใส่ท่อหายใจในเวลา 39.41 $\pm$ 4.64 วินาที โดยไม่พบผลข้างเคียงต่อระบบไหลเวียนเลือด ephedrine–rocuronium จึงน่าจะเป็นอีกทางเลือกหนึ่งของยาหย่อนกล้ามเนื้อเพื่อใส่ท่อหายใจอย่างรวดเร็วและไม่มีภาวะของการใส่ท่อหายใจลำบากร่วมด้วย

คำสำคัญ : การใส่ท่อหายใจ, เอฟรีดีน, รอคคูโรเนียม

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