British Journal of Anaesthesia 1996;77:339–342

Influence of induction technique on intubating conditions after rocuronium in adults: comparison with rapid-sequence induction using thiopentone and suxamethonium

H.J. SPARR, S. GIESINGER, H. ULMER, M. HOLLENSTEIN-ZACKE AND T.J. LUGER

Summary

We have assessed the effect of anaesthetic technique on intubating conditions after rocuronium 0.6 mg kg^{-1} in four groups ($n=25$ each) of unpremedicated patients in whom anaesthesia was induced with either thiopentone 5 mg kg^{-1} or propofol 2.5 mg kg^{-1} alone, or supplemented with alfentanil 20 μg kg^{-1}. Fifty control patients were anaesthetized with thiopentone followed by suxamethonium. Laryngoscopy was commenced at 45 s. Overall intubating conditions after rocuronium were similar to those after suxamethonium (good and excellent ≥96%) only when alfentanil was part of the induction regimen. However, intubation time was similar in all five groups and averaged 55 (SD 3.2) s, and the tube could be passed through open vocal cords within 70 s. After rocuronium the response of the diaphragm to intubation was more pronounced in the two groups of patients not receiving alfentanil ($P<0.0001$) and in patients anaesthetized using propofol with alfentanil ($P<0.01$) than in the control group. Opioids (in doses equivalent to alfentanil 20 μg kg^{-1}) constitute an integral part of an induction regimen containing rocuronium 0.6 mg kg^{-1}, regardless of whether or not thiopentone or propofol is used, in order to achieve overall intubating conditions similar to those after suxamethonium. (*Br. J. Anaesth.* 1996;**77**:339–342)

Key words

Anaesthetic techniques, induction. Intubation, tracheal. Neuromuscular block, rocuronium. Neuromuscular block, suxamethonium. Anaesthetics i.v., thiopentone. Analgesics opioid, alfentanil.

Rocuronium offers the fastest onset of action of all clinically available non-depolarizing neuromuscular blocking agents. Intubating conditions at 60 s after administration of rocuronium 0.6 mg kg^{-1} have been reported to be similar to those after suxamethonium[1–3]. This similarity in intubating conditions is surprising, because the onset of action of rocuronium at the laryngeal adductor muscles is slower than that after suxamethonium, and the degree of block at these muscles is less intense[4].

Anaesthetic techniques used in previous studies[1–3], in particular the use of opioids, may have improved intubating conditions after rocuronium. When increasing doses of opioids were added to propofol, intubating conditions were similar to those after suxamethonium, even in the absence of a neuromuscular blocking agent[5 6]. Propofol rather than thiopentone may further facilitate intubation, as propofol was shown to depress laryngeal reflexes to a greater extent than thiopentone in comparable doses[7]. When anaesthesia was induced with thiopentone alone in unpremedicated adult patients, intubating conditions produced by rocuronium were less favourable than those produced by suxamethonium[8].

Consequently, we hypothesized that opioids should be used with an induction regimen containing rocuronium in order to achieve tracheal intubation within 60 s. In addition, we were interested in whether or not intubating conditions after rocuronium are more favourable if anaesthesia is induced with thiopentone rather than with propofol. Therefore, in this study we administered rocuronium to four groups of unpremedicated patients in whom anaesthesia was induced in a rapid-sequence manner, either with thiopentone or propofol alone, or supplemented with the opioid alfentanil. Rapid-sequence induction with thiopentone and suxamethonium was used in a control group.

Patients and methods

The study was approved by the Ethics Committee of the Medical Faculty of the University of Innsbruck. After obtaining written, informed patient consent, we studied 150 subjects, ASA I–II, aged 18–65 yr, undergoing minor elective surgery (orthopaedic or gynaecological) under general anaesthesia. None of the patients had a history of malignant hyperthermia or were receiving any medications known to interact with neuromuscular blocking agents. Pregnant patients were excluded. A careful physical examination was performed to exclude patients with potential airway problems.

STUDY DESIGN

Patients were allocated randomly to one of five study groups. In the control group, 50 patients received

H.J. SPARR, MD, S. GIENSINGER, MD, M. HOLLENSTEIN-ZACKE, MD, T.J. LUGER, MD, PHD (Department of Anaesthesia and Intensive Care Medicine); H. ULMER, PHD (Department of Biostatistics); University of Innsbruck, Anichstrasse 35, A-6020 Innsbruck, Austria. Accepted for publication: April 1, 1996.

Correspondence to H. J. S.

thiopentone 5 mg kg^{-1} and suxamethonium 1 mg kg^{-1} in a rapid-sequence manner. Rocuronium 0.6 mg kg^{-1}, twice its ED95, was administered to four other groups of patients (25 patients in each group) in whom anaesthesia was induced with either thiopentone 5 mg kg^{-1} (group T-R) or propofol 2.5 mg kg^{-1} (group P-R) alone, or supplemented with alfentanil 20 μg kg^{-1} (groups AT-R and AP-R). The main variables assessed in these patients were intubation time and intubating conditions.

ANAESTHETIC TECHNIQUE

Patients did not receive premedication. After 3 min of preoxygenation, anaesthesia was induced in a rapid-sequence manner (not applying cricoid pressure) with thiopentone or propofol followed by suxamethonium or rocuronium. When alfentanil was part of the induction technique, it was administered immediately before the i.v. anaesthetic. All drugs were given into a rapidly running infusion of lactated Ringer's solution. Injection times were 10 s for alfentanil and thiopentone, 15 s for propofol, and less than 5 s for rocuronium and suxamethonium. Heart rate (determined by ECG), non-invasive arterial pressure, arterial oxygen saturation (Sp_{O_2}) and endtidal carbon dioxide concentration were monitored in all patients (Cardiocap, Datex, Finland).

TRACHEAL INTUBATION

A tracheal tube (Mallinckrodt Lo-Pro, Mallinckrodt Laboratories, UK) with an internal diameter of 8.5 cm in males and 7.5 cm in females was used. A flexible plastic mounted stylet was inserted into the tube. The same fully trained anaesthetist ("intubator"), who was blinded to the treatment each patient received, performed all intubations using a Macintosh size 4 blade. In order to prevent the intubator from noting suxamethonium-related muscle fasciculations, the intubator was called to enter the study room 40 s after administration of the blocker, and another 5 s later he was instructed to start intubation. The tube was intended to be placed in the trachea as soon as possible, but only when the vocal cords were open and immobile. Otherwise insertion of the tube was delayed until the vocal cords were open and immobile.

ASSESSMENT OF INTUBATION TIME AND INTUBATING CONDITIONS

Intubation time was recorded as the number of seconds from the end of administration of blocker to insertion of the tube in the trachea, as measured by a stop-watch. Intubating conditions were assessed using the criteria of Cooper and colleagues[9] (table 1). In addition, the occurrence of suxamethonium-related muscle fasciculations and movement of the limbs during and immediately after intubation were noted by both the attending anaesthetist and the intubator.

STATISTICAL ANALYSIS

Summary statistics (sample size, mean (SD)) were calculated for all quantitative variables of each group. We used one-way analysis of variance to compare age, weight and height between the five groups, and the chi-square test to compare distribution by sex. In order to evaluate differences between the control and each of the other groups, intubation time was analysed using the Mann–Whitney *U* test, and intubating conditions assessed using the chi-square or Fisher's exact test. Estimation of sample size was based on the results of a previous study[8] in which 60% of patients receiving rocuronium and 92% of patients receiving suxamethonium showed excellent intubating conditions after rapid-sequence induction with thiopentone. Using a two-group chi-square test (0.05 two-sided significance level with a correction factor for the four comparisons, 80% power) the minimum sample size thus determined was 45 patients for the control and 23 patients for each of the groups given rocuronium. Calculations were carried out using the software package SPSS (version 6.0 for Windows, SPSS Inc., Chicago, IL, USA).

Table 1 Scoring of intubating conditions[9]. A total score of 8–9 = excellent; 6–7 = good; 3–5 = fair; 0–2 = poor

Score	Jaw relaxation (ease of laryngoscopy)	Vocal cords	Response to intubation
0	Poor (impossible)	Closed	Severe coughing or bucking
1	Minimal (difficult)	Closing	Mild coughing
2	Moderate (fair)	Moving	Slight diaphragmatic movement
3	Good (easy)	Open	None

Results

Mean age, weight and height of the 150 patients were 34 (range 18–55) yr, 69 (SD 12.0) kg and 172 (8.7) cm.

Intubation time was similar in all groups with a mean value of 55.0 (3.4) s. In seven patients (two patients in the control group, three in group T-R, and one each in groups P-R and AT-R) the tube was positioned after 60 s because of problems with laryngoscopy or closed and mobile vocal cords. However, in all patients the tracheal tube was passed easily through open vocal cords within 70 s. Intubating conditions approximately 60 s after suxamethonium (control group) were rated as excellent in 88% and good in 12% of patients. Intubating conditions 60 s after rocuronium differed between the control and groups T-R and P-R, but were similar between the control and groups AT-R and AP-R, in which alfentanil was given during induction of anaesthesia. In groups T-R and P-R, intubating conditions were rated as excellent in only 40% and 32%, good in 40% and 60%, and fair in 20% and 8% of patients, respectively ($P<0.0001$ *vs* control) (fig. 1).

Among the three variables contributing to assessment of intubating conditions, ease of laryngoscopy was similar in all patients. On average, laryngoscopy was judged to be easy in 80% and fair in 20% of patients. However, the condition of the vocal cords differed between the control group and rocuronium-treated patients who did not receive alfentanil (fig. 2). In addition, in groups T-R and P-R and also in

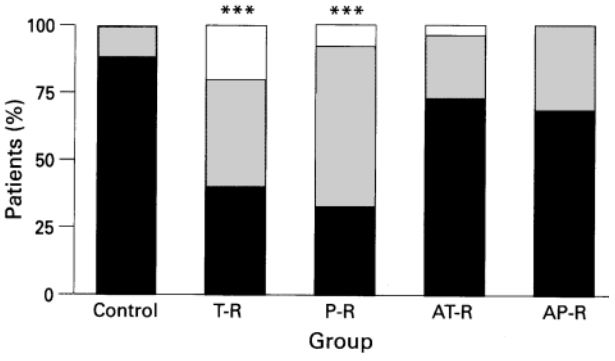

Figure 1 Intubating conditions after suxamethonium (control group; $n=50$) or rocuronium (groups T-R, P-R, AT-R and AP-R; $n=25$ each) after rapid-sequence induction using different anaesthetic techniques. (Solid bars = excellent, shaded bars = good, open bars = fair.) ***$P<0.0001$ compared with control value.

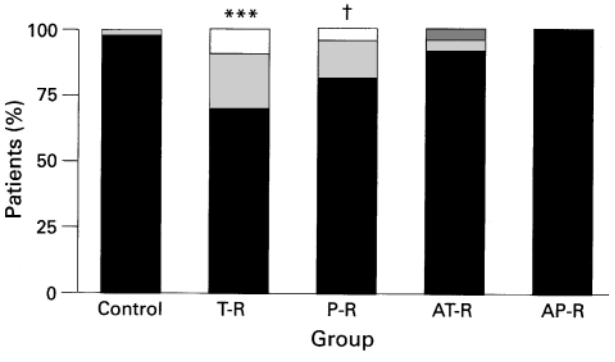

Figure 2 Initial aspect of the vocal cords on laryngoscopy, ⩾45 s after suxamethonium (control group; $n=50$) or rocuronium (groups T-R, P-R, AT-R and AP-R; $n=25$ each) after rapid sequence induction using different anaesthetic techniques. (Solid bars = open, lightly shaded bars = moving, open bars = closing, darkly shaded bars = closed.) ***$P<0.001$, group T-R compared with control; †$P<0.05$, group P-R compared with control.

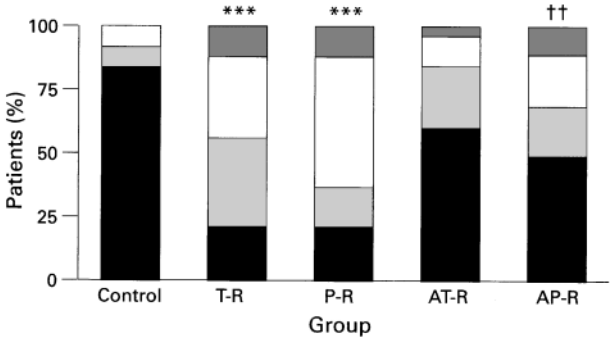

Figure 3 Response of the diaphragm to intubation after suxamethonium (control group; $n=50$) or rocuronium (groups T-R, P-R, AT-R and AP-R; $n=25$ each) after rapid-sequence induction with different anaesthetic techniques. (Solid bars = none, lightly shaded bars = diaphragmatic movement, open bars = mild coughing, darkly shaded bars = severe coughing.) ***$P<0.0001$, groups T-R and P-R compared with control; ††$P<0.01$, group AP-R compared with control.

group AP-R, the response of the diaphragm to intubation was more pronounced than in the control group (fig. 3).

Suxamethonium-related muscle fasciculations were not seen by the intubator, whereas the attending anaesthetist observed muscle fasciculations in 85% of patients given suxamethonium. During or immediately after intubation, or both, movement of the limbs (most frequently the hand, lower arm and foot) were observed in 8% of patients after suxamethonium, but in 40% of patients in group T-R ($P<0.002$ *vs* control), and 56% of patients in group P-R ($P<0.001$ *vs* control). In contrast, there was no difference in the incidence of movement of the limbs between the control and groups AT-R and AP-R, who were given alfentanil during induction.

Discussion

The results of this study indicated that in unpremedicated adult patients, intubating conditions after rocuronium were influenced by the induction technique. However, the anaesthetic technique used for induction of anaesthesia had no significant influence on intubation time after rocuronium 0.6 mg kg^{-1} compared with suxamethonium. Overall intubating conditions after rocuronium were similar to those after suxamethonium when alfentanil 20 μg kg^{-1} was part of the induction regimen. However, they differed from those after suxamethonium when anaesthesia was induced with either thiopentone or propofol alone in equipotent doses[10].

The findings of this study are supported by the results of previous studies in which intubating conditions after rocuronium were assessed. In one group of studies, where opioids were part of the induction regimen or used for premedication, intubating conditions at 60 s after rocuronium 0.6 mg kg^{-1} were similar to those after suxamethonium[1–3]. Although opioids and i.v. anaesthetics had no influence on the neuromuscular blocking effects of rocuronium[11], the use of opioids in these studies might have contributed to the favourable intubating conditions 60 s after rocuronium. After addition of increasing doses of alfentanil to propofol or thiopentone, both used as induction agents, intubating conditions became more favourable[6 12] and were even similar to those after suxamethonium[5 6]. However, when no neuromuscular blocking agent was administered, intubation failed in 50% of patients anaesthetized with propofol 1.5–2 mg kg^{-1} and alfentanil 1 mg[1].

In another set of two studies, intubating conditions were found to be less favourable after rocuronium than after suxamethonium[8 9]. In one of these studies, in unpremedicated adult patients, anaesthesia was induced in a rapid-sequence manner with thiopentone alone (6 mg kg[1])[8]. In the other, patients were premedicated orally, and anaesthesia was induced with small dose of thiopentone and fentanyl and maintained with increments of these agents for approximately 10 min before rocuronium was administered[9].

Evidence suggesting that anaesthesia does have an impact on intubating conditions after rocuronium is supported by the findings of another study on rocuronium, in patients undergoing Caesarean section. The dose of thiopentone was increased from 4 to 6 mg kg^{-1}, and intubation was commenced at 80 s instead of 60 s in order to achieve good or excellent intubating conditions in 90% of patients[13].

In contrast with other investigators[1–3 9], we did not measure the time course of action of rocuronium, as the main purpose of this study was to challenge the efficacy of rocuronium in providing smooth intubating conditions within 60 s by using different techniques of induction of anaesthesia. In addition, until now no conclusive correlation between onset

time at the adductor pollicis muscle and intubating conditions has been shown[14]. In our study, laryngoscopy revealed that the vocal cords were moving or closing in about 25% of rocuronium-treated patients who did not receive alfentanil during induction. The response of the diaphragm to intubation was more pronounced after rocuronium than after suxamethonium, but was attenuated by alfentanil (fig. 3).

These findings are supported by recent investigations[4 15 16]. The laryngeal adductor muscles and the diaphragm are more resistant to the effects of rocuronium than the adductor pollicis muscle[15 16]. However, the onset of action of small doses of rocuronium (0.4 and 0.5 mg kg^{-1}) at the laryngeal adductor pollicis muscle[4 16]. In contrast, the onset of rocuronium at the diaphragm was found to be slower than at the adductor pollicis muscle[15]. In addition, even after administration of higher doses of rocuronium (0.8 and 1.2 mg kg^{-1}), the onset of action at the laryngeal adductor muscles was slower than that after suxamethonium 1 mg kg^{-1} [4].

Hence, signs of incomplete neuromuscular block at the vocal cords, the diaphragm and other muscles may be observed more frequently after administration of rocuronium 0.6 mg kg^{-1} than after suxamethonium, if laryngoscopy with subsequent tracheal intubation is commenced at 45 s, in particular with a light plane of anaesthesia. In this study, movement of the limbs was noted only in exceptional cases after suxamethonium, and after rocuronium with alfentanil, but were observed frequently (≥40%) after rocuronium without alfentanil.

Acknowledgements

Rocuronium (Esmeron) and financial support were received from Organon GmbH, Division Organon Teknika, Vienna, Austria. We acknowledge the support of Professor K. P. Pfeiffer, Werner Lingnau, MD, Hubert Krimbacher, MD, and Ms Helga Oberhollenzer.

References

1. Huizinga ACT, Vandenbrom RHG, Wierda JMKH, Hommes FDM, Hennis PJ. Intubating conditions and onset of neuromuscular block of rocuronium (Org 9426); a comparison with suxamethonium. *Acta Anaesthesiologica Scandinavica* 1992; **36**: 463–468.
2. Pühringer FK, Khuenl-Brady KS, Koller J, Mitterschiffthaler G. Evaluation of the endotracheal intubating conditions of rocuronium (Org 9426) and succinylcholine in outpatient surgery. *Anesthesia and Analgesia* 1992; **75**: 37–40.
3. Magorian T, Flannery KB, Miller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. *Anesthesiology* 1993; **79**: 913–918.
4. Wright PM, Caldwell JE, Miller RD. Onset and duration of rocuronium and succinylcholine at the adductor pollicis and laryngeal adductor muscles in anesthetized humans. *Anesthesiology* 1994; **81**: 1110–1115.
5. Beck BN, Masterson GR, Richards J, Bunting P. Comparison of intubation after propofol and alfentanil with intubation after thiopentone and suxamethonium. *Anaesthesia* 1993; **48**: 876–880.
6. Scheller MS, Zornow MH, Saidman LJ. Tracheal intubation without the use of muscle relaxants: A technique using propofol and varying doses of alfentanil. *Anesthesia and Analgesia* 1992; **75**: 788–793.
7. McKeating K, Bali IM, Dundee JW. The effects of thiopentone and propofol on upper airway integrity. *Anaesthesia* 1988; **43**: 638–640.
8. Sparr HJ, Luger TJ, Heidegger T, Putensen-Himmer G. Comparison of intubating conditions after rocuronium and suxamethonium after 'rapid-sequence induction' with thiopentone in elective cases. *Acta Anaesthesiologica Scandinavica* 1996; **40**: 425–430.
9. Cooper R, Mirakhur RK, Clarke RS, Boules Z, Clarke RSJ. Comparison of intubating conditions after administration of Org 9246 (rocuronium) and suxamethonium. *British Journal of Anaesthesia* 1992; **69**: 269–273.
10. Van Hemelrijck J, Muller P, Van Aken H, White PF. Relative potency of eltanolone, propofol, and thiopental for induction of anesthesia. *Anesthesiology* 1994; **80**: 36–41.
11. Olkkola KT, Tammisto T. Quantifying the interaction of rocuronium (Org 9426) with etomidate, fentanyl, midazolam, propofol, thiopental, and isoflurane using closed-loop feedback control of rocuronium infusion. *Anesthesia and Analgesia* 1994; **78**: 691–696.
12. Helbo-Hansen S, Ravlo O, Trap-Andersen S. The influence of alfentanil on the intubating conditions after priming with vecuronium. *Acta Anaesthesiologica Scandinavica* 1988; **32**: 41–44.
13. Abouleish E, Abboud T, Lechevalier T, Zhu J, Chalian A, Alford K. Rocuronium (Org 9426) for Caesarean section. *British Journal of Anaesthesia* 1994; **73**: 336–341.
14. Agoston S. Onset time and evaluation of intubating conditions: rocuronium in perspective. *European Journal of Anaesthesiology* 1995; **12** (Suppl. 11): 31–37.
15. Cantineau JP, Porte F, D'Honneur G, Duvaldestin P. Neuromuscular effects of rocuronium on the diaphragm and adductor pollicis muscles in anesthetized patients. *Anesthesiology* 1994; **81**: 585–590.
16. Plaud B, Proost JH, Wierda JM, Barre J, Debaene B, Meistelman C. Pharmacokinetics and pharmacodynamics of rocuronium at the vocal cords and the adductor pollicis in humans. *Clinical Pharmacology and Therapeutics* 1995; **58**: 185–191.