Anesthesiology
79:913–918, 1993


# Comparison of Rocuronium, Succinylcholine, and Vecuronium for Rapid-sequence Induction of Anesthesia in Adult Patients

Toni Magorian, M.D.,* K. B. Flannery,† Ronald D. Miller, M.D.‡

***Background:*** **Succinylcholine has been the agent of choice when clinical conditions require emergency airway protection during a rapid-sequence induction of anesthesia. Rocuronium, a new nondepolarizing muscle relaxant with a brief onset of action, but devoid of the adverse reactions associated with succinylcholine, may be an alternative to succinylcholine. To test this hypothesis, the authors compared rocuronium with succinylcholine and vecuronium for rapid-sequence induction of anesthesia.**

***Methods:*** **Fifty patients, ASA 1–3, were randomly designated to receive one of three intravenous doses of rocuronium (0.6, 0.9, and 1.2 mg/kg), vecuronium (0.1 mg/kg), or succinylcholine (1.0 mg/kg). Patients were premedicated with midazolam and fentanyl, and received 2–7 mg/kg thiopental for induction of anesthesia. Sixty seconds after receiving a muscle relaxant, intubation of the trachea was attempted by a clinician who was blinded to the muscle relaxant administered. Neuromuscular monitoring was established before administration of the muscle relaxant. The time from injection of muscle relaxant until complete ablation of T1 (onset) and recovery of T1 to 25% (duration) were recorded. Tracheal intubating conditions were evaluated, and the presence or absence of fasciculations was noted.**

***Results:*** **Onset times for patients receiving 0.9 mg/kg (75 ± 28 s) and 1.2 mg/kg rocuronium (55 ± 14 s), and succinylcholine (50 ± 17 s) were similar. Onset times for the groups given 0.6 mg/kg rocuronium (89 ± 33 s) and vecuronium (144 ± 39 s) were significantly longer. Clinical duration of action was longest with 1.2 mg/kg rocuronium, similar with 0.6 and 0.9 mg/kg rocuronium, and vecuronium, and least with succinylcholine.**

***Conclusions:*** **There is a dose-dependent decrease in onset time with rocuronium. The onset times for the two larger doses of rocuronium were similar to that for succinylcholine, but clinical duration of action with rocuronium was significantly longer. The brief onset time achieved with rocuronium indicates that administration of 0.9–1.2 mg/kg is an acceptable alternative to succinylcholine for rapid-sequence induction of anesthesia. (Key words: Anesthetic techniques: rapid-sequence induction. Neuromuscular relaxants: ORG 9426 (rocuronium); succinylcholine; vecuronium.)**

BOWMAN *et al.* proposed that muscle relaxants with low potency may have shorter onset times (time from drug administration to peak effect) than those of high potency. This hypothesis was confirmed in studies using steroidal muscle relaxants in animals[1] and humans.[2] This concept was, in part, the basis for the development of rocuronium.

The structure of this new relaxant and its dose-response characteristics, interaction with other anesthetics, and lack of adverse effects have been reported elsewhere.[3–8] Several clinical studies have confirmed rocuronium's brief onset time.[8,9] However, previous studies have not usually compared the use of rocuronium with that of muscle relaxants in current common use, vecuronium and succinylcholine, for rapid-sequence induction of anesthesia.

In the current study, we compare the effects of two, three, and four times the ED95 of 0.6, 0.9, or 1.2 mg/kg rocuronium with the effects of 0.1 mg/kg vecuronium and 1.0 mg/kg succinylcholine for rapid-sequence anesthetic induction in adults. Our study differs from previous investigations because it includes a succinylcholine group as control, and because it compares multiple doses of rocuronium, thus confirming a dose-response relationship for rocuronium. In addition, we blinded the investigators who were evaluating relaxant effects to the muscle relaxant administered.

## Materials and Methods

With approval from our Committee on Human Research, we obtained written informed consent from 50

* Assistant Professor of Anesthesia.

† Research Assistant.

‡ Professor and Chairman, Department of Anesthesia; Professor of Pharmacology.

Received from the Department of Anesthesia, University of California, San Francisco, California. Accepted for publication June 21, 1993. Supported in part by Organon, Inc., and the Anesthesia Research Foundation.

Address reprint requests to Dr. Magorian: Department of Anesthesia, University of California, Mount Zion, Box 1610, 1600 Divisadero, San Francisco, California 94115.

patients who were ASA physical status 1–3, and aged 18–70 yr. Patients were excluded from the study if they had evidence of neuromuscular disease or were receiving medications known to influence neuromuscular function. All patients enrolled had either Mallampati class 1 or 2 airway anatomy and no contraindications to undergoing a rapid-sequence induction of anesthesia.

*Anesthetic Management*

Patients were premedicated with 0.02–0.05 mg/kg intravenous midazolam, and then breathed 100% oxygen *via* mask with cricoid pressure. Conventional rapid-sequence induction (RSI) (intravenous thiopental→muscle relaxant→tracheal intubation) was modified to obtain baseline measurements of neuromuscular function. That is, thiopental was injected in incremental doses of 1–2 mg/kg before muscle relaxant administration to permit baseline train-of-four monitoring without patient discomfort. Patients were randomized to receive one of three doses of rocuronium (0.6, 0.9, or 1.2 mg/kg), or 0.1 mg/kg vecuronium or 1.0 mg/kg succinylcholine. No additional doses of thiopental were given once muscle relaxant was administered. Routine monitoring consisted of electrocardiography (ECG), automatic blood-pressure monitoring, and pulse oximetry.

*Monitoring of Neuromuscular Transmission*

Before the administration of the muscle relaxant, the mechanical evoked response of the adductor pollicis muscle to the first stimulus (T1) in a train-of-four sequence was determined. A Digistim 2 Plus (Neurotechnology, Houston, TX) nerve stimulator delivered supramaximal, square-wave impulses of 0.2-ms duration in a train-of-four sequence (2 Hz) *via* surface electrodes placed near the ulnar nerve at the wrist. Trains of stimuli were repeated at intervals of 12 s, and the evoked mechanical response of the adductor pollicis muscle was quantified by a force-displacement transducer (Professional Instruments APM-X, Houston, TX) and displayed on a polygraph. When the amplitude of the first twitch response of each train-of-four (T1) reached a stable plateau (*i.e.*, twitch tension remained the same for several minutes), this peak amplitude response was used as the control with which all subsequent responses were compared.

*Clinical Protocol*

The times from injection of muscle relaxant to complete ablation of T1 (onset), from injection to recovery of T1 to 25% of baseline (clinical duration of action), and from recovery of T25 to T75% (recovery index) were recorded. Sixty seconds after muscle relaxant administration, tracheal intubation was performed. Anesthesia was maintained with 0.7–1.3% isoflurane (end-tidal concentration measured by mass spectrometry) in 60% nitrous oxide and oxygen. Ventilation was controlled to maintain end-tidal $P_{CO_2}$ at 35–40 mmHg. Esophageal temperature was maintained at 36–37.5° C by surface warming. Patients in whom the T4/T1 ratio was less than 70% at the completion of the study received neostigmine (30 μg/kg) with glycopyrrolate (15 μg/kg) for antagonism of neuromuscular blockade.

Tracheal intubating conditions were judged by each clinician, and the presence or absence of fasciculations was noted. Intubating conditions in each patient were assessed using the following criteria: excellent = jaw relaxed, vocal cords apart and immobile, and no diaphragmatic movement; good = jaw relaxed, vocal cords apart and immobile, and some diaphragmatic movement; poor = jaw relaxed, vocal cords moving, and "bucking"; and inadequate = jaw not relaxed and vocal cords closed.

All investigators, with the exception of the one designated to dispense the study drug, were blinded to the choice of muscle relaxant throughout the study.

*Statistical Analysis*

Patients were divided into five study groups, with those given succinylcholine as the control group. Onset time, clinical duration of action, and recovery indices for the five groups were compared using one-way ANOVA. Pairwise comparisons and pharmacodynamic variables were obtained for each group using Student-Newman-Keuls test for multiple comparisons. Differences were considered significant when $P < 0.05$. Intubating conditions were analyzed by Kruskall-Wallis test after assigning a numeric value to each intubation score.

## Results

The study groups did not differ in age, gender distribution, or weight, with one exception: the mean weight for patients given rocuronium 1.2 mg/kg was significantly greater than that for the succinylcholine group ($P = 0.02$) (table 1). Intubating conditions also did not differ in the five groups (table 2). Fasciculations were observed in only three patients, all of whom received succinylcholine.

**Table 1. Demographics of Patient Population**

| | Rocuronium 0.6 mg/kg | Rocuronium 0.9 mg/kg | Rocuronium 1.2 mg/kg | Vecuronium 0.1 mg/kg | Succinylcholine 1 mg/kg |
|---|---|---|---|---|---|
| M/F | 5/5 | 5/5 | 8/2 | 7/3 | 3/7 |
| Age (yr) | 37 ± 12 | 30 ± 7 | 32 ± 13 | 34 ± 11 | 45 ± 16 |
| Weight (kg) | 64 ± 11 | 73 ± 12 | 77 ± 16 | 69 ± 12 | 58 ± 13 |
| Smokers/nonsmokers | 6/4 | 7/3 | 6/4 | 4/6 | 6/4 |

Values are means ± SD.

The mean dose of thiopental for each group ranged from 5.1 to 6.4 mg/kg, with no significant difference in the mean dose per group. Mean time from initial injection of thiopental to administration of muscle relaxant ranged from 5.2 to 10.3 min for all groups, with no difference in the mean time per group.

Onset times, clinical duration of action, and recovery indices for all study groups are summarized in tables 3 and 4. Onset times of rocuronium 0.9 and 1.2 mg/kg did not differ significantly from that for succinylcholine (table 3). Vecuronium onset time was significantly longer than that in each of the other study groups (fig. 1; table 4). Clinical duration of action (recovery to T25) was significantly greater with rocuronium 1.2 mg/kg than with all other doses and agents, similar with rocuronium 0.6 and 0.9 mg/kg and vecuronium, and briefest with succinylcholine (fig. 2; table 4). The recovery index (recovery from T25 to T75) was significantly lower for the succinylcholine group, but statistically similar for all other study groups. *Post hoc* power analysis revealed an 80% certainty in detecting a 15-s difference in onset time between succinylcholine and rocuronium 1.2 mg/kg.

## Discussion

Is rocuronium's onset time sufficient to replace succinylcholine in rapid-sequence induction of anesthesia? Despite the multiple adverse effects of succinylcholine (*e.g.*, hyperkalemia and malignant hyperthermia), this drug often is preferred because it offers a brief onset time, reliably optimal intubating conditions, and a brief duration of action. Rocuronium is the first nondepolarizing muscle relaxant having an onset time as short as that of succinylcholine without adverse side effects.

In our patients, rocuronium onset time appeared to be shorter than that of other nondepolarizing muscle relaxants in clinically relevant doses, ranging from 1 to 1.5 min. Optimal intubating conditions were obtained with all three rocuronium doses 1 min after muscle relaxant administration, similar to conditions achieved with succinylcholine, a finding also reported by Püringer *et al.*[9] Consistent with the latter's data, we also found that intubating conditions did not differ significantly after vecuronium or rocuronium (table 2). However, if the criteria for rapid-sequence induction of anesthesia is complete neuromuscular blockade at the time of tracheal intubation, then only doses of 0.9 and 1.2 mg/kg rocuronium were adequate in our patients. Conversely, the duration of action of these two doses of rocuronium was sufficiently long to present a clinical disadvantage when a short-acting muscle relaxant is required (table 3). Despite its brief onset, rocuronium's duration of action is not comparable with that of succinylcholine.

**Table 2. Intubating Conditions by Neuromuscular Blockade Group**

| | Rocuronium 0.6 mg/kg | Rocuronium 0.9 mg/kg | Rocuronium 1.2 mg/kg | Vecuronium 0.1 mg/kg | Succinylcholine 1.0 mg/kg |
|---|---|---|---|---|---|
| Excellent | 10 | 8 | 7 | 6 | 8 |
| Good | 0 | 2 | 3 | 3 | 2 |
| Poor | 0 | 0 | 0 | 1 | 0 |
| Inadequate | 0 | 0 | 0 | 0 | 0 |
| Fasciculations | 0 | 0 | 0 | 0 | 3 |

Criteria for intubating conditions: excellent = jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement; good = jaw relaxed, vocal cords apart and immobile, some diaphragmatic movement; poor = jaw relaxed, vocals cords moving, "bucking"; inadequate = jaw not relaxed, vocal cords closed.

**Table 3. Group Comparisons: Statistical Significance**

| | | Onset | Duration $T_{25}$* |
|---|---|---|---|
| Rocuronium 0.6 mg/kg *vs*: | Vecuronium | Yes | No |
| | Succinylcholine | Yes | Yes |
| | Rocuronium 0.9 mg/kg | No | No |
| | Rocuronium 1.2 mg/kg | Yes | Yes |
| Rocuronium 0.9 mg/kg *vs*: | Vecuronium | Yes | No |
| | Succinylcholine | No | Yes |
| | Rocuronium 1.2 mg/kg | No | Yes |
| Rocuronium 1.2 mg/kg *vs*: | Vecuronium | Yes | Yes |
| | Succinylcholine | No | Yes |
| Vecuronium *vs.*: | Succinylcholine | Yes | Yes |

* $P > 0.05$.

The above comparisons resulted from analysis of variance and multigroup comparison by the Student–Newman–Keuls test for multiple comparisons. Each neuromuscular blockade group is compared for each pharmacodynamic variable.

Although there are various techniques to allow tracheal intubation without the use of muscle relaxants,[10–12] neuromuscular blockade has been an integral component of the rapid-sequence approach to induction of anesthesia. Thus, to compare the use of different muscle relaxants for rapid-sequence induction requires excluding the influence of other anesthetic agents, determining the degree of neuromuscular blockade achieved, and judging ease of tracheal intubation by scoring intubating conditions.

We controlled for the influence of other anesthetics in several ways. First, the mean thiopental dose was similar for all patient groups; moreover, the total mean dose ranged from 5.1 to 6.4 mg/kg, only slightly greater than the conventional dose range of 4–6 mg/kg. Second, our use of incremental, rather than single-bolus, administration of thiopental is unlikely to have confounded results, because thiopental *per se* does not affect twitch tension or reliably provide adequate intubating conditions.[11–13] Similarly, the presence of the 5–10-min period between initial thiopental dose and muscle relaxant administration is unlikely to have affected results, because intubation occurred 60 s after muscle relaxant administration, consistent with the timing required for rapid-sequence induction. Finally, all patients received the same doses of the premedicant drugs, thus eliminating any potentially confounding drug interaction.

We chose to monitor twitch tension as an endpoint defining optimal intubating conditions, because this technique is quantifiable and reliable. Twitch tension alone provides the necessary pharmacodynamic information, and can provide a reliable indicator of inadequate muscle relaxation. Furthermore, maximal twitch depression is essential in circumstances that require placement of a tracheal tube without increasing intracranial pressure or intraocular pressure.

In contrast to twitch tension, intubation score provides a qualitative measure of intubating conditions.

**Table 4. Onset and Recovery Data**

| | Rocuronium 0.6 mg/kg | Rocuronium 0.9 mg/kg | Rocuronium 1.2 mg/kg | Vecuronium 0.1 mg/kg | Succinylcholine 1 mg/kg |
|---|---|---|---|---|---|
| Onset (s) | | | | | |
| n | 10 | 10 | 10 | 10 | 10 |
| Mean | 89 | 75 | 55 | 144 | 50 |
| SD | 33 | 28 | 14 | 39 | 17 |
| Range | 48–156 | 48–144 | 36–84 | 96–204 | 24–84 |
| Duration (min) | | | | | |
| n | 10 | 9 | 9 | 10 | 10 |
| Mean | 37 | 53 | 73 | 41 | 9 |
| SD | 15 | 21 | 32 | 19 | 2 |
| Range | 23–75 | 25–88 | 38–150 | 17–82 | 5–14 |
| Recovery index (min) | | | | | |
| n | 9 | 8 | 8 | 10 | 10 |
| Mean | 14 | 22 | 24 | 20 | 2 |
| SD | 8 | 14 | 11 | 18 | 1 |
| Range | 6–27 | 8–29 | 11–43 | 6–57 | 1–3 |

Variables: onset = the time interval between the completion of injection of NMB and time to maximal depression $T_1$; duration = the time interval between the completion of injection of NBM and time to maximal depression $T_1$ to 25% of control; recovery index = the time from $T_{25}$ to $T_{75}$% of recovery.

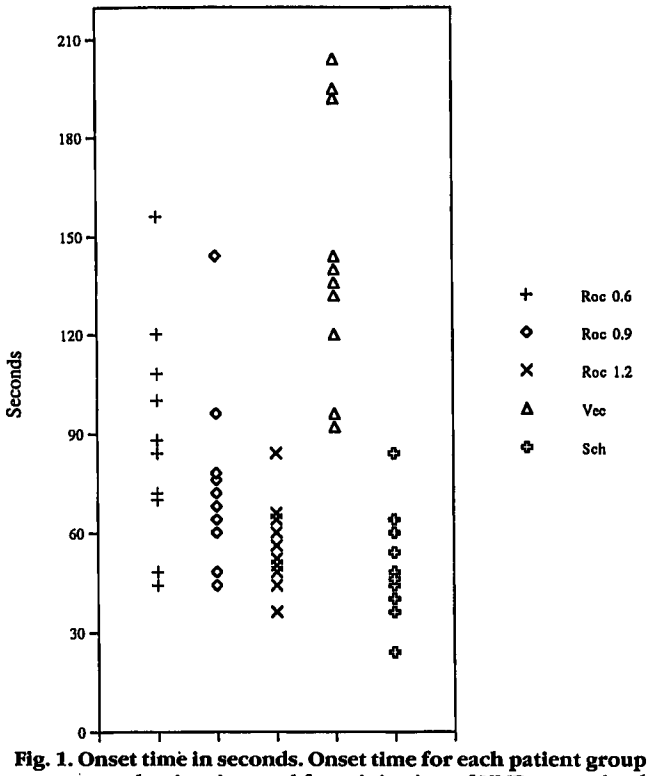


**Fig. 1. Onset time in seconds. Onset time for each patient group represents the time interval from injection of NMB to maximal twitch depression. Roc 0.6 = 0.6 mg/kg rocuronium; Roc 0.9 = 0.9 mg/kg rocuronium; Roc 1.2 = 1.2 mg/kg rocuronium; Vec = 0.1 mg/kg vecuronium; SCH = 1.0 mg/kg succinylcholine.**

One risk associated with the use of the intubation score alone is that the point at which intubating conditions become optimal can vary by protocol, drug, and clinician. Data may, therefore, be misleading. For example, McKeating *et al.*[12] demonstrated that propofol produced greater depression of pharyngeal and laryngeal reactivity than thiopental based on the intubation score, but achieved these results using only laryngoscopy without actual insertion of a tracheal tube. Conversely, Hovorka *et al.*[11] reported higher intubation scores with thiopental than propofol, but concluded that neither drug ensured "acceptable intubation conditions," even when supplemented by 1.5 mg/kg lidocaine and 30 μg/kg alfentanil. Finally, Scheller *et al.*[10] scored satisfactory intubating conditions, but only at relatively large doses of alfentanil (>40 μg/kg). In the current study, there was no difference between groups in intubation scores, and good-to-excellent intubation scores were achieved before obtaining maximal twitch tension in some patients. These inconsistencies indicate that evaluation of a muscle relaxant's effects cannot be based solely on intubation score.

Finally, the experience of the clinician, individual patient airway anatomy, patient history (smoking or bronchospastic disease), and study design may influence the comparison of intubating conditions. Although it was generally evident when our patients had received succinylcholine, we believed it necessary to blind investigators to the muscle relaxant administered to permit evaluation of the other muscle relaxant groups without bias.

We chose to measure both twitch tension and intubation score to combine reproducible quantitative criteria with qualitative clinical criteria. Only one other study has measured both indicators, reporting findings similar to our own. Pühringer *et al.*[9] compared the effects of 1 mg/kg succinylcholine and 0.6 mg/kg ro-

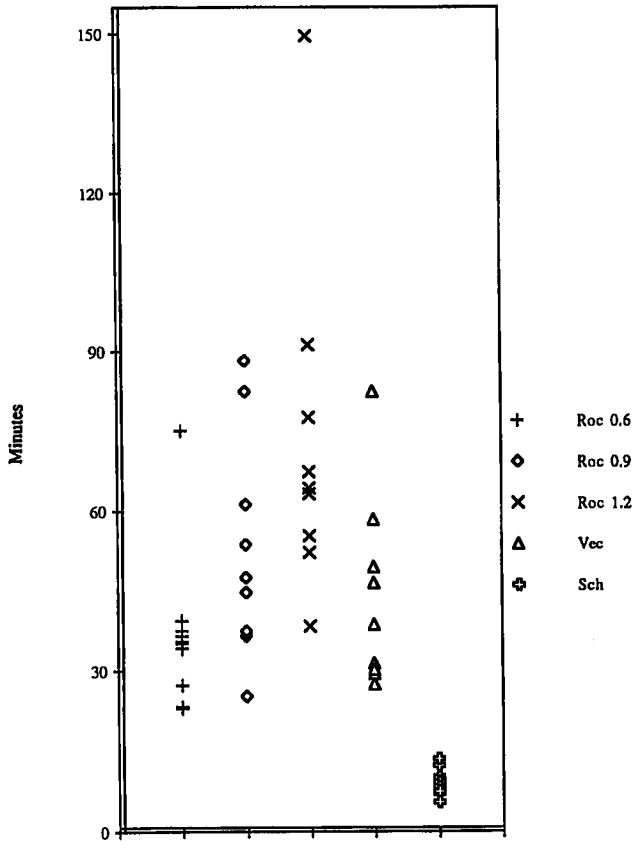


**Fig. 2. Duration of action in minutes. Duration for each patient group represents the time interval from injection of NMB to recovery of T1 to 25% of control twitch height. Roc 0.6 = 0.6 mg/kg rocuronium; Roc 0.9 = 0.9 mg/kg rocuronium; Roc 1.2 = 1.2 mg/kg rocuronium; Vec = 0.1 mg/kg vecuronium; SCH = 1.0 mg/kg succinylcholine.**

curonium after administration of 2.5 mg/kg propofol and 25 μg/kg alfentanil in outpatients. They found onset times of 1.2 and 0.8 min for rocuronium and succinylcholine, respectively, with no difference in the ability to intubate the trachea. Their onset time for rocuronium is consistent with that in our intermediate- and low-dose groups (0.6 and 0.9 mg/kg), but slower than onset with our high-dose rocuronium group (table 4).

In summary, the purpose of our study was to determine whether rocuronium onset time was sufficiently short to permit its use for rapid-sequence induction of anesthesia. We compared the effects of three doses of rocuronium with those of succinylcholine and of vecuronium. Only after 0.9 or 1.2 mg/kg rocuronium were intubating conditions and onset time comparable to those with succinylcholine. However, the duration of clinical action (>50 min) of rocuronium at these doses may present a clinical disadvantage, particularly in patients whose surgery is of short duration. Nonetheless, rocuronium may be a suitable alternative for succinylcholine during rapid-sequence induction of anesthesia, particularly in patients who are at risk for the adverse sequellae of succinylcholine.

The authors wish to thank Winifred von Ehrenburg, for her editorial contributions in the writing of this manuscript; and Valerie J. Perring, C.R.N.A., for her dedication and clinical expertise in the completion of this study.

## References

1. Bowman WC, Rodger IW, Houston J, Marshall RJ, McIndewar I: Structure:action relationships among some desacetory analogous of pancuronium and vecuronium in the anesthetized cat. ANESTHESIOLOGY 69:57–62, 1988

2. Kopman AF; Pancuronium, gallamine, and d-tubocurarine compared: Is speed of onset inversely related to drug potency? ANESTHESIOLOGY 70:915–920, 1989

3. Wierda JM, Kleef UW, Lambalk LM, Kloppenburg WD, Agoston S: The pharmacodynamics and pharmacokinetics of ORG 9426, a new non-depolarizing neuromuscular blocking agent, in patients anaesthetized with nitrous oxide, halothane and fentanyl. Can J Anaesth 38:430–435, 1991

4. Quill TJ, Begin M, Glass PS, Ginsberg B, Gorback MS: Clinical responses to ORG 9426 during isoflurane anesthesia. Anesth Analg 72:203–206, 1991

5. Wierda JM, de Wit AP, Kuizenga K, Agoston S: Clinical observations on the neuromuscular blocking agent of ORG 9426, a new steroidal non-depolarizing agent. Br J Anaesth 64:521–523, 1990

6. Foldes FF, Nagashima H, Nguyen HD, Schiller WS, Mason MM, Ohta Y: The neuromuscular effects of ORG 9426 in patients receiving balanced anesthesia. ANESTHESIOLOGY 75:191–196, 1991

7. Booij LH, Knape HTA: The neuromuscular blocking effect of ORG 9426. Anaesthesia 46:341–343, 1991

8. Szenohradszky J, Fisher DM, Segredo V, Caldwell JE, Bragg P, Sharma ML, Gruenke L, Miller RD: Pharmacokinetics of rocuronium bromide (ORG 9426) in patients with normal renal function or patients undergoing cadaver renal transplantation. ANESTHESIOLOGY 77: 899–904, 1992

9. Pühringer RK, Khuenl-Brady KS, Koller J, Mitterschiffthaler G: Evaluation of the endotracheal intubating conditions of rocuronium (ORG 9426) and succinylcholine in outpatient surgery. Anesth Analg 75:37–40, 1992

10. Scheller MS, Zornow MH, Saidman LJ: Tracheal intubation without the use of muscle relaxants: A technique using propofol and varying doses of alfentanil. Anesth Analg 75:788–793, 1992

11. Hovorka J, Honkavaara P, Korttila K: Tracheal intubation after induction of anaesthesia with thiopentone or propofol without muscle relaxants. Acta Anaesthesiol Scand 35:326–328, 1991

12. McKeating K, Bali IM, Dundee JW: The effects of thiopentone and propofol on upper airway integrity. Anaesthesia 43:638–640, 1988

13. Kallar SK: Propofol allows intubation without relaxants (abstract). ANESTHESIOLOGY 73:A22, 1990