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Rocuronium (Org 9426) for Caesarean section

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Summary

This was a prospective, non-randomized, multicentre study of rocuronium (Org 9426) in 40 elective Caesarean section patients at full term without fetal distress. Anaesthesia was induced with thiopentone 4–6 mg kg^{-1} i.v. and rocuronium 0.6 mg kg^{-1} and maintained with isoflurane and nitrous oxide in oxygen. Monitors included ECG, arterial pressure, pulse oximeter and train-of-four (TOF) produced by ulnar nerve stimulation. In all patients, full neuromuscular block at the hand indicating the maximum effect of rocuronium (T1 = 0) occurred at a mean time of 98.1 (SE 9.4) s. However, after 79.3 (2.9) s, excellent to good intubating conditions were achieved in 90% of patients. Injection to delivery time was 12.7 (0.9) min and the surgical procedure lasted 53.1 (3.5) min. After administration of rocuronium, T2 appeared after 32.7 (1.8) min (indicating duration of effect). At the end of the surgical procedure in 39 patients, glycopyrronium 0.2 mg and neostigmine 1 mg were given every 5 min to antagonize residual neuromuscular effect. The mean dose of neostigmine required was 1.54 (0.1) mg. Rocuronium had no clinically significant effect on maternal heart rate or arterial pressure. After administration of thiopentone and rocuronium in two patients, temporary erythema occurred, one along the site of injection and the other on the chest wall. Rocuronium had no untoward effects on the neonates, evaluated by 1- and 5-min Apgar scores, time to sustained respiration, total and muscular neuroadaptive capacity scores, acid–base status and blood-gas tensions in umbilical arterial and venous blood. At delivery in 32 patients, concentrations of rocuronium in maternal venous (MV) and umbilical venous (UV) plasma were 2412 (180) ng ml^{-1} and 389.6 (27.8) ng ml^{-1}, respectively (UV/MV ratio 0.16). In 12 patients, the mean concentration of rocuronium in umbilical arterial (UA) plasma was 271.2 (34.7) ng ml^{-1} with a UA/UV ratio of 0.62. 17-Desacetylrocuronium (Org 9943), the main metabolite of rocuronium, was below the sensitivity level (25 ng ml^{-1}) in umbilical venous and arterial plasma; the maternal venous plasma concentration was 178 (31) ng ml^{-1}. (*Br. J. Anaesth.* 1994; **73**: 336–341)

Key words

Anaesthesia, obstetric. Neuromuscular block, rocuronium.

Rocuronium (Org 9426) is a steroidal, non-depolarizing neuromuscular blocking agent related chemically to vecuronium. Compared with the latter, rocuronium is less potent, has a shorter onset of action, comparable duration, no cumulative effect and is more stable [1–9]. The plasma clearance of rocuronium is primarily via liver uptake and biliary excretion, while renal elimination is less than 9% [8, 10].

When rapid sequence induction is required, the relatively slow onset of action of vecuronium (3–4 min) makes it inappropriate [11]. Suxamethonium has a faster onset of action (60 s) [12] but it is a depolarizing agent associated with undesirable side effects and is inadvisable in some conditions (e.g. susceptibility to hyperpyrexia, abnormal cholinesterase genotypes, susceptibility to hyperkalaemia). When rocuronium was used in non-pregnant patients, adequate intubating conditions were achieved in 60–90 s [13–16], a desirable feature when rapid sequence induction is required, for example in Caesarean section.

Our study was conducted to evaluate the suitability of rocuronium for Caesarean section, its effects on the mother and fetus, and its placental transfer in humans.

Patients and methods

This was a prospective, non-randomized, multicentre study which was approved by the hospital and university committees overseeing human research. Written, informed consent was obtained from each patient. This study included 40 parturients, ASA I or II, undergoing Caesarean section at full term. Exclusion criteria included fetal distress, preterm labour, intrauterine fetal death or known congenital anomalies, multiple gestations, patients with predictable difficult airway or obesity (weight exceeding 100 kg), patients of ASA class III or more, patients receiving drugs that might alter the effect of neuromuscular blocking agents, for example magnesium sulphate, anticonvulsants or polypeptide antibiotics, and patients from whom informed consent could not be obtained.

Within 30 min of anaesthesia, patients received 30 ml of sodium citrate 0.3 mol $litre^{-1}$ orally. No premedication was used. After left uterine displacement, using a wedge under the right hip, monitors were applied, including ECG, automated non-

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invasive arterial pressure (AP), pulse oximeter and a continuous monitoring system for respiratory gases including oxygen, carbon dioxide and anaesthetics, using mass spectrometry (Perkin-Elmer). Neuromuscular function was assessed by stimulating the ulnar nerve at the wrist, using surface electrodes with train-of-four (TOF) supramaximal square wave impulses of 0.2-s duration administered at 2 Hz every 10 s using a battery-operated stimulator (Digi-Stem II, Neurotechnology). The resulting force of contraction of the adductor pollicis muscle (Myotrace, Professional Instruments) was measured and recorded continuously using a force transducer. After a few minutes of oxygen administration, rapid sequence induction was performed with thiopentone via a rapidly running i.v. infusion, followed by rocuronium 0.6 mg kg^{-1} ($2 \times ED_{95}$) which was injected as a single bolus in 5 s immediately after loss of consciousness. Cricoid pressure was applied from loss of consciousness to confirmation of tracheal tube placement and inflation of the tracheal tube cuff. In the first eight patients, the dose of thiopentone was 4 mg kg^{-1} and intubation was started at the disappearance of T3 of the TOF or 60 s from administration of rocuronium, whichever occurred first. Because of inadequate neuromuscular block and patient movement, we increased the dose of thiopentone to 6 mg kg^{-1} and the time to intubation to 90 s or disappearance of T3, whichever occurred first.

The condition at intubation was rated as *excellent* when the jaw was relaxed, vocal cords apart and immobile, and no movement on intubation; *good* when the jaw was relaxed, vocal cords apart and immobile, and some diaphragmatic movement on intubation; *poor* when the jaw was relaxed, vocal cords moving, and strong diaphragmatic movement (bucking) on intubation; *inadequate* when the jaw was not relaxed and vocal cords were closed. Anaesthesia was maintained with 0.75% isoflurane and 50% nitrous oxide in oxygen until the fetus was delivered. After delivery, the isoflurane concentration was reduced to 0.5% and anaesthesia was supplemented with a mean dose of morphine of 7 (SD 2.4) mg and diazepam 2.6 (1.9) mg. I.v. fluid before delivery comprised lactated Ringer's solution. After delivery, 5% glucose 1 litre, to which added oxytocin 20 u. was infused. After delivery of the fetus and return of T2, increments of rocuronium 0.12 mg kg^{-1} were administered if additional neuromuscular block was required. Maternal heart rate and AP were measured and recorded before induction of anaesthesia, after thiopentone and before rocuronium, then every 1 min for 5 min after administration of rocuronium and at least once every 5 min until the end of the procedure. A mixture of glycopyrronium 0.2 mg and neostigmine 1 mg was administered at the end of the procedure every 5 min to antagonize residual neuromuscular block, if required.

Maternal blood samples were obtained for measurement of plasma concentrations of rocuronium and its metabolite, 17-desacetyl-rocuronium (Org 9943), before induction of anaesthesia and at delivery. Blood from the umbilical vein (UV) and artery (UA) was collected also for measurement of blood-gas tensions and plasma drug concentrations.

The plasma concentrations of drugs were determined by Pharmaco Analytical Laboratories. After centrifuging the blood samples, plasma was separated and stored at −20 °C until analysed. Rocuronium, Org 9943 and an internal standard (Org 9273) were extracted from plasma using ion pair extraction followed by derivatization with *t*-butyldimethylsilyl-trifluoroacetate. Analysis was performed with capillary gas chromatography with nitrogen phosphorus detection. This method was validated with a minimum quantifiable concentration of 25.0 ng ml^{-1} for either rocuronium or Org 9943 and required 1.00 ml per plasma sample. The overall percent coefficient of variation for rocuronium was 6.72% and that for Org 9943 10.9%.

The neonate was evaluated using time to sustained respiration, 1- and 5-min Apgar scores, blood-gas tensions, acid–base status and neuroadaptive capacity scores (NACS) [17] (total score, maximum 40; muscular component, maximum 26) at 15 min, 2 h and 24 h after delivery.

Data were analysed using the statistical package Stanview 4.0.1 (FPU version, Abacus Concepts, Inc, CA, USA). Data are expressed as mean (SE) or median and range, when applicable. The relationship between intubation score and the other variables was tested using Kruskall–Wallis one-way analysis of variance. The relationship between the neonatal NACS and thiopentone dosage was tested using Mann–Whitney non-parametric ANOVA since NACS were considered non-parametric. The relationship between NACS at 15 min, 2 h and 24 h and mean fetal plasma concentration was evaluated by linear correlations. $P < 0.05$ was considered significant.

Results

Patient weight, doses of thiopentone and rocuronium and the recorded times are shown in table 1. When the dose of thiopentone was 4 mg kg^{-1}, the intubation score was significantly inferior to the larger dose of 6 mg kg^{-1} ($P = 0.03$) (table 2). Although prolonging the waiting period from 60 to 90 s showed a tendency towards improvement in intubating conditions, this was not statistically significant. At least two twitches had to disappear before good to excellent intubating conditions were provided. The mean times from rocuronium injection to disappearance of T4, T3, T2 and T1 were 81 (10.8), 84.2 (12.5), 91.6 (10.7) and 98.1 (9.4) s, respectively; the latter indicated the

Table 1 Mean (SE) patient weight, doses and operating details ($n = 40$)

Weight (kg)	77.8 (1.7)
Thiopentone dose (mg)	422.8 (14.0)
Intubating rocuronium dose (mg)	47.6 (1.2)
Injection to start of intubation (s)	79.3 (2.9)
Onset time, time to maximum effect (s)	98.1 (9.4)
Duration of effect, time to return of T2 (min)	32.7 (1.8)
Injection to delivery time (min)	12.7 (0.9)
Duration of surgery (min)	53.1 (3.5)
Injection to extubation time (min)	58.2 (3.3)

Table 2 Intubation scores (excellent = jaw relaxed, cords immobile and apart, no movement on intubation; good = jaw relaxed, cords immobile and apart, some diaphragmatic movement; poor = jaw relaxed, cords moving, strong diaphragmatic movement; inadequate = jaw not relaxed and cords closed) (No. (%)) and intubation conditions (mean (SE)). Significant differences ($P < 0.05$) *vs*: † excellent, * good and excellent scores (Kruskal–Wallis one-way ANOVA)

	No. (%)	No. of twitches present	Injection to start of intubation (s)	Onset time(s) (injection to max. effect)	Thiopentone dose (mg kg^{-1})
Inadequate	1 (2.5)	4*	72	132†	4.0†
Poor	3 (7.5)	4*	63.7 (14.3)	156 (94)†	4.0
Good	16 (40.0)	2	82.6 (4.3)	124 (12)†	5.6 (0.2)
Excellent	20 (50.0)	0.79	79.4 (2.9)	72 (11)	5.9 (0.1)

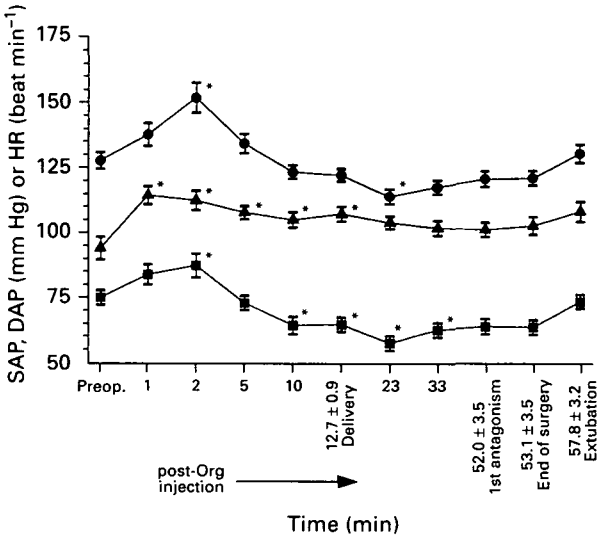

Figure 1 Mean (SE) systolic (SAP, ●) and diastolic (DAP, ■) arterial pressure and heart rate (HR, ▲) after administration of rocuronium. *$P < 0.05$ compared with preoperative value.

time for onset of action of rocuronium. With an excellent intubation score, onset of action was significantly shorter than with the other intubation scores ($P < 0.01$), indicating variability in response to drug administration. At 79.3 (2.9) s, excellent to good intubating conditions were present in 90% of patients.

A second dose of rocuronium (0.12 mg kg^{-1}) was required in five patients. With intubating doses, the recovery times of TOF, as indicated by return of T1, T2 (duration of effect), T3 and T4 were 29.6 (1.5), 32.7 (1.8), 35.6 (1.4) and 39.4 (1.8) min, respectively. With maintenance doses, the respective times were significantly shorter, for example, administration to return of T2 was 13.5 (1.6) min ($P < 0.05$). At the end of the surgical procedure (53.1 (3.5) min), glycopyrronium and neostigmine were required for complete antagonism in 39 patients, the dose of neostigmine being 1.54 (0.1) mg.

There were statistically significant increases in heart rate and AP 2 min after administration of rocuronium, coinciding with completion of intubation and skin incision (fig. 1).

One patient had a localized erythema along the vein where the drugs (thiopentone and rocuronium) were given. This resolved spontaneously in 20 min without any other skin manifestations, bronchospasm or cardiovascular depression. After induction of anaesthesia, another patient had localized erythema on the chest wall which lasted 2 min and resolved spontaneously. During surgery, one patient

Table 3 Neonatal condition (No. or mean (SEM))

Apgar scores	1 min	5 min
0–3	5	0
4–6	2	0
7–10	33	40

Time to sustained respirations (s)
Mean (SEM) 46.6 (6.7)

Total NAC scores (maximum = 40)

	Minimum	Maximum	Median
15 min	30	39	35
2 h	33	40	37
24 h	35	40	38
Muscle NAC scores (maximum = 26)			
15 min	18	26	24
2 h	20	26	25
24 h	22	26	25

Fetal acid–base and blood-gas tensions

	pH	Pco_2 (kPa)	Po_2 (kPa)	Base excess (mmol litre^{-1})
Umbilical venous blood	7.30 (0.01)	6.7 (0.1)	3.7 (0.2)	−1.8 (0.4)
Umbilical arterial blood	7.29 (0.01)	6.9 (0.2)	3.3 (0.2)	−1.8 (0.4)

Table 4 Maternal and fetal plasma concentrations of rocuronium (ng ml^{-1})

	Mean (SE)	Range	Median	Ratio of means
Maternal venous (n = 32)	2412 (180)	1120–6300	2200	
Umbilical venous (n = 32)	389.6 (27.8)	50–931	349.5	
Umbilical arterial (n = 12)	271.2 (34.7)	72–495	277	
Ratio UV/MV				0.161
Ratio UA/UV				0.62

Figure 2 Relationship between maternal plasma concentrations and time after administration of rocuronium (r^2 = 0.552, n = 32, P < 0.05).

developed uterine atony and excessive bleeding requiring hysterectomy. The neuromuscular effect was not antagonized and the patient was transferred to the intensive care unit. This patient received a total of 8000 ml of blood. This was the only patient who received fluid other than crystalloid solutions.

On the whole, neonatal conditions were good, as evaluated by Apgar scores, time to sustained respiration, total NACS and muscular NACS at 15 min, 2 h and 24 h, and umbilical arterial and venous acid–base status, and blood-gas tensions (table 3). None of the neonates required tracheal intubation. In seven neonates, the 1-min Apgar score was less than 7, but the 5-min Apgar score was 7 or more in all neonates. One of the neonates who had a transverse lie, was breathing within 30 s of delivery, had Apgar scores of 8 and 9, total NACS of 32 and muscular NACS of 21 at 15 min. At 1 h after delivery, while being bottle fed, he held his breath and was noted to have chest retraction and tachypnoea. He was admitted to the observation unit overnight. Chest x-ray was negative. No further episodes occurred and his hospital stay was uneventful. Maternal and fetal plasma concentrations of rocuronium were 2210 ng ml^{-1} and 396 ng ml^{-1}, respectively. Umbilical blood-gas tensions and acid–base status were normal.

In 32 patients, maternal venous and umbilical

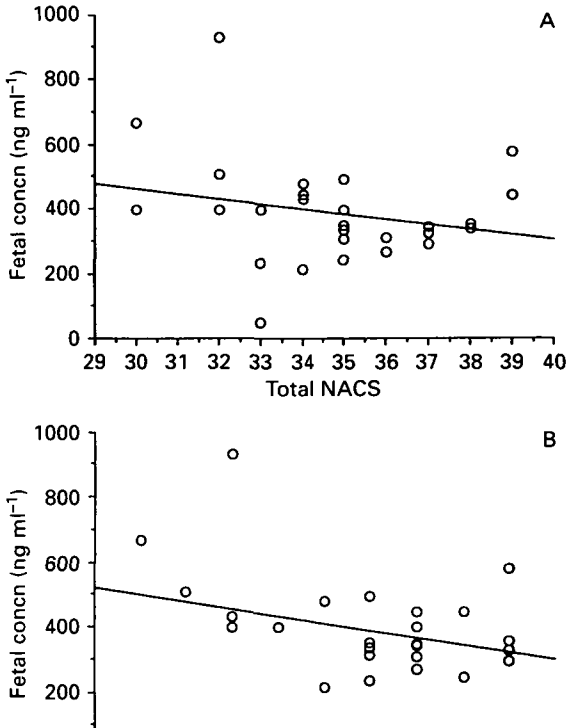

Figure 3 A: Correlation between fetal plasma concentrations of rocuronium and total NACS at 15 min (r^2 = 0.055). B: Correlation between fetal plasma concentration of rocuronium and muscular NACS at 15 min (r^2 = 0.097).

Table 5 Correlation between NACS and thiopentone dose. No significant differences (Mann–Whitney U test)

	NACS (15 min)	
Thiopentone dose	Total	Muscle
4 mg kg^{-1} (n = 8)		
Median	35	23.5
Range	32–39	20–26
6 mg kg^{-1} (n = 32)		
Median	35	24
Range	30–39	18–26
P	0.97	0.88

venous plasma concentrations of rocuronium were measured. Plasma concentrations for the mother (MV) and fetus (UV) at delivery are presented in table 4 with a UV/MV ratio of 0.16. In 12 patients, the umbilical arterial plasma concentration of rocuronium was also measured (table 4), with a UA/UV ratio of 0.62. The plasma concentration of 17-desacetylrocuronium, the main metabolite of rocuronium which has a weak neuromuscular blocking effect, was below the sensitivity level (< 25 ng ml^{-1}) in umbilical venous and arterial plasma. In maternal venous plasma, mean concentration of 17-desacetylrocuronium was 178 (31) ng ml^{-1} and the median was 158 (0–794) ng ml^{-1}.

The maternal concentration of rocuronium declined rapidly after i.v. administration; there was a significant correlation with time (fig. 2). However, there was no correlation between fetal concentrations

and either delivery time or NACS (total and muscular) at 15 min, 2 h or 24 h (figs 3A and 3B). Also, changing the dose of thiopentone from 4 to 6 mg kg^{-1} had no significant effect on NACS (table 5).

Discussion

Based on previous studies in adults indicating that $2 \times ED_{95}$ had a rapid onset of action and a duration of about 30 min [1, 2], we arbitrarily used a dose of rocuronium of 0.6 mg kg^{-1}. In one study, increasing the dose to $3 \times ED_{95}$ did not shorten the onset of action, but prolonged the duration [18]. Using the same dose of rocuronium 0.6 mg kg^{-1}, the onset time in our study (98.1 (9.4) s) was comparable with previous studies (96.7 s [6] and 95.8 (12.2) s [2]) in non-pregnant patients. The more rapid onset of action of rocuronium compared with vecuronium or pancuronium is probably partially a result of its lower potency as the time of onset of action of these drugs is proportional to their potency [16].

Previous studies have shown that, compared with suxamethonium 1 mg kg^{-1}, rocuronium 0.6 mg kg^{-1} produced similar intubating conditions and similar mean times to complete intubation [13–15, 19]. However, such an intubating dose of rocuronium was associated with a longer time to maximum depression of T1 and a longer clinical duration than suxamethonium. Prior administration of suxamethonium decreased the time to maximum depression of T1, and increased the clinical duration of subsequently administered rocuronium 0.6 mg kg^{-1}. Another study similarly showed that prior administration of suxamethonium reduced by 50% the dose of pancuronium required to achieve the same effect [20]. Recently it was found that increasing the dose of rocuronium to 3 or $4 \times ED_{95}$ (0.9 or 1.2 mg kg^{-1}) significantly shortened the onset time to a value the same as that for suxamethonium 1 mg kg^{-1} [21]. However, increasing the dose of rocuronium with Caesarean section carries the risk of increasing fetal transmission of the drug.

In our study, increasing the dose of thiopentone from 4 to 6 mg kg^{-1} improved intubating conditions without adversely affecting neonatal outcome. Kosaka, Takahashi and Mark [22] found that a dose of 6 mg kg^{-1} had no harmful effect on the neonate, but when increased to 8 mg kg^{-1}, neonatal depression was observed.

Our study was in agreement with previous studies in non-pregnant patients, where rocuronium was found to have little effect on the cardiovascular system [6, 12, 13, 23]. Our case of uterine atony leading to hysterectomy was most probably unrelated to rocuronium because no other incidence of uterine atony occurred and the neuromuscular blocking agents have no known effect on the smooth muscle of the uterus. The cutaneous reaction in two patients was transient, localized and mild. The aetiology was not clear but in neither case could the reaction be ascribed solely to rocuronium.

By simultaneously recording the force of muscle contraction at both the adductor pollicis and adductor muscles of the larynx, Meistelman, Plaud and Donati found that onset time was more rapid at the vocal cords than at the adductor pollicis [24]. In our study, intubating conditions were excellent to good in the presence of one or two twitches of the TOF at the adductor pollicis muscle and occurred in about 80 s, which was earlier than the full effect on the adductor pollicis muscle (about 98 s).

We found that placental transfer of rocuronium, as indicated by a UV/MV ratio of 0.16, was between that of vecuronium (0.11) [25] and pancuronium (0.21) [20]. The more rapid decline of rocuronium in maternal plasma, compared with vecuronium, may have been a factor in the higher UV/MV ratio with rocuronium.

17-Desacetylrocuronium has approximately 5% of the potency of rocuronium as a neuromuscular blocking agent [Organon Inc, data on file]. The concentration of this metabolite in adults necessary to produce any significant neuromuscular effect has to exceed 1000 ng ml^{-1} and for surgical neuromuscular block, 1200–2000 μg ml^{-1} [Organon Inc, data on file]. Therefore, the maternal concentration of 17-desacetylrocuronium of 178 (31) ng ml^{-1} is likely to have had no significant clinical effects. The fetal concentration of 17-desacetylrocuronium (less than 25 ng ml^{-1}) suggests that the metabolite had no effect on the fetus.

The low 1-min Apgar scores in seven neonates were related to prolonged uterine incision to delivery times, difficulty in delivery (large fetus, abnormal position) or vigorous suctioning of the pharynx causing laryngospasm. Drug concentrations and the NACS in these neonates were within the range of the group as a whole. In all patients, the 5-min Apgar scores were normal. In the one neonate that showed tachypnoea 1 h after delivery and during feeding, it is most unlikely that this effect was related to rocuronium because of the late onset and normality of the other features, including plasma concentrations of rocuronium.

The absence of a correlation between NACS (total and muscular) and fetal plasma concentrations of rocuronium is indirect evidence of the absence of any significant effect of rocuronium on the neonate. Brandom found that with 75% depression of T1 in 12 neonates between 3 and 10 months of age, the median plasma venous concentration of rocuronium was 654 (417–852) ng ml^{-1} and the mean value was 654 (SD 119) ng ml^{-1} [Brandom B. Intubation with rocuronium in pediatric patients under halothane anesthesia (unpublished observations)]. These concentrations are much higher than corresponding concentrations in umbilical arterial plasma.

In conclusion, our study showed that rocuronium 0.6 mg kg^{-1} provided excellent to good intubating conditions in 90% of Caesarean section patients when combined with thiopentone 6 mg kg^{-1} and a waiting period of 80 s after injection. Also, its use was found to be safe for mother and fetus.

References

1. Quill TJ, Begin M, Glass PSA, Ginsberg B, Borback MS. Clinical responses to ORG 9426 during isoflurane anesthesia. *Anesthesia and Analgesia* 1991; 72: 203–206.

2. Booij LHDJ, Knape HTA. The neuromuscular blocking effect of ORG 9426. *Anaesthesia* 1991; **46**: 341–343.
3. Mark J, Wierda KH, Kleef UW, Lambalk LM, Kloppenburg WD, Agoston S. The pharmacodynamics and pharmocokinetics of ORG 9426, a new non-depolarizing neuromuscular blocking agent, in patients anaesthetized with nitrous oxide, halothane and fentanyl. *Canadian Journal of Anaesthesia* 1992; **38**: 420–435.
4. Muir AW, Houston J, Green KL, Marshall RJ, Bowman WC, Marshall IG. Effects of a new neuromuscular blocking agent (ORG 9426) in anesthetized cats and pigs and in isolated nerve–muscle preparations. *British Journal of Anaesthesia* 1989; **63**: 400–410.
5. Dubois M, Kataria B, Lea D, Lapeyre G. Neuromuscular effects of ORG 9426 in humans during general anesthesia with and without enflurane. *Anesthesia and Analgesia* 1991; **72**: S57.
6. Nagashima H, Nguyen HD, Mason MM, Schiller WS, Goldiner PL, Foldes FF. Muscular relaxation with ORG 9426 under balanced anesthesia. *Anesthesiology* 1990; **73**: A890.
7. Tullock WC, Wilks DH, Brandom BW, Diana P, Cook DR. ORG 9426: single dose response, onset and duration with halothane anesthesia. *Anesthesiology* 1990; **73**: A877.
8. Khuenl-Brady K, Castagnoli KP, Canfell PC, Caldwell JE, Agoston S, Miller RD. The neuromuscular block effects and pharmacokinetics of ORG 9426 and ORG 9616 in the cat. *Anesthesiology* 1990; **72**: 669–674.
9. Mayer M, Doenicke A, Hofmann A, Peter K. Onset and recovery of rocuronium (ORG 9426) and vecuronium under enflurane anaesthesia. *British Journal of Anaesthesia* 1992; **69**: 511–512.
10. Szenohradszky J, Fisher DM, Segredo V, Caldwell JE, Bragg P, Sharma ML, Gruenke LD, Miller RD. Pharmacokinetics of rocuronium bromide (ORG 9426) in patients with normal renal function undergoing cadaver renal transplantation. *Anesthesiology* 1992; **77**: 899–904.
11. Krieg N, Crul JF, Booij LHJ. Relative potency of ORG NC 45, pancuronium, alcuronium and tubocurarine in anaesthetized man. *British Journal of Anaesthesia* 1980; **52**: 783–788.
12. Wierda JMKH, Agoston S. Human pharmacology of two steroidal, non-depolarizing, neuromuscular block agents: pipecuronium and ORG 9426. In: Mitterschiffthaler G, Denissen P, eds. *Neuromuscular Blocking Agents in Development for Operating Theatre and Intensive Care Unit*. The Netherlands: Medicom Europe, 1990; 67–81.
13. Puhringer FK, Khuenl-Brady KS, Killer 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.
14. 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.
15. Cooper R, Mirakhur RK, Clarke RSJ, Boules Z. Comparison of intubating conditions after administration of ORG 9426 (rocuronium) and suxamethonium. *British Journal of Anaesthesia* 1992; **69**: 269–273.
16. Min JC, Bekavac I, Glavinovic MI, Donati F, Bevan DR. Iontophoretic study of speed of action of various muscle relaxants. *Anesthesiology* 1992; **77**: 351–356.
17. Amiel-Tison C, Barrier B, Shnider SH, Levinson G, Hughes SC, Stefani SJ. A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. *Anesthesiology* 1982; **56**: 340–350.
18. Dubois MY, Lapeyre G, Lea D, Tran DQ, Kataria BK. Pharmacodynamic effects of three doses of ORG 9426 used for endotracheal intubation in humans. *Journal of Clinical Anesthesia* 1992; **4**: 472–475.
19. Muir AW, Houston J, Marshall RJ, Bowman WC, Marshall IG. A comparison of the neuromuscular blocking and autonomic effects of two new short-acting muscle relaxants with those of succinylcholine in the anesthetized cat and pig. *Anesthesiology* 1989; **70**: 533–540.
20. Abouleish E, Wingard LBJ, de la Vega S, Uy N. Pancuronium in Caesarean section and its placental transfer. *British Journal of Anaesthesia* 1980; **52**: 531–536.
21. 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.
22. Kosaka Y, Takahashi T, Mark LC. Intravenous thiobarbiturate anesthesia for Caesarean section. *Anesthesiology* 1969; **31**: 489–506.
23. Cason B, Baker DG, Hickey RF, Miller RD, Ogoston S. Cardiovascular and neuromuscular effects of three steroidal neuromuscular blocking drugs in dogs (ORG 9616, ORG 9426, ORG 9991). *Anesthesia and Analgesia* 1990; **70**: 382–388.
24. Meistelman C, Plaud B, Donati F. Rocuronium (ORG 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. *Canadian Journal of Anaesthesia* 1992; **39**: 665–669.
25. Dailey PA, Fisher DM, Shnider SM, Baysinger CL, Shinohara Y, Miller RD, Abboud TE, Kim KC. Pharmacokinetics, placental transfer, and neonatal effects of vecuronium and pancuronium administered during Cesarean section. *Anesthesiology* 1984; **60**: 599–605.