Rocuronium prevents succinylcholine-induced fasciculations

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Purpose: The aim of this study was to assess the effect of rocuronium pretreatment at 3 and 1.5 min before succinylcholine administration on fasciculations, neuromuscular blockade and intubating conditions.

Methods: Sixty ASA I or II adults scheduled for elective surgery were anaesthetised with midazolam, fentanyl, propofol, N_2O and isoflurane. They were randomised in a double blind manner into three groups: group ROC-3 min (n = 22) received 0.05 mg·kg^{-1} rocuronium, 3 min before 2 mg·kg^{-1} succinylcholine; group ROC-1.5 min (n = 20) received 0.05 mg·kg^{-1} rocuronium 1.5 min before 2 mg·kg^{-1} succinylcholine; and group NO ROC (n = 18) had no rocuronium before injection of 2 mg·kg^{-1} succinylcholine. Fasciculations and intubating conditions were evaluated by the same physician who was unaware of the randomisation. Neuromuscular block was measured at the adductor pollicis with an accelerometer.

Results: The incidence of fasciculations was lower in the ROC-3 min (9%) and ROC-1.5 min (30%) groups than in the NO ROC group (83%; $P < 0.001$). The intensity of fasciculations was also less in both pretreatment groups. No statistical difference was noted between pretreatment at 3 and 1.5 min. Intubating conditions, onset time and duration of succinylcholine blockade were comparable in all three groups.

Conclusion: The incidence and severity of succinylcholine fasciculations can be reduced by giving 0.05 mg·kg^{-1} rocuronium either 1.5 min or 3 min before succinylcholine. The effects of 2 mg·kg^{-1} succinylcholine with rocuronium pretreatment, and 1 mg·kg^{-1} succinylcholine, without pretreatment, are similar with respect to intubating conditions, onset of paralysis and duration of blockade.

Objectif : Évaluer l'influence du rocuronium administré 3 et 1,5 min avant la succinylcholine sur les fasciculations, le bloc neuromusculaire et les conditions d'intubation,

Méthodes : Soixante patients ASA I et II programmés pour une chirurgie non urgente ont été anesthésiés avec du midazolam, du fentanyl, du propofol et de l'isoflurane. Ils ont été assignés aléatoirement et en double aveugle à trois groupes : le groupe ROC-3 min (n = 22) a reçu le rocuronium 0,05 mg·kg^{-1} 3 min avant la succinylcholine 2 mg·kg^{-1} ; le groupe ROC-1,5 min (n = 20) a reçu le rocuronium 0,05 mg·kg^{-1} 1,5 min avant la succinylcholine 2 mg·kg^{-1} et le groupe NO ROC (n = 18) n'a pas reçu de rocuronium avant l'injection de la succinylcholine 1 mg·kg^{-1}. Un même médecin non informé de la randomisation a évalué les fasciculations et les conditions d'intubation. Un accéléromètre a servi à mesurer le bloc neuromusculaire au niveau de l'adducteur du pouce.

Résultats : L'incidence des fasciculations était plus faible dans les groupes ROC-3 min (9%) et ROC-1,5 min (30%) que dans le groupe NO ROC (83% ; $P < 0,001$). Les fasciculations étaient aussi moins intenses dans les deux groupes prétraités mais sans différence statistique entre 3 et 1,5 min. Les conditions d'intubation, la vitesse d'installation et la durée d'action du bloc à la succinylcholine ne différaient pas entre les trois groupes.

Conclusion : L'administration de rocuronium, que ce soit 1,5 ou 3 min avant la succinylcholine, peut réduire l'incidence et l'intensité des fasciculations. L'effet de la succinylcholine 2 mg·kg^{-1} avec prétraitement au rocuronium est comparable avec celle de la succinylcholine 1 mg·kg^{-1} sans prétraitement au regard des conditions d'intubation, de la vitesse d'installation de la paralysie et de la durée du bloc.

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SUCCINYLCHOLINE is still widely used to facilitate tracheal intubation because of its short onset of action and rapid recovery. It is especially recommended in patients with full stomachs.[1] However, succinylcholine has many side effects, including fasciculations and post-operative muscle pain.[2] Succinylcholine-induced fasciculations probably have a presynaptic origin,[3] and generally a small dose of non-depolarising muscle relaxant is effective in reducing their incidence.[4] All non-depolarising muscle relaxants do not have the same effectiveness against succinylcholine-induced fasciculations. For example, *d*-tubocurarine, even in relatively low doses was found to be superior to pancuronium, vecuronium, and atracurium in reducing fasciculations.[5] These variations might be related to differences in presynaptic activity. The optimal time interval before succinylcholine injection is also uncertain although it appears that better results are associated with long intervals (three to five minutes).[6]

Rocuronium has certain characteristics that make it a potential candidate as a defasciculant. It is a non-depolarising muscle relaxant with fast onset of action,[1] which suggests that the interval between defasciculant and succinylcholine could be shortened. Rocuronium might have a greater presynaptic activity than other muscle relaxants[7] and fasciculations have a presynaptic origin.[3] Therefore it could be effective against succinylcholine-induced fasciculations at intervals shorter than three to five minutes which are necessary for most of the currently used non-depolarising defasciculants.

The aim of this study was to assess the defasciculant properties of rocuronium bromide, a low potency non-depolarising muscle relaxant with fast onset of action, at three minutes (traditional interval) and at 1.5 min (short interval) before the injection of succinylcholine. To determine the effectiveness of succinylcholine preceded by rocuronium, neuromuscular blockade and intubation conditions were also assessed.

Patients and methods

After approval by the local ethics committee and informed written consent, 60 ASA I or II adults aged 18–65 yr and scheduled for elective surgery necessitating tracheal intubation were enrolled in this double blind study. Patients with known or suspected hepatic, renal or neuromuscular disorders were excluded, as were patients with electrolyte abnormality, diabetes or those taking medications known or suspected to interfere with neuromuscular function. Patients with an anticipated difficult airway or with a history of malignant hyperthermia were also excluded.

Premedication was at the discretion of the anaesthetist. In the operating room, ECG, pulse oximeter and non- invasive blood pressure were monitored. Before induction of anaesthesia, the hand and forearm contralateral to the blood pressure cuff were immobilised. Supra-maximal (60 mA) train of four stimulation every 15 sec was delivered through surface electrodes applied over the ulnar nerve at the wrist. The piezoelectric device of a *TOF- GUARD* accelerometer (Biometer International, Odense, Denmark.) was taped on the internal aspect of the distal phalanx of the corresponding thumb to assess neuromuscular blockade of the adductor pollicis muscle.

Patients were randomised into three groups. They all received 1 mg midazolam, and 1–2 $\mu g \cdot kg^{-1}$ fentanyl, after the intravenous line was inserted. Anaesthesia was induced with 2–3 $mg \cdot kg^{-1}$ propofol, given as a slow injection (15–20 sec). The accelerometer was turned on after loss of consciousness, at which time control twitch height (T_1 control) was obtained. Succinylcholine was given one minute after the start of the propofol injection. In group ROC-3 min, patients received 0.05 $mg \cdot kg^{-1}$ (0.005 $ml \cdot kg^{-1}$) rocuronium, three minutes before 2 $mg \cdot kg^{-1}$ succinylcholine, and the same volume (0.005 $ml \cdot kg^{-1}$) of normal saline was given 1.5 min before succinylcholine. In group ROC-1.5 min, normal saline was administered three minutes before 2 $mg \cdot kg^{-1}$ succinylcholine, and 0.05 $mg \cdot kg^{-1}$ rocuronium was injected at 1.5 min before 2 $mg \cdot kg^{-1}$ succinylcholine. Patients in group NO ROC received normal saline at 3 and 1.5 min before 1 $mg \cdot kg^{-1}$ succinylcholine (Table I). The dose of succinylcholine in group ROC-3 min and ROC-1.5 min was greater than in group NO ROC because pretreatment with a non-depolarising muscle relaxant increases the onset time and reduces the duration of succinylcholine blockade.[4,8] The presence of fasciculations and their severity in the upper trunk and limbs were evaluated by the same physician who was unaware of the randomisation. Both a five point scoring system and a visual analog scale were used (Table II).

Tracheal intubation was performed 60 sec after the injection of succinylcholine. If fasciculations persisted after 60 sec, intubation was delayed until their disappearance. Intubating conditions were also evaluated by the same individual as excellent, good, fair, poor or impossible (Table III). Anaesthesia was maintained with N_2O 60% and isoflurane 1–1.2% inspired while muscle relaxation was achieved with 0.2 $mg \cdot kg^{-1}$ rocuronium, once 75% first twitch (T_1) recovery (compared with pre-succinylcholine control) was attained. An additional dose of 0.1 $mg \cdot kg^{-1}$ was injected if maximum blockade achieved with 0.2 $mg \cdot kg^{-1}$ rocuronium was less than 70% ($T_1 > 30\%$).

The following variables were measured: [1] maximum sux blockade, defined as lowest (T_1) after

TABLE I Study design

Time	*−3 min*	*−1.5 min*	*−1 min*	*0 min*	*1 min*
Group ROC-3 min	0.05 mg·kg^{-1} rocuronium + 1–2 μg·kg^{-1} fentanyl	saline	2–3 mg·kg^{-1} propofol 1	2 mg·kg^{-1} succinylcholine	intubation
Group ROC-1.5 min	saline + 1–2 μg·kg^{-1} fentanyl	0.05 mg·kg^{-1} rocuronium	2–3 mg·kg^{-1} propofol	2 mg·kg^{-1} succinylcholine	intubation
Group NO ROC	saline + 1–2 μg·kg^{-1} fentanyl	saline	2–3 mg·kg^{-1} propofol	1 mg·kg^{-1} succinylcholine	intubation

TABLE II Fasciculations score

Five-point scale		*Visual analogue scale*	
0	no fasciculations	0	no fasciculations
1	minimal visible fibrillation	↓	↓
2	moderate contractions		
3	severe fasciculations		
4	maximum fasciculations	10	maximum fasciculations

succinylcholine injection; [2] sux onset time, defined as the interval between succinylcholine injection and maximum succinylcholine blockade; [3] duration to 25% recovery and duration to 75% recovery, defined as the time from injection to recovery of T_1 =25% and T_1=75%, compared with pre-succinylcholine control; [4] maximum rocuronium blockade defined as the largest T_1 depression after 0.2 mg·kg^{-1} rocuronium.

Sigmastat JANDEL statistical software was used to analyse the data. ANOVA, Kruskall-Wallis ANOVA on ranks, Fisher exact test and Tukeys test were used

TABLE III Intubation scores

Assessment					
vocal cords	open	open	moving	closing	closed
coughing	no	(while cuff inflation) with diaphragm	with diaphragm	clear	severe
laryngoscopy	easy	easy	fair	difficult	impossible
Classification					
intubating conditions	excellent	good	fair	poor	impossible

TABLE IV Demographic data

GROUP	*ROC-3 min*	*ROC-1.5 min*	*NO ROC*	*TEST*	*P*
Number of patients	22	20	18		
Age (yr)	42.2 ± 10.3	43.2 ± 13.9	39.8 ± 13.5	ANOVA*	NS
Sex : male/female	4/18	6/14	4/18	Fisher Exact test	NS
Weight (kg)	66.1 ± 13.8	70.0 ± 11.9	69.5 ± 9.9	ANOVA	NS
Height (cm)	170.6 ± 9.7	170.3 ± 8.2	169.1 ± 9.2	ANOVA	NS
Propofol dose (mg)	178 ± 28	189 ± 43	186 ± 28	ANOVA KW†	NS
Fentanyl dose (μg)	138 ± 25	152 ± 30	138 ± 39	ANOVA KW	NS

*= One way analysis of variance
†= Kruskall Wallis ANOVA on ranks
NS = non significant, ROC= rocuronium, (mean ± SD, where applicable)

TABLE V Incidence and intensity of fasciculations

	ROC -3 min	*ROC -1.5 min*	*NO ROC*
Number of patients who fasciculated	2*(9%)	6*(30%)	15 (86%)
Intensity: five-point scale median ± quartile	0 ± 0†	0 ± 1†	2 ± 1
Intensity: visual analogue score median ± quartile	0 ± 0†	0 ± 0†	5.5 ± 3

*= $P < 0.001$ Fisher exact test, †= $P < 0.001$ compared with NO-ROC group, Kruskall-Wallis one way ANOVA on ranks followed by multiple comparisons procedure, Dunns method

TABLE VII Intubating conditions

Intubating conditions	*ROC-3 min*	*ROC-1.5 min*	*NO ROC*
excellent	11	13	7
good	11	3	6
fair	0	4	5
poor	0	0	0
impossible	0	0	0

No statistically significant difference (Kruskall -Wallis one way ANOVA on ranks)

TABLE VI Characteristics of Neuromuscular Block

	ROC -3 min	*ROC -1.5 min*	*NO ROC*	*P*
Sux onset time (sec)	94 ± 28	81 ± 22	93 ± 39	NS
Maximum sux blockade (%)	100 ± 0	100 ± 0	100 ± 0	NS
Duration to 25% recovery (min)	6.2 ± 1.9	6.7 ± 3.0	5.9 ± 1.9	NS
Duration to 75% recovery (min)	9.0 ± 2.8	10.0 ± 3.3	9.2 ± 3.4	NS
Maximum roc blockade (%)	73 ± 18	74 ± 11	54 ± 19	$P < 0.05$*

(mean ± SD)

sux = succinylcholine; roc = rocuronium, *= NO-ROC versus both pretreated groups, NS = non significant, Kruskall Wallis one way ANOVA on ranks and multiple comparison procedure (Tukeys test).

when appropriate and a difference associated with a P value of less than 0.05 was considered statistically significant.

Results

There was no difference among the three groups with respect to age, sex distribution, weight, height and dose of anaesthetics (Table IV). Fasciculations occurred in 23 patients: two in the ROC-3 min group, (9%), six in the ROC-1.5 min group, (30%), and 15 in the NO ROC group (83%), $P < 0.001$ (Table V). The severity of fasciculations was lower in the pretreatment groups compared with the NO ROC group $P < 0.001$, (Table V). There was no difference between both pretreatment groups with respect to incidence and severity of fasciculations (Table V).

Onset time and duration of succinylcholine blockade did not differ among the three groups (Table VI). Maximum blockade after 0.2 mg·kg^{-1} rocuronium was less in the NO ROC group than in the pretreatment groups ($P < 0.05$; Table VI).

Intubating conditions were rated as excellent, good, or fair in all patients. There was no difference among groups (Table VII).

Discussion

This study shows that 0.05 mg·kg^{-1} rocuronium, 3 min or 1.5 min before succinylcholine administration reduces the incidence of succinylcholine-induced fasciculations. This regimen has no effect on the neuromuscular characteristics of succinylcholine provided that the dose of the depolarising agent is increased from 1 to 2 mg·kg^{-1}. In addition, injection of rocuronium after recovery from succinylcholine blockade produces a more profound blockade if rocuronium has been used as pretreatment. The incidence of fasciculations and the characteristics of succinylcholine blockade were not altered when the pre-curarisation interval was reduced from 3 to 1.5 min.

Pretreatment with a non-depolarising muscle relaxant is commonly used in clinical practice to prevent fasciculations and post-operative myalgias.[9] A large number of non depolarising muscle relaxants have been assessed in this setting.[4–6,10–15] It seems that *d*-tubocurarine is the most appropriate drug to prevent fasciculations.[5] The optimal time interval between precurarisation and injection of succinylcholine has also been studied and it appears that a waiting time of three to four minutes is optimal.[6] It is likely that the onset of the defasciculating effect of non-depolarising muscle relaxants is similar to the onset of neuromuscular blockade. Thus, the probability of fasciculations decreases with longer time intervals between pretreatment and succinylcholine administration. The speed of action of non-depolarising muscle relaxants is inversely related to drug potency[16] and this

probably explains the effectiveness of rocuronium, a low potency drug,[17] as a defasciculant, even if the interval is short.

When the interval was 1.5 min, 30% of patients given rocuronium fasciculated compared with 9% with a 3-min interval. The difference was not statistically significant. Assuming a real difference of 20% between the two time intervals, power analysis shows that a study involving 130 patients (65 per group) would be required to demonstrate a statistically significant difference with a probability of 80%. Considering that the intensity of fasciculations was small in both precurarisation groups, demonstrating a difference between the 3 and 1.5 min intervals might not be worth the effort. The reported incidence of fasciculations with 0.05 $mg \cdot kg^{-1}$ *d*-tubocurarine administered three to four minutes before succinylcholine is between 10 and 30%.[4,13,14] We found a similar incidence (9% and 30%) in our rocuronium pretreated groups. A large number of patients would be required to demonstrate which pretreatment (*d*-tubocurarine or rocuronium) is superior because the reported incidence of fasciculations is similar with both groups. Comparison between rocuronium and a non-depolarising agent other than *d*-tubocurarine is not necessary since 0.05 $mg \cdot kg^{-1}$ *d*-tubocurarine, three to four minutes before succinylcholine has been reported to be the optimal pretreatment regimen.[5]

Neuromuscular blockade was monitored with accelerography because it is an easy and convenient method in current clinical practice and results are comparable with other techniques.[18] The other advantage of accelerography that a stabilisation period is not required.[19] Thus, the drugs were given in a sequence which mimics the clinical situation. However, it was impossible to determine whether the pre-curarising doses of rocuronium had any detectable neuromuscular effect. It is unlikely that 0.05 $mg \cdot kg^{-1}$ rocuronium produced any neuromuscular block because it is one quarter of the ED_{50} dose.[17,20]

The mean onset time to maximum succinylcholine blockade was longer here (89 sec) than in a previous study.[21] Duration to T25% T_1 recovery was also shorter (6.2 min *vs* 9.8 min), probably because nitrous oxide, which is known to potentiate succinylcholine,[22] was not used before succinylcholine. In addition, if a mechanomyographic device is used, the duration and type of stimulation before stabilisation can affect neuromuscular blockade.[24] A long stabilisation period, as in the previous study,[21] is associated with shorter onset times and long duration.[23] The dependence of onset time on stabilisation period has not been observed with accelerography.[19]

Our intubating scores were lower (80% good or excellent conditions) compared with some other studies (over 95% good or excellent conditions).[4,14,21] One of the reasons for this discrepancy might be our use of a five point scoring system instead of a four point scale as in other studies. We considered total absence of any movement or cough following intubation and cuff inflation as excellent. In other studies minimal cough during laryngoscopy was considered excellent whether or not movement occurred with cuff inflation. However, intubating conditions were adequate for all patients and scores were comparable to a previous study with a five point evaluation.[12] The use of propofol as an induction agent in this study is unlikely to make intubating conditions worse than with thiopentone. A recent study suggests that intubating conditions are worse with thiopentone than with propofol.[24]

Fasciculations were assessed using two different scales, a five point system and a visual analogue scale. Both scales gave similar results and probably can be used interchangeably. The incidence of succinylcholine induced fasciculations in the general population varies between 78% and 90%,[25] which is comparable with our findings (83%), and it appears that there is no sex or age predilection in the adult population.[25] In our study there were more female than male patients (46 *vs* 14).

The dose of 0.05 $mg \cdot kg^{-1}$ rocuronium was chosen because it has approximately equipotent to 0.007 $mg \cdot kg^{-1}$ vecuronium, since the ED_{95} of rocuronium, (0.3 $mg \cdot kg^{-1}$),[17,20] is approximately seven times the ED_{95} of vecuronium, (0.04 $mg \cdot kg^{-1}$).[26] This dose is slightly less than 0.01 $mg \cdot kg^{-1}$ vecuronium, which has been shown to cause symptoms of weakness (heavy eyelids, blurring of vision) in awake patients.[27,28] Reducing the interval between pre-treatment and induction of anaesthesia, which is possible with rocuronium, also decreases the possibility of these symptoms. The potency of rocuronium is also close of that of *d*-tubocurarine (ED_{95} = 0.34–0.5 $mg \cdot kg^{-1}$).[29] Therefore, the dose of rocuronium used here was the same as that of *d*-tubocurarine commonly used for pretreatment.

Onset and duration of neuromuscular blockade was similar after 2 $mg \cdot kg^{-1}$ succinylcholine with pretreatment and 1 $mg \cdot kg^{-1}$ succinylcholine without pretreatment. This indicates that, with rocuronium pretreatment, doubling the succinylcholine dose is necessary to achieve the same effect. This is in accordance with a previous dose-response study,[8] where succinylcholine ED_{50} was increased two-fold after precurarisation with *d*-tubocurarine.

Although absence of fasciculations in any patient does not guarantee freedom from post-operative myalgias,[2,15] pretreatment with non depolarising muscle relaxants has been shown to reduce the incidence of both fasciculations and myalgias.[9] The effect of rocuronium pretreatment on post-operative myalgias needs to be assessed in a further study. However, a pretreatment regimen which reduces the incidence of fasciculations is likely to decrease the incidence of myalgias and tends to be more acceptable clinically.

In a recently published study, Findlay and Spittal[30] found, in adults, that a single dose (6 mg) of rocuronium one minute before the injection of 1.5 $mg \cdot kg^{-1}$ succinylcholine was effective as a defasciculant and prevented myalgias. However, assessment of fasciculations was not double blind and neuromuscular block was not measured. In addition, the dose of rocuronium used in that study (6 mg) might be unnecessarily high. The present study shows a considerable reduction in the incidence and severity of fasciculations with a much smaller dose (3.5 mg in the 70 kg patient). A dose of 6 mg rocuronium before induction is approximately equivalent to 0.015 $mg \cdot kg^{-1}$ vecuronium. It might produce symptoms of neuromuscular weakness[27,28] and predispose patients to the risk of aspiration. Another recent report[31] compared saline, 0.05 $mg \cdot kg^{-1}$ *d*-tubocurarine, and 0.03 $mg \cdot kg^{-1}$ rocuronium two minutes before 1.5 $mg \cdot kg^{-1}$ succinylcholine. This small dose of rocuronium was reported to be effective against both fasciculations and myalgias. In both these studies, the succinylcholine dose was not increased in precurarised groups to compensate for its reduced effectiveness, and neuromuscular blockade was not measured.

Rocuronium has been reported to produce pain on injection.[32] The same problem also occurs with administration of propofol. To minimise patient discomfort, intravenous fluid was infused rapidly before and during induction of anaesthesia, and our subjects were warned that any drug might cause pain on injection. Although the evaluation of pain was not the purpose of the study, it appears that rocuronium causes less pain than does propofol.

In summary, 0.05 $mg \cdot kg^{-1}$ rocuronium injected either at 3 or 1.5 min before succinylcholine reduced the incidence of fasciculations with no difference in neuromuscular block and intubating conditions. Because of the effectiveness of rocuronium in succinylcholine induced fasciculations, it would be appropriate to evaluate this regimen for postoperative myalgias. However, such a study would require a large number of patients because the incidence of myalgias is lower than the incidence of fasciculations.

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References

1 *Magorian T, Flannery KB, Miller RD.* Comparison of rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients. Anesthesiology 1993; 79: 913–8.

2 *Silverman DG, Donati F.* Undesirable effects of succinylcholine. *In*: Silverman DG (Ed.). Neuromuscular Block in Perioperative and Intensive Care. Philadelphia: J.B.Lippincott Co., 1994: 276–96.

3 *Hartman GS, Fiamengo SA, Riker WFJr.* Succinylcholine: mechanism of fasciculations and their prevention by *d*-tubocurarine or diphenylhydantoin. Anesthesiology 1986; 65: 405–13.

4 *Cullen DJ.* The effect of pretreatment with nondepolarizing muscle relaxants on the neuromuscular blocking action of succinylcholine. Anesthesiology 1971; 35: 572–8.

5 *Pinchak AC, Smith CE, Shepard LS, Patterson L.* Waiting time after non-depolarizing relaxants alter muscle fasciculation response to succinylcholine. Can J Anaesth 1994; 41: 206–12.

6 *Horrow JC, Lambert DH.* The search for an optimal interval between pretreatment dose of *d*-tubocurarine and succinylcholine. Can Anaesth Soc J 1984; 31: 528–33.

7 *England AJ, Richards KM, Feldman SA.* The effect of rate of stimulation on force of contraction in a partially paralyzed rat phrenic nerve hemidiaphragm preparation. Anesth Analg 1997; 84: 882-5.

8 *Szalados JE, Donati F, Bevan DR.* Effects of *d*-tubocurarine pretreatment on succinylcholine twitch augmentation and neuromuscular blockade. Anesth Analg 1991; 71: 55–9.

9 *Pace NL.* Prevention of succinylcholine myalgias: a meta-analysis. Anesth Analg 1990; 70: 477–83.

10 *Masey SA, Glazebrook CW, Goat VA.* Suxamethonium: a new look at pretreatment. Br J Anaesth 1983; 55: 729–33.

11 *Manchikanti L, Grow JB, Colliver JA, Canella MG, Hadley CH.* Atracurium pretreatment for succinylcholine-induced fasciculations and postoperative myalgia. Anesth Analg 1985; 64: 1010–4.

12 *Blitt CD, Carlson GL, Rolling GD, Hameroff SR, Otto CW.* A comparative evaluation of pretreatment with nondepolarizing neuromuscular blockers prior to the administration of succinylcholine. Anesthesiology 1981; 55: 687–9.

13 *Sosis M, Broad T, Larijani GE, Marr AT.* Comparison of atracurium and *d*-tubocurarine for prevention of succinylcholine myalgia. Anesth Analg 1987; 66: 657–9.

14 *Virtue RW.* Comparison of gallamine with d-tubocurarine effects on fasciculations after succinylcholine. Anesth Analg 1975; 54: 81–2.
15 *O'Sullivan EP, Williams NE, Calvey TN.* Differential effects of neuromuscular blocking agents on suxamethonium-induced fasciculations and myalgias. Br J Anaesth 1988; 60: 367–71.
16 *Law Min JC, Bekavac I, Glavinovic MI, Donati F, Bevan DR.* Iontophoretic study of speed of action of various muscle relaxants. Anesthesiology 1992; 77: 351–6.
17 *Cooper RA, Mirakhur R K, Elliot P, McCarthy GJ.* Estimation of the potency of ORG 9426 using two different modes of nerve stimulation. Can J Anaesth 1992; 39: 139–42.
18 *Lepage JY, Malinovsky JM, Lechevalier T, Cozian A, Pinaud M.* Neuromuscular transmission analyser: mechanomyography *vs* acceleromyography. Anesthesiology 1995; 83: A891.
19 *Girling KJ, Mahajan RP.* The effect of stabilization on the onset of neuromuscular block when assessed using accelerometry. Anesth Analg 1996; 82: 1257–60.
20 *Bevan DR, Fiset P, Balendran P, Law-Min JC, Ratcliffe A, Donati F.* Pharmacodynamic behaviour of rocuronium in the elderly. Can J Anaesth 1993; 40: 127–32.
21 *Maddineni VR, Mirakhur R.K , McCoy EP, Fee JPH, Clarke RSJ.* Neuromuscular effects and intubating conditions following mivacurium: a comparison with suxamethonium. Anaesthesia 1993; 48: 940–5.
22 *Szalados JE, Donati F, Bevan DR.* Nitrous oxide potentiates succinylcholine neuromuscular blockade in humans. Anesth Analg 1991; 72: 18–21.
23 *McCoy ÉP, Mirakhur R K, Connolly FM, Loan PB.* The influence of the duration of control stimulation on the onset and recovery of neuromuscular block. Anesth Analg 1995; 80: 364–7.
24 *Stevens JB, Vescovo MV, Harris KC, Walker SC, Hickey R.* Tracheal intubation using alfentanil and no muscle relaxant: is the choice of hypnotic important? Anesth Analg 1997; 84: 1222–6.
25 *Manchikanti L.* Diazepam does not prevent succinylcholine-induced fasciculations and myalgia. A comparative evaluation of the effect of diazepam and *d*-tubocurarine pretreatments. Acta Anaesthesiol Scand 1984; 28: 523–8.
26 *Krieg N, Crul JF, Booij LHDJ.* Relative potency of ORG NC 45, pancuronium, alcuronium, and tubocurarine in anaesthetized man. Br J Anaesth 1980; 52: 783–8.
27 *Mahajan RP, Laverty J.* Lung function after vecuronium pretreatment in young, healthy patients. Br J Anaesth 1992; 69: 318–9.
28 *Engbæk J, Howardy-Hansen, Ørding H, Viby-Mogensen J.* Precurarization with vecuronium and pancuronium in awake, healthy volunteers: the influence of neuromuscular transmission and pulmonary function. Acta Anaesthesiol Scand 1985; 29: 117–20.
29 *Ali HH, Savarese JJ.* Stimulus frequency and dose-response curve to *d*-tubocurarine in man. Anesthesiology 1980; 52: 36–9.
30 *Findlay GP, Spittal MJ.* Rocuronium pretreatment reduces suxamethonium-induced myalgia: comparison with vecuronium. Br J Anaesth 1996; 76: 526–9.
31 *Thompson-Bell G, Joshi GP, Whitten CW.* Effects of pretreatment with rocuronium on succinylcholine-induced fasciculations and myalgia: a comparison with tubocurarine and placebo. Anesthesiology 1996; 85: A828.
32 *Moorthy SS, Dierdorf SF.* Pain on injection of rocuronium bromide (Letter). Anesth Analg 1995; 80: 1067.