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Rocuronium is the best non-depolarizing relaxant to prevent succinylcholine fasciculations and myalgia

Purpose: To determine which non-depolarizing relaxant among *d*-tubocurarine, vecuronium, atracurium, mivacurium and rocuronium prevented muscular fasciculations and myalgia following succinylcholine.

Methods: In this double blind randomized study, 120 female patients scheduled for laparoscopic procedures were studied. They were divided into six groups of 20 according to the non-depolarizing pretreatment used: NaCl 0.9% (control), 0.05 mg·kg⁻¹ *d*-tubocurarine, 0.01 mg·kg⁻¹ vecuronium, 0.05 mg·kg⁻¹ atracurium, 0.02 mg·kg⁻¹ mivacurium and 0.06 mg·kg⁻¹ rocuronium. Four minutes after the pretreatment, 1.5 mg·kg⁻¹ succinylcholine was injected. Side effects of the pretreatment, the presence and magnitude of fasciculations, the ease of tracheal intubation, myalgia 1, 24 and 48 hr after surgery were observed. A Puritan Bennett Datex™ 221 NMT Relaxograph monitor was used to evaluate the neuromuscular block.

Results: Muscle fasciculations were observed in 19 of the 20 patients in the control group and in 3 of the 20 patients in the rocuronium group, the best of the pretreatments in that aspect. Four patients in the mivacurium group were unable to sustain more than four seconds head-lift after pretreatment ($P < 0.05$). Tracheal intubation conditions were better and the onset of block was faster and longer after succinylcholine in the control group ($P < 0.05$). Myalgias were present in 71 % of the patients 24 hr postoperatively and the frequency was not different among the groups.

Conclusion: Among the pretreatments tested, 0.06 mg·kg⁻¹ rocuronium was the best to prevent muscular fasciculations following succinylcholine injection. In the population studied, pretreatment did not prevent postoperative myalgia. Succinylcholine 1.5 mg·kg⁻¹ was more effective without a non-depolarizing pretreatment.

Objectif : Déterminer quel myorelaxant non dépolarisant, dont la *d*-tubocurarine, le vécuronium, l'atracurium, le mivacurium et le rocuronium, saura le mieux prévenir éles myofasciculations et les myalgies qui suivent l'utilisation de succinylcholine.

Méthode : Dans cette étude randomisée en double insu, 120 patientes devant subir une laparoscopie ont été étudiées. Elles ont été réparties en six groupes de 20 selon le prétraitement non dépolarisant utilisé : NaCl 0,9 % (témoin), 0,05 mg·kg⁻¹ de *d*-tubocurarine, 0,01 mg·kg⁻¹ de vécuronium, 0,05 mg·kg⁻¹ d'atracurium, 0,02 mg·kg⁻¹ de mivacurium et 0,06 mg·kg⁻¹ de rocuronium. Quatre minutes après le prétraitement, on a administré par injection 1,5 mg·kg⁻¹ de succinylcholine. Les effets secondaires du prétraitement, la présence et l'intensité des fasciculations, l'aisance de l'intubation endotrachéale, les myalgies 1h, 24h et 48h post chirurgicales ont été colligés. Un moniteur Relaxographe 221 NMT de Datex® Puritan Bennet a été utilisé pour quantifier le bloc neuromusculaire.

Résultats : Des myofasciculations ont été observées chez 19 des 20 patientes du groupe témoin et chez 3 des 20 patientes du groupe rocuronium, groupe affichant les meilleurs résultats au prétraitement. Du groupe mivacurium, 4 patientes étaient incapables de soulever la tête pendant plus de quatre secondes après ce prétraitement ($P < 0,05$). Les conditions d'intubation endotrachéale ont été meilleures et le bloc neuromusculaire a été plus précoce et plus prolongé après la succinylcholine chez le groupe témoin ($P < 0,05$). Des myalgies étaient manifestes chez 71 % des patientes, 24 heures après l'opération et l'incidence était similaire dans tous les groupes.

Conclusion : Parmi les types de prétraitements utilisés, c'est le rocuronium à raison de 0,06 mg·kg⁻¹ qui présentait la meilleure capacité de prévention des myofasciculations à la suite d'injection de succinylcholine. Dans la population étudiée, les prétraitements n'ont pu prévenir les myalgies postopératoires. La succinylcholine à raison de 1,5 mg·kg⁻¹ était plus efficace sans prétraitement avec un bloqueur non dépolarisant.

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THE administration of a small dose of a non-depolarizing muscle relaxant (pretreatment) is a prophylaxis for succinylcholine fasciculations and, possibly, for postoperative myalgia. A meta-analysis concluded that pretreatment with several non-depolarizing muscle relaxants, a benzodiazepine or a local anaesthetic decreased, by about 30%, the incidence of muscle aches after succinylcholine.¹ The pretreatment used the most often was *d*-tubocurarine.¹ We planned to examine the efficacy of the new short and intermediate neuromuscular relaxants in preventing fasciculations and myalgia following succinylcholine injection in patients scheduled for a laparoscopic surgery.

Material and methods

One hundred and twenty women scheduled, on an outpatient basis, for laparoscopic surgery and gynecological procedure during general anaesthesia were studied prospectively. Carbon dioxide was used to create a pneumoperitoneum. The observer and the patient were unaware of the pretreatment used and the patients were randomized into six groups of 20 patients according to pretreatment: NaCl 0.9% (control), 0.05 mg·kg⁻¹ *d*-tubocurarine, 0.01 mg·kg⁻¹ vecuronium, 0.05 mg·kg⁻¹ atracurium, 0.02 mg·kg⁻¹ mivacurium and 0.06 mg·kg⁻¹ rocuronium. The doses represent approximately 10% of the intubating dose providing good intubating conditions under light anaesthesia,² and are in the range of the doses suggested in the literature.³ Patients were excluded with known allergy to the pretreatment, with atypical plasma cholinesterase, hyperkalaemia, intra-cranial hypertension, intra-ocular hypertension, malignant hyperthermia or presenting a difficult airway. The actual weight of the patient was used if it was in the range accepted for their height (Build Study Chart, Society of actuaries and association of life insurance, 1979). If the patient was overweight, the maximal acceptable weight for the patient according to her height was used. Standard monitoring including ECG, non-invasive oscillometric blood pressure, pulse oximeter and capnometer was used. A Puritan Bennett Datex™ 221 NMT Relaxograph monitor was used. The stimulating electrodes were at the wrist over the ulnar nerve, with the recording electrodes on the thenar eminence. Supramaximal currents were determined by the Relaxograph, and TOF stimuli were applied every 20 sec. The pretreatment was always adjusted to a 3 ml volume.

At time 0, pretreatment was injected; two minutes later, the patient was evaluated for side effects including diplopia, difficulty to protrude the tongue, to open the eyes, to swallow, to breathe or to sustain a head lift

for more than four seconds. At three minutes, 1 µg·kg⁻¹ fentanyl and 2.5 mg·kg⁻¹ propofol were injected followed, four minutes later, by a bolus of 1.5 mg·kg⁻¹ succinylcholine. The Relaxograph monitor was calibrated after propofol and fentanyl injections. Following succinylcholine, the patient was observed for possible fasciculations which were graded 0 to 3 : 0 = no fasciculation at all, 1 = fasciculation in the face and/or hand, 2 = small fasciculations on the trunk and/or extremities and 3: strong fasciculations in the trunk and/or extremities. At 5.5 min, the trachea was intubated by an experienced anaesthetist unaware of the pretreatment. Intubation conditions were graded as : 0 = impossible, 1 = difficult, 2 = easy, 3 = optimal, according to the jaw relaxation, vocal cord relaxation and postintubation reaction.⁴

Anaesthesia was maintained with incremental doses of fentanyl, an infusion of 120-200 µg·kg⁻¹·min propofol, and a mixture of N₂O/O₂ 70%/30% with isoflurane 0.5% inspired. When the twitch had recovered to 20% of its control value, 0.1 mg·kg⁻¹ mivacurium was injected. Further boluses of 1 to 2 mg mivacurium were injected when TOF values were > 0. The time for maximal depression of twitch and for its recovery to 20% of control value was verified, as was the time for the TOF ratio to recover to a value >0 after 0.1 mg·kg⁻¹ mivacurium.

The tracheas were extubated when the patients were awake and breathing. Patients were evaluated one hour after their arrival in the recovery room and 24 and 48 hr later for the presence and intensity of myalgia on a 0 - 10 pain scale, in the face, jaws, thighs, calves, shoulders, back, neck and thorax. No patient received NSAID prophylaxis for pain, which was treated with fentanyl in the recovery room, and with acetaminophen with or without codeine at home. Chi-squared and Kruskal-Wallis tests were used to analyze non-parametric data. Analysis of variance with Fisher PLSD and Bonferroni-Dunn tests when indicated were used for parametric data. A probability level < 0.05 was considered significant. Means and standard deviation are used in the presentation of results.

Results

Demographic data showed that the patients did not differ (Table I). Side effects were mainly ocular in all non-control pretreatment groups, but four patients in the mivacurium group were unable to sustain a head lift for more than four seconds, complaining of difficulty in swallowing and of a subjective difficulty in breathing for two of them (*P* < 0.05). Fasciculations were observed more frequently in the control group than in all other groups and less frequently in the

TABLE I Demographic data

Pretreatment	NaCl	Vecuronium	Atracurium	Mivacurium	<i>d</i> -Tubocurarine	Rocuronium
Age (yr)	31 ± 7	34 ± 5	30 ± 6	33 ± 5	31 ± 6	30 ± 4
Weight (kg)	59 ± 12	62 ± 8	60 ± 18	66 ± 16	58 ± 7	66 ± 1
Height (cm)	160 ± 6	161 ± 3	158 ± 5	162 ± 5	161 ± 5	163 ± 4
Duration of surgery (min)	21 ± 11	25 ± 17	25 ± 11	29 ± 13	25 ± 11	23 ± 11

TABLE II Effect of pretreatment on muscular fasciculations and tracheal intubation

Pretreatment	Patients with / without fasciculations* (n)	Grade of fasciculations (0-3)	Conditions of intubation (0-3)†
NaCl	19 / 1	2.2 ± 0.5	2.9 ± 0.3
Vecuronium	11 / 9	2 ± 0.7	2.5 ± 0.5
Atracurium	7 / 13	2.4 ± 0.5	2.3 ± 0.5
Mivacurium	14 / 6	1.7 ± 0.7	2.2 ± 0.4
<i>d</i> -Tubocurarine	10 / 10	1.8 ± 0.6	2.3 ± 0.6
Rocuronium	3 / 17	2 ± 1	2.4 ± 0.5

* $P < 0.05$: NaCl and rocuronium *vs* all others

† $P < 0.05$: NaCl *vs* all others

TABLE III Effect of pretreatment on succinylcholine block

Pretreatment	Twitch at intubation*	Time to maximal twitch depression†	Time for 20% twitch recuperation‡	Time for TOF>0§
	(%)	(sec)	(min)	(min)
NaCl	0.2 ± 0.8	75 ± 25	8 ± 3	10 ± 5
Vecuronium	0.7 ± 2	83 ± 23	4 ± 1	14 ± 5
Atracurium	2 ± 3	92 ± 26	4 ± 1	14 ± 3
Mivacurium	2 ± 6	83 ± 29	5 ± 4	11 ± 4
<i>d</i> -Tubocurarine	0.3 ± 1	86 ± 33	6 ± 5	17 ± 5
Rocuronium	8 ± 11	114 ± 38	3 ± 2	12 ± 5

* $P < 0.05$: rocuronium *vs* all others groups.

† $P < 0.05$: rocuronium *vs* NaCl, vecuronium, mivacurium.

‡ $P < 0.05$: NaCl *vs* vecuronium and rocuronium; *d*-tubocurarine *vs* rocuronium.

§ $P < 0.05$: NaCl *vs* vecuronium, atracurium, *d*-tubocurarine; *d*-tubocurarine *vs* mivacurium and rocuronium.

rocuronium group than in all other groups ($P < 0.05$) (Table II). The grade of fasciculations, when present, was not different among the six groups. Intubation conditions were better in the control group than in all other group ($P < 0.05$) (Table II).

The effect of pretreatment on succinylcholine efficiency is summarized in Table III. Twitch was less depressed in the rocuronium group than in all other groups at the time of tracheal intubation, and rocuronium pretreatment slowed the onset of succinylcholine block ($P < 0.05$). Recovery of twitch to 20% was longer in the NaCl group than in all other groups and mivacurium 0.1 mg·kg⁻¹ after twitch recuperation lasted longer in the *d*-tubocurarine group.

Finally, postoperative muscular pains were more frequent at 24 hr than at 1 and 48 hr and were uni-

formly distributed among the six groups (Table IV). The muscular pain sites from the pooled data of the six pretreatment groups were usually multiple, shoulder and thoracic areas being the more frequent sites of complaint (Table V). Pain intensity was worse 24 hr postoperatively and did not differ among the most frequent sites involved (Table VI).

Discussion

Our results demonstrated the efficacy of 0.06 mg·kg⁻¹ rocuronium in preventing succinylcholine fasciculations. This was the best pretreatment among those tested. The study also confirmed the relative efficacy of all pretreatments as reported in other studies,⁵ and the diminished efficacy of succinylcholine following such pretreatment.⁶ However, the controversy concerning

TABLE IV Postoperative muscular pains

Postoperative period (hr)	Pretreatment groups						
	Patients with muscular pains	0.9 NaCl	Vecuronium	Atracurium	Mivacurium	d-Tubocurarine	Rocuronium
	(n and %)	(n)	(n)	(n)	(n)	(n)	(n)
1	5 (4.1%)	1	2	0	0	0	2
24	86 (71.6%)	16	13	13	12	15	17
48	62 (51.6%)	11	10	10	10	10	11

TABLE V Sites of muscular pain

Postoperative period (hr)	One site (n and %)	Many sites (n and %)	Shoulder (%)	Thorax (%)	Neck (%)	Back (%)	Calf (%)	Thigh (%)
1	4 (80)	1 (20)	20	—	—	20	20	40
24	27 (31.3)	59 (68.7)	41.3	22.2	19.7	10.5	3.7	2.5
48	26 (41.9)	36 (58.1)	31.3	32.3	19.6	10.7	3.9	1.9

TABLE VI Pain intensity*

Postoperative period (h)	Shoulder	Thorax	Neck	Back
1	2	—	—	—
24	6.5 ± 2	6.8 ± 1.9	6.9 ± 1.8	6.7 ± 1.9
48	4.4 ± 1.8	4.6 ± 2.1	4.7 ± 1.8	5 ± 1.9

* 0 - 10 scale

the decrease of postoperative myalgia with the use of pretreatment remains. In the present study which concerned women submitted to laparoscopic surgery on an outpatient basis, myalgia was not diminished by pretreatment.

The incidence of myalgia in the control group (without pre-treatment) where succinylcholine was used is usually > 50%¹ and the myalgia is moderate to severe.^{1,7} This is the incidence observed in the present study. Pretreatment is generally reported to reduce the incidence of myalgia by 30%.¹ We did not observe any diminution. However, pain in the shoulders and thorax represented more than 60% of the muscular pain in our study, and could have been related to the laparoscopic procedure itself and not with succinylcholine.^{8,9} Moreover, in our study, prevention of fasciculations seemed to be an all-or-none phenomenon. For example, only three patients of 20 had fasciculations in the rocuronium group. However, the intensity of fasciculations in these three patients was as great as in the 19 patients who fasciculated in the control group (2 vs 2.2/3). A lack of relationship between succinylcholine induced fasciculations and myalgia was reported many years ago.¹⁰

The electromyographic neuromuscular monitoring used allowed evaluation of the effect of 0.1 mg·kg⁻¹

mivacurium following the recovery of the twitch to 20% of the control value after pretreatment, and succinylcholine injection. It showed that pretreatment increased the duration of mivacurium, especially when a long acting neuromuscular blocker as d-tubocurarine was used (seven minute increase). This result was expected,¹¹ although electromyography monitoring differs from mechanomyography monitoring.¹²

Rocuronium was followed by atracurium, d-tubocurarine, vecuronium, mivacurium and NaCl (control) in regard to their efficacy to prevent fasciculations. Rocuronium has recently been reported effective in that function.⁷⁻¹³ The reason for this rank could be related to the greater prejunctional effect of rocuronium and atracurium.¹⁴ Succinylcholine was given 5.5 min after the pretreatment. This is longer than the usual three minute waiting period after pretreatment and should have favoured the slow acting relaxant such as mivacurium and d-tubocurarine. The side effects of pretreatment with 10% of the intubating dosage of the neuromuscular relaxant were mainly ocular and occurred in 90% of all the pretreated patients. However, four patients in the mivacurium group, the worst of the pretreatments used to prevent fasciculations, could not sustain more than a four second head lift, complained of difficulty in swallowing, with two of them reporting difficulty in breathing. This suggests that the magnitude of side effects does not correlate with the ability to prevent fasciculations.

In summary, no advantage was observed with the pretreatment, except that it prevented fasciculations. This was particularly true for rocuronium. Adverse effects included side effects of the pretreatment which were potentially dangerous with mivacurium, a need for a greater dose of succinylcholine, and a longer

duration of action of mivacurium when a longer neuromuscular blocker than this drug was used as pretreatment.

In conclusion, in ambulatory female patients having laparoscopic procedures, rocuronium was the best pretreatment in the prevention of fasciculations. The prevention of fasciculations was not related to a decrease in the incidence of myalgia in the population studied.

References

- 1 Pace NL. Prevention of succinylcholine myalgias: a meta-analysis. *Anesth Analg* 1990; 70: 477–83.
- 2 Savarese JJ, Miller RD, Lien CA, Caldwell JE. Pharmacology of muscle relaxants and their antagonists. In: Miller RD (Ed). *Anesthesia*, 4th ed. New York: Churchill-Livingstone Inc., 1994: 430.
- 3 Bevan DR, Bevan JC, Donati F. Muscle Relaxants in Clinical Anesthesia. Chicago: Year Book Medical Publishers Inc., 1988: 260.
- 4 Hawkins JL, Johnson TD, Kubicek MA, Skjonsby BS, Morrow DH, Joyce TH III. Vecuronium for rapid-sequence intubation for cesarean section. *Anesth Analg* 1990; 71: 185–90.
- 5 Jansen EC, Hansen PH. Objective measurement of succinylcholine-induced fasciculations and the effect of pretreatment with pancuronium or gallamine. *Anesthesiology* 1979; 51: 159–60.
- 6 Miller RD. The advantages of giving *d*-tubocurarine before succinylcholine (Letter). *Anesthesiology* 1972; 37: 568–9.
- 7 Findlay GP, Spittal MJ. Rocuronium pretreatment reduces suxamethonium-induced myalgia: comparison with vecuronium. *Br J Anaesth* 1996; 76: 526–9.
- 8 Mingus M, Shamsi H, Recant J, Eisenkraft J. Propofol does not affect succinylcholine postoperative myalgias. *Anesthesiology* 1993; 79: A17.
- 9 Zahl K, Apfelbaum JL. Muscle pain occurs after outpatient laparoscopy despite substitution of vecuronium for succinylcholine. *Anesthesiology* 1989; 70: 408–11.
- 10 Churchill-Davidson HC. Suxamethonium (succinylcholine) chloride and muscle pains. *BMJ* 1954; 1: 74–5.
- 11 Savarese JJ, Miller RD, Lien CA, Caldwell JE. Pharmacology of muscle relaxants and their antagonists. In: Miller RD (Ed.). *Anesthesia*, 4th ed. New York: Churchill-Livingstone Inc., 1994: 466.
- 12 Kopman AF. The relationship of evoked electromyographic and mechanical responses following atracurium in humans. *Anesthesiology* 1985; 63: 208–11.
- 13 Demers-Pelletier J, Drolet P, Girard M, Donati F. Comparison of rocuronium and *d*-tubocurarine for prevention of succinylcholine-induced fasciculations and myalgia. *Can J Anaesth* 1997; 44: 1144–7.
- 14 McCoy EP, Connolly FM, Mirakhur RK, Loan PB, Paxton LD. A comparison of train-of-four fade with different neuromuscular blocking agents. *Anesthesiology* 1994; 81: A1111.