Comparison of rocuronium and *d*-tubocurarine for prevention of succinylcholine-induced fasciculations and myalgia

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Purpose: We compared *d*-tubocurarine and rocuronium for the prevention of succinylcholine-induced fasciculations and postoperative myalgia (POM) and evaluated the influence of both drugs on the speed of onset and recovery of succinylcholine.

Methods: Seventy-five women undergoing surgery of short duration were studied. They were randomized to one of three groups: group SAL received normal saline followed three minutes later by 1.0 $mg \cdot kg^{-1}$ succinylcholine; group ROC received 0.05 $mg \cdot kg^{-1}$ rocuronium + 1.5 $mg \cdot kg^{-1}$ succinylcholine; group DTC received 0.05 $mg \cdot kg^{-1}$ *d*-tubocurarine + 1.5 $mg \cdot kg^{-1}$ succinylcholine. Single-twitch stimulation was applied to the ulnar nerve every 10 sec and the EMG response of the adductor pollicis was recorded. Fasciculations were assessed by a blinded observer on a scale of 0–3. Patients were asked 24 and 48 hr later to rate POM using a scale of 0–10.

Results: The interval needed for twitch height to decrease to 10% of initial value after succinylcholine was longer in group ROC (58 ± 20 sec) (mean ± SD) compared with group SAL (44 ± 13 sec) ($P < 0.05$). Recovery to 20% occurred faster in group ROC (324 ± 83 sec) than in groups SAL (456 ± 103 sec) and DTC (450 ± 132 sec) ($P < 0.05$). Fasciculations were more intense in groups SAL than in groups ROC and DTC ($P < 0.001$). Patients rated POM as less intense 24 hr postoperatively only in group ROC (1.2 ± 2.4) compared with group SAL (3.3 ± 3.5) ($P < 0.05$).

Conclusion: Rocuronium prevents succinylcholine-induced fasciculations and POM. Rocuronium also delays the onset of succinylcholine and shortens its duration compared with *d*-tubocurarine.

Objectif : Comparer la *d*-tubocurarine avec le rocuronium sous l'angle de la prévention des fasciculations et de la myalgie postopératoire (MPO) et évaluer l'influence des deux myorelaxants sur la vitesse d'installation et de récupération du bloc neuromusculaire à la succinylcholine.

Méthodes : Soixante-quinze femmes soumises à une chirurgie de courte durée ont participé à l'étude. Elles étaient réparties aléatoirement entre trois groupes : le groupe SAL recevait du sol. phys. suivi trois minutes plus tard de succinylcholine 1,0 $mg \cdot kg^{-1}$; le groupe ROC, rocuronium 0,05 $mg \cdot kg^{-1}$ + succinylcholine 1,0 $mg \cdot kg^{-1}$; le groupe DTC, *d*-tubocurarine 0,05 $mg \cdot kg^{-1}$ + succinylcholine 1,5 $mg \cdot kg^{-1}$. Le nerf cubital était stimulé au twitch simple aux 10 secondes et la réponse ÉMG de l'adducteur du pouce était enregistrée. Un observateur indépendant évaluait la réponse ÉMG sur une échelle de 0–3. Vingt-quatre et 48 h plus tard, on demandait aux patientes de coter la MPO sur une échelle de 0–10.

Résultats : L'intervalle requis pour abaisser le niveau du twitch à 10 % de la valeur initiale après la succinylcholine était plus long dans le groupe ROC (58 ± 20 s ; moyenne ± ÉT) comparativement aux groupes SAL (44 ± 13 s) ($P < 0,05$)). La récupération à 20% survenait plus rapidement dans le groupe ROC (324 ± 83 s) que dans le groupe SAL (456 ± 103 s) et DTC (450 ± 132 s) ($P < 0,05$). Seules les patientes du groupe ROC évaluaient la MPO comme moins intense 24 h après l'intervention (1,2 ± 2,4) comparativement au groupe SAL (3,3 ± 3,5) ($P < 0,05$).

Conclusion : Le rocuronium prévient les fasciculations et la MPO induites par la succinylcholine. Comparativement à la *d*-tubocurarine, le rocuronium retarde aussi le début d'action de la succinylcholine et raccourcit sa durée.

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SINCE its introduction in 1951,[1] succinylcholine has been used extensively in anaesthesia to produce profound neuromuscular blockade of rapid onset and short duration. However, succinylcholine commonly produces a number of undesirable effects, including muscle fasciculations and postoperative myalgia (POM). These phenomena can be modified by pretreatment with small doses of non-depolarizing neuromuscular blockers. Among these, *d*-tubocurarine was generally considered the most effective[2] until it recently became unavailable. Since it was suggested that the efficacy of *d*-tubocurarine could be attributed to its ability to interfere rapidly with depolarization at pre-junctional sites of the neuromuscular junction,[3,4] we speculated that rocuronium bromide, a newly introduced non-depolarizing blocker with rapid onset and pre-junctional effects,[5] would prevent some of the side effects of succinylcholine.

The aim of this study was to compare the efficacy or *d*-tubocurarine and rocuronium in preventing succinylcholine-induced fasciculations and POM. In addition, we wished to evaluate the influence of both drugs on the speed of onset and the recovery from the neuromuscular blockade produced by succinylcholine.

Methods

Approval for the study was given by the Institutional Review Board of Maisonneuve-Rosemont Hospital. We studied 75 ASA I and II women aged 18–50 yr undergoing elective surgery of short duration. All patients gave written consent. Patients with known neuromuscular disorders, those taking drugs known to alter the action of neuromuscular blockers and those with a body mass index[6] exceeding 30 were excluded. Anaesthesia was induced with 10 $\mu g \cdot kg^{-1}$ alfentanil and 2–3 $mg \cdot kg^{-1}$ propofol followed by a 120–250 $\mu g \cdot kg^{-1} \cdot min^{-1}$ propofol infusion. After loss of consciousness, supramaximal stimulation of the ulnar nerve at the lower forearm was determined automatically by searching for the stimulus current needed to activate all the stimulated muscle fibres (0–70 mA) and then adding 20% to this maximal current (Relaxograph NMT-100, DATEX, Helsinki, Finland). Single twitch stimulation with square pulses of 0.1 msec duration, delivered every 10 sec then began and the resultant summated muscle action potential of the adductor pollicis was recorded (T) (integrated EMG). After a stable neuromuscular response was obtained (T_c), the subjects were randomly assigned to one of three groups: group "SAL" received intravenous saline followed three minutes later by 1.0 $mg \cdot kg^{-1}$ succinylcholine, group "ROC" received 0.05 $mg \cdot kg^{-1}$ rocuronium followed three minutes later by 1.5 $mg \cdot kg^{-1}$ succinylcholine, and group "DTC" received 0.05 $mg \cdot kg^{-1}$ *d*-tubocurarine followed three minutes later by 1.5 $mg \cdot kg^{-1}$ succinylcholine. The drugs were administered from syringes, all containing the same volume, in a double-blind manner. Succinylcholine was given over five seconds. The intensity of fasciculations was assessed by an observer blinded to the medication administered. The following scale was used to characterize fasciculations: nil [0]; mild fine fasciculations of the face or neck [1]; moderate fasciculations affecting neck or limbs [2]; severe vigorous and widespread fasciculations possibly requiring forceful retention [3]. The patients' trachea was then intubated and anaesthesia was maintained with nitrous oxide, propofol infusion, and boluses of 3–5 $\mu g \cdot kg^{-1}$ alfentanil. Rocuronium bromide was administered to maintain relaxation but not before the height of T recovered to 20% of T_c following intubation. Neuromuscular blockade was reversed at the end of surgery with 0.05 $mg \cdot kg^{-1}$ neostigmine and 0.02 $mg \cdot kg^{-1}$ atropine.

Patients were contacted 24 and 48 hr postoperatively. They were asked if they suffered from diffuse muscular pain (excluding specifically pain at the surgical site or at the shoulder in the case of laparoscopic surgery) and, if so, to rate it on a scale of 0–10. They were also asked to report analgesic intake and the reason for it (surgical pain *vs* POM).

Data are expressed as mean ± SD. Quantitative variables were analysed with one-way ANOVA followed by multiple comparison test (Tukey procedure) to identify which groups were different from the others. Ordinal data were compared with the Kruskal-Wallis test followed, when indicated, with Dunn's multiple comparison test. Levels of $P < 0.05$ were considered significant. Relative risks of exhibiting fasciculations and suffering from POM were also analysed and are reported with 95% confidence limits.

Results

There were no differences among the groups in terms of age, weight, height or type of surgery (Table I). The interval needed for T to decrease to 10% of T_c following succinylcholine injection was longer only in group ROC (58 ± 20 sec) than in group SAL (44 ± 13 sec) (Table II). The time necessary for T to recover to 20% of T_c following succinylcholine administration was shorter in group ROC (324 ± 83 sec) than in groups SAL (456 ± 103 sec) and DTC (450 ± 132 sec) (Table II). The intensity of fasciculations (scale 0–3) was higher in group SAL than in groups ROC and DTC (Table III). There was more intense POM (scale 0–10) 24 hr postoperatively in group SAL (3.3 ± 3.5) than in group ROC (1.2 ± 2.4) (Figure).

TABLE I Demographic data

GROUP	*SAL*	*ROC*	*DTC*
Age (yr)	35.0 ± 6.1	32.2 ± 6.5	33.5 ± 6.5
Weight (kg)	60.3 ± 8.6	63.2 ± 10.5	68.4 ± 9.1
Height (cm)	161 ± 7	162 ± 7	163 ± 7
Surgery*	18/5/2	17/6/2	19/5/1

Values are expressed as mean ± SD (n = 25 per group)
*abdominal laparoscopic/abdominal non-laparoscopic/others

TABLE II Onset and recovery following suxamethonium

GROUP	*SAL*	*ROC*	*DTC*
Time between succinylcholine and decrease of T to 10% of T_c (sec)	44 ± 13*	58 ± 20	50 ± 16
Time between succinylcholine and recovery of T to 20% of T_c (sec)	456 ± 103†	324 ± 83	450 ± 132†

Values are expressed as mean ± SD (n = 25 per group)
*$P < 0.05$ *vs* group ROC
†$P < 0.05$ *vs* group ROC

TABLE III Intensity of fasciculations (scale 0–3)
(Kruskal-Wallis followed with Dunn's multiple comparison)

GROUP	*SAL (n = 25)**	*ROC (n = 25)*	*DTC (n = 25)*
0 (none)	0	13	9
1 (mild)	4	11	17
2 (moderate)	11	0	0
3 (severe)	10	1	0

*$P < 0.001$ *vs* group ROC and group DTC

TABLE IV Relative risks with regard to fasciculations and myalgia

GROUP (n)	*n*	*relative risk compared with SAL (95% confidence bounds)*
fasciculations		
SAL (25)	25	
ROC (25)	12	2.1 (1.4–3.1)*
DTC (25)	17	1.5 (1.1–1.9)*
severe myalgia (24 hr)†		
SAL (25)	8	
ROC (25)	1	8.0 (1.1–59.3)*
DTC (25)	2	4.0 (0.9–17.0)
severe myalgia (48 hr)†		
SAL (25)	2	
ROC (23)‡	1	1.8 (0.2–19.0)
DTC (24)‡	1	1.9 (0.2–19.8)

*significant risk
†intensity ≥6 (scale 0–10)
‡3 patients, 2 in group ROC and 1 in group DTC could not be reached at 48 hr

The relative risk of exhibiting fasciculations in group SAL was 2.1 (1.4–3.1) compared with group ROC and 1.5 (1.1–1.9) compared with group DTC (Table IV). The relative risk of suffering from severe POM (≥6 on a scale of 0–10) 24 hr postoperatively in group SAL was 8.0 (1.1–59.3) compared with group ROC, and 4.0 (0.9–17.0) compared with group DTC (Table IV). No differences existed between the groups at 48 hr with regard to POM intensity (Figure) or relative risk of severe POM (Table IV). A total of 69 patients (23 in each group) took analgesics. Nine patients in group SAL, six in group ROC and four in group DTC admitted taking them because of POM (P: NS).

Discussion

The present study demonstrates that rocuronium reduces the fasciculations and POM associated with succinylcholine.

Although the need for succinylcholine in modern anaesthesia is diminishing, its unique pharmacodynamic profile combining fast onset and short recovery will probably secure its presence in our armamentarium until a non-depolarizing neuromuscular relaxant can duplicate its attributes. Thus, a reliable method of reducing succinylcholine-induced fasciculations and POM is still needed.

Hartman *et al.* demonstrated that fasciculations are caused by axonal depolarization initiated by the action of succinylcholine on pre-junctional nicotinic receptors at the neuromuscular junction.[7] The effectiveness of *d*-tubocurarine in reducing fasciculations might be related to its important pre-synaptic effects.[8] Erkola showed that the ability of *d*-tubocurarine to induce a strong train-of-four fade, an indicator of pre-junctional effects,

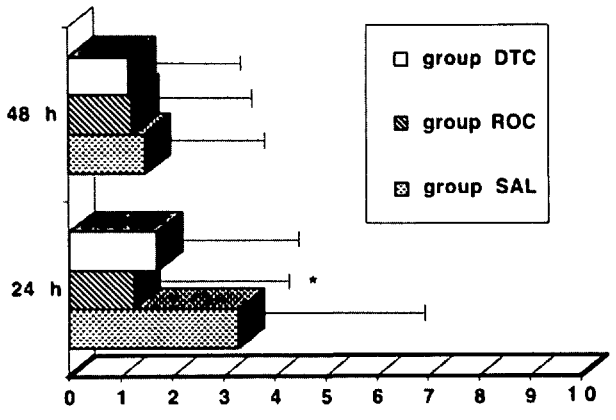

FIGURE Intensity of postoperative myalgia (scale 0–10) at 24 and 48 hr. (ANOVA followed with Tukey procedure).
Values are expressed as mean ± SD.
*$P < 0.05$ *vs* group SAL

correlated with its ability to prevent fasciculations.[4] Although our study showed that rocuronium effectively prevented fasciculations, its effect on the paralysing action of succinylcholine was also considerable. Rocuronium bromide, at the dose administered in this study, delayed the onset of succinylcholine and shortened its duration. These findings suggest that rocuronium is more likely than *d*-tubocurarine to interfere with the post-junctional (paralysing) effects of succinylcholine. This could be because the doses of rocuronium and *d*-tubocurarine used in this study were not exactly equipotent, rocuronium being slightly more potent than *d*-tubocurarine. We waited three minutes between the administration of the non-depolarizing relaxant and succinylcholine because this was described as the optimal interval with *d*-tubocurarine.[9] Since rocuronium exhibits a faster onset than *d*-tubocurarine, we may speculate that a shorter interval, or the administration of a smaller dose of rocuronium, could also have been effective in reducing fasciculations while interfering less with the paralysing action of succinylcholine.

The relation between fasciculations and POM is controversial.[3,10] While it is generally agreed that pretreatment with a non-depolarizing relaxant could reduce POM,[11,12] it is not clear that *d*-tubocurarine is the most effective drug to do so.[13–15] In our study, only rocuronium decreased the intensity of POM 24 hr postoperatively compared with placebo (Figure). It was also effective in reducing the risk of suffering from severe POM (Table IV).

Although our study suggests that rocuronium can be an effective substitute to *d*-tubocurarine with regard to preventing fasciculations and POM associated with succinylcholine, it still leaves some questions unanswered. First, both the optimal dose of rocuronium and pretreatment interval need to be determined. Second, we elected to induce anaesthesia before administering the pretreatment drugs. We did so in order to perform calibration of the Relaxograph NMT-100® while patients were anaesthetised to minimize discomfort. We need confirmation, in awake patients, that rocuronium does not induce clinical weakness. It has also been suggested that rocuronium could produce pain at the site of injection.[16,17] Again studies in awake patients are needed to evaluate this phenomenon.

In summary, rocuronium is as effective as *d*-tubocurarine in preventing fasciculations following the administration of succinylcholine. It is also reliable with regard to reducing POM.

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