Reports of Investigation

A rapid precurarization technique using rocuronium

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Purpose: To evaluate a rapid and time-saving precurarization technique using rocuronium to prevent succinylcholine-induced myalgia.

Method: In a prospective, double blind randomized study, 42 ASA 1–2 patients were assigned to one of three pretreatment groups: 0.01 ml·kg^{-1} normal saline, 0.1 mg·kg^{-1} atracurium, and 0.1 mg·kg^{-1} rocuronium. Anaesthesia commenced with 1.5 μg·kg^{-1} fentanyl and 0.5 mg·kg^{-1} lidocaine at time zero. Pretreatment was administered 60 sec later, followed by 2.5 mg·kg^{-1} propofol. At 90 sec, 1.5 mg·kg^{-1} succinylcholine was injected and 30 sec later, the trachea was intubated and the ease of intubation was graded. The patient was observed for the presence and severity of fasciculations. Myalgias were recorded on postoperative days 1, 2 and 7.

Results: The incidence of fasciculations in the rocuronium group (21.4%) was lower ($P < 0.001$) than atracurium (78.5%) or placebo (92.8%) groups. On postoperative day 1, the incidence of postoperative myalgia in the rocuronium group (14.2%) was less than the placebo group (78.2%; $P < 0.002$) and atracurium group (85.7%; $P < 0.001$). The incidence of myalgia in the rocuronium group (7.1%) was lower than in the placebo group (78.5%; $P < 0.001$) but not different from the atracurium group (42.8%; $P = 0.077$) on postoperative day 2. On postoperative day 7, there was no difference among the three groups. Fasciculations were related to postoperative myalgia. There was no difference in intubating conditions among the three groups.

Conclusion: Rocuronium pretreatment given just before induction of anaesthesia with propofol reduces fasciculations and succinylcholine-induced myalgia.

Objectif : Évaluer une technique de précurarisation rapide à base de rocuronium pour prévenir les myalgies causées par la succinylcholine, tout en sauvant du temps.

Méthode : Dans une étude prospective, à double insu et aléatoire, 42 patients de classe ASA 1 et 2 ont été répartis en 3 groupes selon le prétraitement reçu : 0,01 ml·kg^{-1} de NaCl 0,9%, 0,1 ml·kg^{-1} d'atracurium et 0,1 mg·kg de rocuronium. Au temps zéro de l'anesthésie, les patients ont reçu 1,5 mg·kg^{-1} de fentanyl et 0,5 mg·kg^{-1} de lidocaïne. Soixante secondes plus tard, on a administré le prétraitement suivi de 2,5 mg·kg^{-1} de propofol. À 90 secondes, on a injecté 1,5 mg·kg^{-1} de succinylcholine et 30 secondes plus tard la trachée a été intubée et on a évalué la facilité de l'intubation. On a recherché chez les patients la présence de fasciculations, dont on a évalué la sévérité. On a évalué les myalgies en postopératoire aux jours 1, 2 et 7.

Résultats : L'incidence de fasciculations a été plus faible dans le groupe rocuronium (21,4%, P 0,001) que dans le groupe atracurium (78,5%) ou le groupe placebo (92,8%). Au jour 1, l'incidence des myalgies était plus faible dans le groupe rocuronium (14,2%) que dans le groupe placebo (78,2%, P 0,002) et dans le groupe atracurium (85,7%, P 0,001). Au jour 2, l'incidence des myalgies dans le groupe rocuronium demeurait plus faible que dans le groupe placebo (78,5%, P 0,001) mais n'était pas différente du groupe atracurium (42,8%, P=0,077). Au jour 7, il n'existait plus de différence entre les 3 groupes. Les myalgies postopératoires étaient en relation avec les fasciculations. On n'a constaté aucune différence dans les conditions d'intubation.

Conclusion : Le prétraitement avec le rocuronium administré immédiatement avant une induction au propofol réduit les fasciculations et les myalgies provoquées par la succinylcholine.

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DESPITE the recent arrival of short-acting, nondepolarizing neuromuscular blockers, succinylcholine continues to be a commonly used neuromuscular blocker to facilitate tracheal intubation.[1,2] However, the prevalence of fasciculations and myalgias is high after the injection of succinylcholine, especially in women and muscular adults.[3] This complaint is most common in healthy female outpatients.[4] Although the relationship between muscle pains and fasciculations is not well established, recent studies suggest that there may be a protective effect from precurarization with a small dose of a nondepolarizing neuromuscular blocking drug.[3] Many studies have compared various non-depolarizing agents and pretreatment intervals required for precurarization.[1-3] An optimal pretreatment interval of three minutes has been recommended for many commonly used agents such as vecuronium, atracurium and *d*-tubocurarine.[1-3] However, such a lengthy interval is not only impractical with busy operating room lists but it also exposes the awake patient to the potentially unpleasant experiences of difficulty in swallowing or breathing. To avoid these hazards, a more rapid precurarization technique that does not expose the patients to the side effects of the precurarization is desirable. Thus, the prospective doubled blinded study described here was to examine the clinical effectiveness of a new precurarization approach using rocuronium to prevent fasciculations and postoperative myalgia from succinylcholine and to compare it with another commonly used agent atracurium.

Methods

Following ethics approval, institutional review and written informed consent, 42 patients scheduled for elective gynaecological (tubal ligation or diagnostic) laparoscopic procedures, requiring tracheal intubation were studied in a double blind randomized study. Patients were divided into three groups. Fourteen patients were allocated randomly to each pretreatment group: 0.01 $ml \cdot kg^{-1}$ normal saline (placebo), 0.1 $mg \cdot kg^{-1}$ atracurium, and 0.1 $mg \cdot kg^{-1}$ rocuronium.

Pain on injection is a common problem with both propofol and rocuronium. In this study, a small dose of lidocaine was injected one minute before the pretreatment in order to reduce the incidence of local irritation. After the installation of a standard infusion pump, Ringers lactate was started at a flow rate of 600 $ml \cdot hr^{-1}$ into the patients *iv* catheter. The induction regimen (Figure 1) was as follows: at time zero, 1.5 $\mu g \cdot kg^{-1}$ fentanyl and 0.5 $mg \cdot kg^{-1}$ lidocaine was administered: one minute later, the blinded pretreatment study drug was injected followed 10 sec later by 2.5 $mg \cdot kg^{-1}$ propofol. At 90 sec, 1.5 $mg \cdot kg^{-1}$ succinylcholine was injected. Thirty seconds later, the trachea was intubated and the ease of intubation was assessed[1] as good (easy intubation with no reaction from the patient), adequate intubation with reaction of slight coughing or bucking) or poor (intubation with marked patient response). The patient was observed for two minutes following succinylcholine administration for the presence and severity of fasciculations on a four-point scale[1]: nil = no visible fasciculations; mild = very fine fingertip or facial muscle movements; moderate = minor fasciculations on trunk and extremities, severe = vigorous fasciculations on trunk and extremities. Anaesthesia was maintained with isoflurane 1–2% in a mixture of nitrous oxide and oxygen (50%/50%). Using train-of-four measurement, mivacurium was given when needed to some of the patients to facilitate surgery. We did not measure twitch height during induction phase as it is not our routine practice. At the end of the procedure, neuromuscular blockade was reversed in all patients who received mivacurium with 0.5 $mg \cdot kg^{-1}$ edrophonium (preceded by 7 $\mu g \cdot kg^{-1}$ of glycopyrrolate). All patients were evaluated by telephone interview on postoperative days 1, 2 and 7 by an investigator, blinded to the pretreatment. Myalgia was assessed on a four-point scale[1]: nil = no muscle pains or stiffness; mild = muscle pains or stiffness at one site but not causing disability or limiting activities; moderate = muscle pains or stiffness at more than one site but not causing disability or limiting activities; severe = muscle pains or stiffness at one site or more and causing disability or limiting activities, e.g., difficulty getting out of bed or turning the head. Typical succinylcholine-induced myalgia is generalized aching and stiffness, similar to the one that follows heavy exercise.

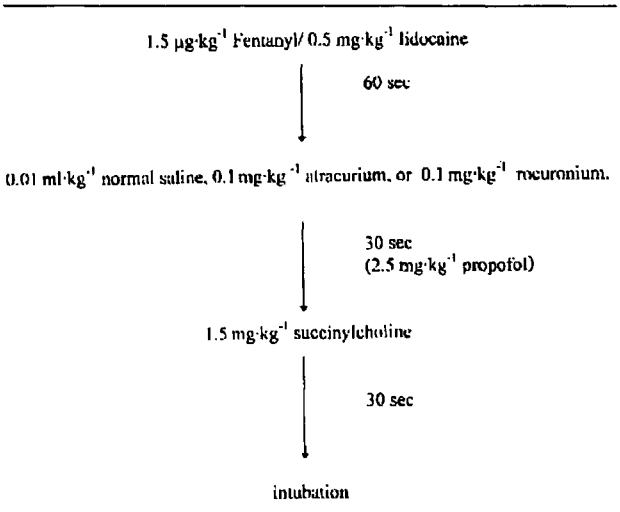

FIGURE 1 Induction regimen

Other symptoms unrelated to the use of succinylcholine such as incisional pain, diffuse abdominal pain and referred shoulder pain from diaphragmatic irritation occur frequently after laparoscopy.[5] These symptoms were not included in the above described assessments. In the postoperative period, patients were asked whether they recalled any blurred vision or difficulty breathing during the induction. For post-operative analgesia, acetaminophen with codeine *po* was given when needed.

The statistical significance of the data was analysed using the Chi-square test and Fishers exact test. Statistical significance was assumed when $P < 0.05$. In addition, the association between the appearance of fasciculation and the presence of myalgia in the postoperative period was examined using Kappa analysis.

Results

No patients were able to recall blurred vision or difficulty breathing from the pretreatment. There were no differences in patient characteristics or surgical details (Table I). There was no difference in intubating conditions among the three groups (Table II). The incidence of fasciculations (Table III) in the rocuronium group (21.4%) was lower ($P < 0.001$) than in the atracurium (78.5%) or placebo (92.8%) groups. On postoperative day 1 (Table IV), the incidence of postoperative myalgia in the rocuronium group (14.2%) was less than in the placebo (78.2%; $P < 0.002$) and atracurium (85.7%; $P < 0.001$) groups. The incidence of myalgia in the rocuronium group (7.1%) was lower than in the placebo group (78.5%; $P < 0.001$) but not lower than in the atracurium group (42.8%; $P = 0.077$) on postoperative day 2 (Table IV). On postoperative day 7, all patients were free of myalgia except one from the placebo group who suffered mild myalgia. The appearance of fasciculations was also found to be related to the presence of myalgia in the postoperative period (Table V).

Discussion

Although the relationship between muscle pains and fasciculations is not well established, recent studies suggest that there may be a protective effect from precurarization.[3,6,7] In a recent study by Findlay and Spittal,[1] rocuronium was reported to be effective in preventing fasciculations and postoperative myalgia when it was given one minute before succinylcholine but after induction of anaesthesia with propofol and fentanyl. Despite the unusual sequence of precurarizing with rocuronium after propofol, this study supports the

TABLE I Patient characteristics and surgical details. Mean ±SD

	Group *Placebo*	*Atracurium*	*Rocuronium*
Age (yr)	29.4 ± 6.2	27.3 ± 6.4	31.4 ± 5.4
Weight (kg)	68 ± 16.3	70.2 ± 18.1	67.7 ± 11.8
Surgical time (min)	24.5 ± 5.9	20.9 ± 6.1	22.5 ± 3.5

TABLE II Intubating conditions. No significant differences. (Chi-square)

		Group *Placebo*	*Atracurium*	*Rocuronium*
Intubating Conditions	Good	13	10	13
	Adequate	1	4	1
	Poor	0	0	0

TABLE III Incidence and severity of fasciculations.

Group	*Placebo*	*Atracurium*	*Rocuronium*
None	1	3	11
Mild	2	6	3
Moderate	5	4	0
Severe	6	1	0
Incidence (%)	92.8	78.5	21.4*

Fishers Exact Test (*$P < 0.001$ *vs* placebo group, $P = 0.007$ *vs* atracurium group)

TABLE IV Incidence and severity of myalgia.

	Day 1 *Placebo*	*Atracurium*	*Rocuronium*	*Day 2* *Placebo*	*Atracurium*	*Rocuronium*
Myalgia						
None	3	2	12	3	8	13
Mild	3	6	2	8	3	1
Moderate	5	4	0	3	1	0
Severe	3	2	0	0	2	0
Incidence (%)	78.5	85.7	14.2*	78.5	42.8	7.1†

Fishers Exact Test (Day 1:*$P < 0.002$ *vs* placebo group, $P < 0.001$ *vs* atracurium group; Day 2: †$P < 0.001$ *vs* placebo group, $P = 0.077$ *vs* atracurium)

notion of rocuronium providing rapid effective precurarization within a short interval.

The principal findings of this study were a reduction in the incidence of myalgia in the rocuronium group compared with the placebo and atracurium group on postoperative day 1. On postoperative day 2, the incidence of myalgia in the rocuronium group was lower than in the placebo group ($P < 0.001$) but not significantly lower than in the atracurium group ($P = 0.077$). This may be a reflection of the small size as a reduction of incidence of myalgia from 42.8% with atracurium group to 7.1% may be considered clinically important. In this study, the appearance of fasciculations did seem to be related to the presence of myalgia in the postoperative period ($P = 0.001$).

The post-operative myalgia usually begins 12–48 hr after the patient has received succinylcholine.[3,8] In most cases, the duration of pain persists for one to two days but occasionally it may continue for five to six days.[8] This is consistent with the findings of this study as all patients were free of myalgia except one patient from placebo group having mild myalgia on postoperative day 7.

As pretreatment with a non-depolarizing relaxant may affect intubating conditions, a higher dose of 1.5 $mg \cdot kg^{-1}$ succinylcholine is commonly recommended and was used in this study.[1,4,7] The commonly reported incidence of myalgia varies from 5 to 83% after succinylcholine injection.[3,6] In our study, there was an incidence of myalgia of 78% in the placebo group. The use of a higher dose of succinylcholine (1.5 $mg \cdot kg^{-1}$) in all study groups may have been responsible for the high incidence of myalgia in the placebo group and may have added subtle bias in contrasting and amplifying the improvements from pretreatment groups over the placebo group.

Succinylcholine has a rapid onset (30 to 60 sec) of action.[9] Despite 60 to 90 sec being the recommended time to achieve optimal intubating conditions,[3,4] it is seldom that the anaesthetist waits the recommended full 60 sec before intubation. Since it is not uncommon in clinical practice that the anaesthetist intubates the trachea as early as 30 sec after succinylcholine injection, we chose to intubate the trachea 30 sec after succinylcholine to make the study more applicable to common clinical practice.

A dose of 0.6–1.2 $mg \cdot kg^{-1}$ rocuronium will usually produce good intubating conditions within 60–90 sec.[4,10] To reduce fasciculation, it is commonly recommended that 10–15% of a non-depolarizer intubating dose can be used.[4] Thus, a pretreatment dose of 0.1 $mg \cdot kg^{-1}$ rocuronium was used in this study. For ease of blinded administration, we selected the atracurium pretreatment dose at 0.1 $mg \cdot kg^{-1}$. Despite three minutes being the optimal time to wait after precurarization with atracurium,[3,6,7] we chose to standardize the comparison at 30 sec before succinylcholine administration for all groups. This was done for both ease of comparison and because, in clinical practice, it is seldom that the anaesthetist waits the recommended three minutes. It is speculated that the higher dose used (0.1 $mg \cdot kg^{-1}$ rocuronium) in this study rather than the previously reported dosage (0.06 $mg \cdot kg^{-1}$) of rocuronium[2] may have contributed to enhancement of the rocuronium precurarization effect. In addition to the higher rocuronium dose, the theoretical explanation for this rapid precurarization effect in this new technique (Figure 1) is that the time needed to perform intravenous induction (30 sec) and the onset of succinylcholine (30 sec) is long enough for rocuronium to begin precurarization. It is postulated that rocuronium, because of its rapid onset of action, can provide good intubating conditions within 60 sec presumably it may also precurarize in a relatively short interval, perhaps 60 sec.

In conclusion, our study demonstrated reduction of succinylcholine induced fasciculation and myalgia using a new approach of precurarization with rocuronium. This approach is a time-saving technique which minimizes exposure of the awake patient to the unpleasant experience of partial neuromuscular blockade from precurarization.

TABLE V Severity of fasciculations *vs* postoperative myalgia.

		Fasciculations			
		None	*Mild*	*Moderate*	*Severe*
Myalgia	None	11	3	2	0
	Mild	2	6	3	1
	Moderate	1	1	2	4
	Severe	0	2	2	2

Kappa $P = 0.001$.

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