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Vecuronium for Muscle Relaxation in Patients with Myasthenia Gravis

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The shorter duration of action of atracurium and vecuronium might facilitate inducing controlled muscle relaxation in patients with neuromuscular disease as compared with longer-acting drugs such as pancuronium.[1] After encouraging results with atracurium,[2–6] we examined vecuronium for its neuromuscular blocking potency and duration of action in patients with myasthenia gravis.

METHODS

Five patients undergoing thymectomy for myasthenia gravis (table 1) and five patients without neuromuscular disease scheduled for general surgical procedures gave their informed consent to participate in the study. The patients were not subjected to plasmapheresis before surgery. Anticholinesterase therapy was discontinued the night before the operation. Atropine 0.5 mg, meperidine 50 mg, and trifluprομazine 10 mg were injected im 45 min before induction of anesthesia, which was with thiopental 250 mg to 350 mg and fentanyl 0.5 mg iv. The trachea was intubated following topical anesthesia without the administration of a muscle relaxant. Anesthesia was maintained with 70% nitrous oxide in oxygen with controlled ventilation. Increments of fentanyl 0.1 mg were injected iv as needed. Neuromuscular transmission was monitored by measuring the evoked twitch tension of the left adductor pollicis muscle in response to supramaximal train-of-four stimulation of the ulnar nerve at the wrist every 15 s as previously described.[7] In two myasthenic patients, the evoked compound electromyogram (EMG)[8] of the ipsilateral thenar eminence was recorded simultaneously. At least 30 min after the induction of anesthesia, vecuronium was injected iv in divided doses for 90% twitch depression: 2–5 $\mu g \cdot kg^{-1}$ increments in myasthenic patients and 7.5 $\mu g \cdot kg^{-1}$ increments in control patients. Neuromuscular transmission was then allowed to recover spontaneously. Any further muscle relaxant or anticholinesterase medication was withheld as long as twitch tension had not returned to at least 75% of control. Postoperatively, the trachea remained intubated to facilitate ventilatory support. Twitch tension and EMG recordings were evaluated for cumulative 50% and 90% blocking doses (ED_{50} and ED_{90})[9] and for duration of neuromuscular blockade. All variables were calculated as means and standard deviations. Statistical significance of differences between means and variances were assessed by unpaired Student's t test and F test, respectively.

RESULTS

Compared with healthy individuals, those with myasthenia gravis required an average 61% and 57% dose reduction for 50% and 90% twitch depression, respectively (table 2). The time from maximum twitch depression to 25% recovery had a significantly greater variance in myasthenic than in control patients ($P < 0.01$), while the difference of the means, although amounting almost to a factor of 2, was not significant. The *recovery time* (*i.e.*, the time for recovery from 25% to 75% of control twitch tension), showed a marked individual variation and was three times as long in myasthenic than in normal patients, not including two patients who had failed to recover 75% of control twitch tension (table 2). In two patients with simultaneous twitch and EMG recording (table 3), the 90% blocking doses determined by mechanical twitch tension amounted to 65% and 69% of those determined by EMG. In addition to such increased sensitivity to vecuronium, twitch tension took 25 to 38 min longer than

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TABLE 1. Patient Data

Variable	Patient No. 1	2	3	4	5
Sex	F	M	F	F	F
Age (yr)	19	58	72	25	23
Weight (kg)	55	74	47	55	63
Duration of disease	7 months	16 months	2 yr	1 yr	1 yr
Symptoms	ocular, pharyngeal	pharyngeal	ocular, pharyngeal	general	ocular
Acetylcholine receptor antibodies	+	+	+	+	+
Preoperative pyridostigmine (mg po)	60-60-40	4 × 120	4 × 50	none	3 × 60
Postoperative ventilation support	2 days	2 days	2 days	6 h	24 h
Postoperative pyridostigmine (mg)	3 × 10 iv	4 × 60 po	none	none	none
Surgery duration (min)	125	125	110	85	120

TABLE 2. Pharmacodynamic Data of Vecuronium in Normal Individuals and in Patients with Myasthenia Gravis (mean ± SD; range in parenthesis)

	Normal (n = 5)	Myasthenia Gravis (n = 5)	Significance
ED_{50} ($\mu g \cdot kg^{-1}$)*	18 ± 9 (6–28)	7 ± 5 (0.3–14)	S‡
ED_{90} ($\mu g \cdot kg^{-1}$)†	44 ± 7 (34–52)	19 ± 11 (5–31)	S‡
Duration from maximum block to 25% recovery (min)	11 ± 4 (6–17)	21 ± 18 (4–48)	NS
Recovery time (25–75% of control) (min)	9 ± 3 (6–13)	70 ± 62 (10–>140)§	S‡

NS = not significant.
* Cumulative dose for 50% twitch depression.
† Cumulative dose for 90% twitch depression.
‡ S = significant; $P < 0.005$.
§ Two patients only recovered 50% (# 1) and 69% (# 5) of control twitch tension within the 130- and 140-min time of observation. For statistical analysis, their *recovery times* were taken as 130 and 140 min, respectively.

the EMG to return to 25% of control (table 3). In patient no. 1 (table 3), only the EMG voltage recovered to 75% of control, while the twitch, one h later, had failed to return to the corresponding level. In another case, a persisting 31% twitch depression was reversed by 0.5 mg neostigmine (fig. 1, *bottom trace*). Normal recovery with constant *recovery times* from repeated doses of vecuronium in a myasthenic patient is shown in figure 1 (*upper trace*).

DISCUSSION

The duration of action of equipotent doses of nondepolarizing muscle relaxants was believed to be similar in myasthenic and nonmyasthenic individuals.[10] Yet, our myasthenic patients were hypersensitive to vecuronium, while their duration of blockade, in particular the *recovery time*, was hardly predictable. Failure of the adductor pollicis muscle to reflect accurately the contractile force of the respiratory and pharyngeal muscles in the presence

TABLE 3. Differences Between Evoked Twitch Tension and Evoked Compound Electromyogram (EMG)

Patient		ED_{50} $\mu g \cdot kg^{-1}$	ED_{90} $\mu g \cdot kg^{-1}$	Maximum Depression (% control)	Recovery Time (25–75%) (min)	Interval 25% EMG to 25% Twitch (min)
#1	Twitch	5.4	17.4	5	—*	38
	EMG	6.1	26.8	25	28	
#4	Twitch	6.0	10.7	5	15	25
	EMG	8.6	15.6	23	13	

* During recovery, within 130 min, twitch tension failed to exceed 50% of control.

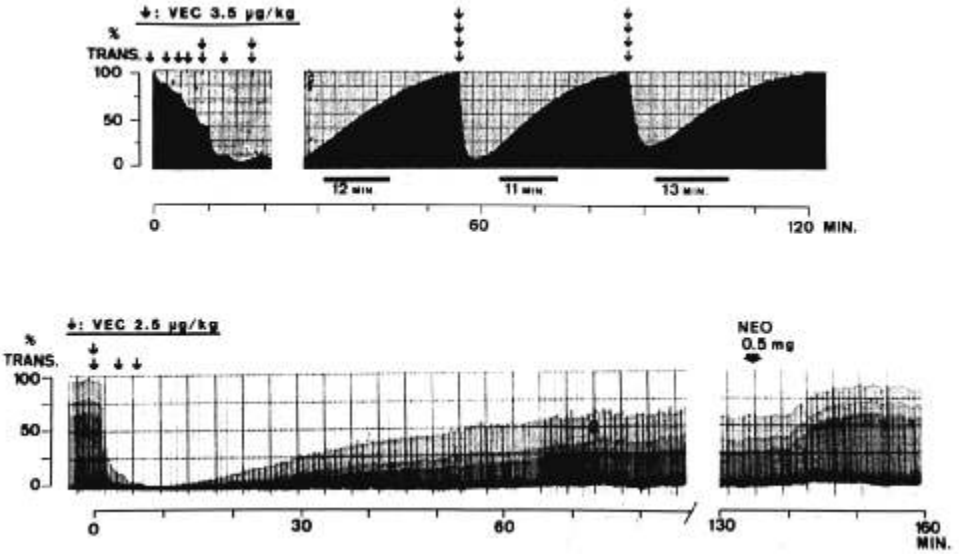

FIG. 1. Response of evoked twitch tension to titrated doses of vecuronium (VEC) in two patients with myasthenia gravis. *Upper trace:* Hypersensitivity to vecuronium followed by regular course of recovery (patient #2) from multiple doses. *Bottom trace:* Hypersensitivity to vecuronium followed by prolonged and incomplete recovery despite titration of the loading dose (patient #5). Residual block reversed by neostigmine (NEO). Note train-of-four (T4) fade before administration of vecuronium (T4 ratio = 0.72).

of neuromuscular disease[11] may account for postoperative ventilatory failure despite complete twitch recovery.

The present data obtained from simultaneous twitch and EMG recording in myasthenic patients suggest a greater than normal difference in sensitivity[12] and a slower recovery of twitch tension relative to the EMG. Although too few for statistical analysis, these results are in line with compromised muscle contractility without a corresponding depression of the EMG, which was observed in partially curarized myasthenic patients.[13]

It may be tempting to compare the present results on vecuronium with published data on atracurium, another nondepolarizing muscle relaxant with intermediate duration of action in normal individuals. However, careful examination of the relevant articles revealed that, in five myasthenic patients, the titration of atracurium guided by the EMG[5] yielded two times higher 80–95% blocking doses than in another seven patients monitored by twitch recording.[2–4,6] Furthermore, pyridostigmine medication, in nine out of 12 myasthenic patients studied for their response to atracurium, was discontinued only on the morning of surgery. The 80–95% blocking doses of these patients (210–471 $\mu g \cdot kg^{-1}$)[2–6] ranged markedly above normal limits (189 ± 8 $\mu g \cdot kg^{-1}$),[14] and their duration of neuromuscular blockade was not prolonged. The significance of both the recording technique and the anticholinesterase medication cannot be quantitated. Thus, due to different methods, the diverging data regarding vecuronium and atracurium are not at all comparable.

We conclude that vecuronium may be safely used in patients with myasthenia gravis. Its dosage should be titrated with the aid of a nerve stimulator. The duration of block may nevertheless be prolonged. Twitch monitoring is more sensitive in reflecting neuromuscular blockade than is the EMG.

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