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Vecuronium Neuromuscular Blockade at the Adductor Muscles of the Larynx and Adductor Pollicis

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The differences between neuromuscular blockade of the adductor muscles of the vocal cords and the adductor pollicis were examined in 20 adult women anesthetized with fentanyl and propofol. Vecuronium 0.04 or 0.07 mg/kg was given as a single bolus by random allocation. The force of contraction of the adductor pollicis was recorded. Laryngeal response was measured as pressure changes in the cuff of the tracheal tube positioned between the vocal cords. Train-of-four stimulation was applied to the recurrent laryngeal nerve at the notch of the thyroid cartilage and to the ulnar nerve at the wrist. Neuromuscular blockade had a faster onset, was less intense, and recovered more rapidly at the vocal cords. With 0.04 mg/kg, maximum blockade of first twitch (T1) was 55 ± 8 (mean ± standard error of the mean [SEM]) and 88 ± 4% at the vocal cords and the adductor pollicis, respectively ($P = 0.006$). Onset time was 3.3 ± 0.1 and 5.7 ± 0.2 min, respectively ($P = 0.000001$), and time to 90% T1 recovery was 11.3 ± 1.6 and 26.1 ± 1.8 min, respectively ($P = 0.001$). With 0.07 mg/kg, onset time was unchanged; maximum blockade was more intense, being 88 ± 4 and 98 ± 1%, respectively ($P = 0.04$ between muscles); and time to 90% T1 recovery was 23.3 ± 1.8 min at the vocal cords *versus* 40.3 ± 2.9 min at the adductor pollicis ($P = 0.001$). Approximately 1.73 times as much vecuronium was required at the larynx compared with the dose required at the adductor pollicis for the same intensity of blockade. It is concluded that total relaxation of the vocal cords requires large doses of vecuronium, but that maximal effect is reached more rapidly than at the adductor pollicis. (Key words: Larynx: vocal cords. Monitoring: neuromuscular blockade. Neuromuscular relaxants: vecuronium. Skeletal muscle: adductor pollicis; larynx.)

IN ANESTHETIC PRACTICE, relaxation of the vocal cords is desirable for laryngoscopy and tracheal intubation and for certain endoscopic procedures. At the end of surgery and anesthesia, airway protection is dependent on the functional integrity of laryngeal muscles.

However, the effects of neuromuscular blocking drugs on laryngeal muscles are not well known. It cannot be assumed that the response of the vocal cords is the same as that of other muscles because wide differences, both in intensity and time course, have been reported among different muscles of the body.[1–5] Laryngeal muscles are important clinically, but their function has been neglected because of a lack of a quantitative technique to study them. With the availability of a convenient method to perform these studies, involving the placement of the inflatable cuff of a tracheal tube between the vocal cords,[6] the action of neuromuscular blocking drugs can be measured.

This study was designed to measure the onset, intensity, and recovery of vecuronium-induced neuromuscular blockade on laryngeal adductor muscles. The data were compared with recordings obtained simultaneously at the adductor pollicis, because this muscle is routinely monitored in clinical practice and research.

Materials and Methods

The protocol was approved by the Institution's Ethics Committee, and informed consent was obtained from the subjects. Twenty women, ASA physical status 1 or 2, scheduled for breast or gynecologic surgery participated in the study. Exclusion criteria included: abnormal airway, cardiovascular, respiratory, neuromuscular, hepatic, or renal disease; previous head and neck surgery or radiotherapy; excessive alcohol intake; chemotherapy; or the concurrent administration or any drug known or suspected of interfering with neuromuscular function.

On arrival in the operating room, ECG, pulse oximetry, and arterial blood pressure were monitored noninvasively. Anesthesia was induced with propofol 2–4 mg/kg and fentanyl 2–5 μg/kg intravenously. A deep level of anesthesia was sought to permit laryngoscopy and tracheal intubation with a Mallinckrodt (Athlone, Ireland) 7.5-mm ID tracheal tube without neuromuscular blocking drugs. No local anesthetic was injected intratracheally. The inflatable cuff of the tracheal tube was positioned under direct vision between the vocal cords, and the cuff was inflated to 10–12 mmHg. The lungs were ventilated mechanically to keep end-tidal carbon dioxide tension (PET_{CO_2}) within the range of 35–40 mmHg. Anesthesia was then maintained with propofol 10–20 $mg \cdot kg^{-1} \cdot h^{-1}$, and intermittent doses of fentanyl. The use of nitrous oxide and halogenated agents was avoided.

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TABLE 1. Demographic Data

Dose (mg/kg)	Age (yr)	Height (cm)	Weight (kg)
0.04	49 ± 2	164 ± 1	60 ± 2
0.07	46 ± 2	159 ± 2	55 ± 1

Mean ± SEM.

Surface electrodes were applied near the ulnar nerve at the wrist. To stimulate the recurrent laryngeal nerve, a negative electrode was placed on the skin overlying the notch of the thyroid cartilage, with a positive electrode on the sternum or the forehead. The force of contraction of the adductor pollicis muscle was recorded with a Bio-Industry Curamètre Module 2 Transducer (Boulogne-sur-Mer, France). Vocal cord response was evaluated by measuring the pressure change produced in the inflatable cuff of the tracheal tube, using an air-filled transducer.[6] The responses from both sites were displayed on a Gould V1000 CRT and recorded simultaneously on paper with a Gould ES1000 chart recorder.

Supramaximal train-of-four stimulations (pulses 0.2 ms in duration; trains 2 Hz, 2 s in duration) were applied at both the ulnar and recurrent laryngeal nerves every 10 s. After a 2–3-min baseline, vecuronium 0.04 or 0.07 mg/kg was injected by random allocation as a rapid bolus. Ten patients received each dose. After maximal blockade was reached, the interval between train-of-four stimulations was increased to 20 s. Neuromuscular monitoring was continued until at least 90% recovery of first twitch (T1) at the adductor pollicis.

Onset time was defined as the interval between injection and maximum T1 blockade. Times from injection to 25, 50, 75, and 90% T1 recoveries were measured. Dose-response relationships also were obtained, by linear regression of the logit of maximum T1 blockade and the logarithm of dose, and ED_{90} and ED_{95} were calculated.

The results are presented as the means ± standard errors of the mean (SEM). The ED_{90} and ED_{95} are given as estimates ± the standard error of the estimate for the mean. Analysis of covariance was used to compare the dose-response data. Paired comparisons were made between data at the larynx and the adductor pollicis. A Student's *t* test for paired data was used for statistical analysis. A *P* value of 0.05 or less was considered to indicate statistically significant differences.

Results

The patients' demographic data are presented in table 1. The two groups did not differ significantly with respect to age, height, or weight.

With either dose, maximum blockade was less intense at the vocal cords (table 2; figs. 1 and 2). Only 2 of 20 patients had more intense laryngeal than adductor pollicis blockade (by 1 and 16%, respectively). However, the time to reach maximum effect at the vocal cords was only half that required at the adductor pollicis (table 2; figs. 1 and 2). This faster onset at the larynx was observed in all individuals. Recovery was much more rapid at the vocal cords, for both doses (table 3; figs. 1 and 2), and this was seen in all subjects.

The dose-response curves had the same slope (3.87 in both cases), but the vocal cord response was shifted to the right by a factor of 1.73 ± 0.13. The ED_{95} was 0.046 ± 0.003 mg/kg at the adductor pollicis, compared with 0.080 ± 0.006 mg/kg at the larynx ($P = 0.00001$). Corresponding values for the ED_{90} were 0.043 ± 0.003 and 0.075 ± 0.005 mg/kg, respectively ($P = 0.00001$). The train-of-four ratio at the larynx was 75 ± 4% before administration of vecuronium, and this value decreased in all cases after the drug was given.

Discussion

This study demonstrated that there are important differences between laryngeal muscles and the adductor pollicis with respect to their response to vecuronium. The laryngeal muscles require a larger dose for comparable blockade, but maximal effect is reached more rapidly. Recovery occurs much sooner at the laryngeal muscles.

In the current investigation, the stimulation modality was the same at both muscles (train-of-four every 10 s), and a measure of force was obtained. Although the pattern and duration of stimulation can influence onset time,[7] both of these variables were the same for both muscles studied, and their effects were likely to be similar. The

TABLE 2. Onset Characteristics

Variable	Dose (mg/kg)	Larynx	Adductor Pollicis	*P*
Maximum blockade (%)	0.04	55 ± 8	89 ± 3	0.006
	0.07	88 ± 4	98 ± 1	0.04
Onset (min)	0.04	3.3 ± 0.1	5.7 ± 0.2	0.000001
	0.07	3.3 ± 0.2	5.7 ± 0.3	0.000002

Mean ± SEM.

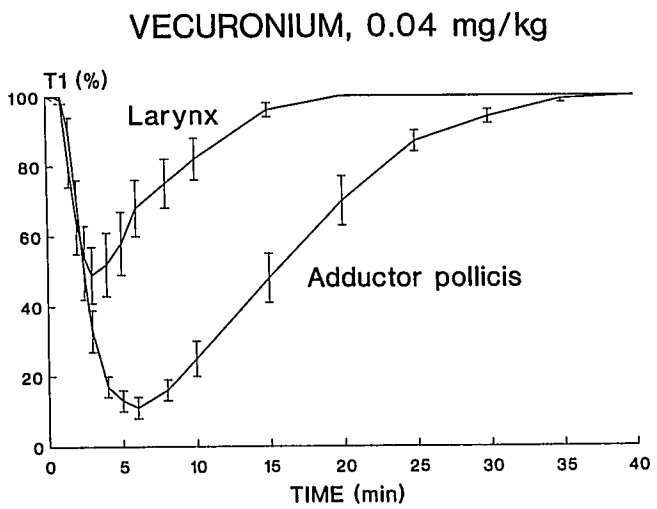

FIG. 1. First twitch height (T1) against time for vocal cords and adductor pollicis, after vecuronium 0.04 mg/kg. Bars indicate SEM.

doses (0.04 and 0.07 mg/kg) were chosen because the former was expected to yield approximately 90–95% blockade at the adductor pollicis,[8] and because the latter is used commonly for short- or medium-duration procedures. Inhalational halogenated agents were avoided because of their possible interaction with vecuronium, and the nitrous oxide was not used because it would have produced diffusion into the inflatable cuff and possible interference with the measurements. The train-of-four ratio was not measured after administration of vecuronium because its value was less than 100% before the relaxant was given. The significance of this finding is uncertain. Full recovery of laryngeal muscles may be associated with a train-of-four ratio as small as 50%. However, the decrease in train-of-four ratio and the abolition of the fourth response with vecuronium effectively rules out the possibility of direct muscle stimulation.

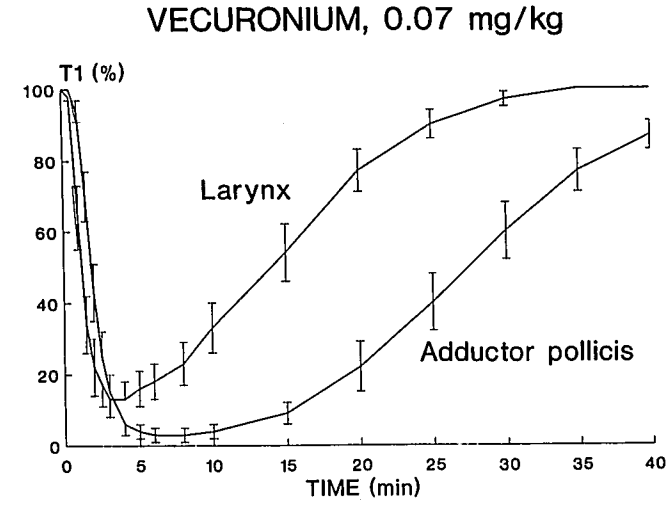

FIG. 2. First twitch height (T1) against time for vocal cords and adductor pollicis, after vecuronium 0.07 mg/kg. Bars indicate SEM.

TABLE 3. Recovery Characteristics

Time Recovery (min)	Dose (mg/kg)	Larynx	Adductor Pollicis	P
25%	0.04	—	10.6 ± 1.6	
	0.07	9.3 ± 1.5	22.5 ± 1.8	0.0005
50%	0.04	—	15.7 ± 1.4	
	0.07	14.4 ± 1.6	27.9 ± 2.0	0.0005
75%	0.04	—	20.4 ± 1.5	
	0.07	19.4 ± 1.8	34.1 ± 2.4	0.001
90%	0.04	11.3 ± 1.6	26.1 ± 1.8	0.001
	0.07	23.3 ± 1.8	40.3 ± 2.9	0.001

Mean ± SEM.

Dose-response data are normally obtained with three doses or more, but adequate estimates of potency have been obtained with two doses.[9] In the present context, only two doses were given because dose-response relationships of the two muscles studied overlapped over a narrow range. Using a larger or smaller dose would have produced 0 and 100% responses, which are difficult to analyze with logit or probit transformation. The transducer applied to the adductor pollicis was sufficiently sensitive to measure 99.8% blockade, so that analysis of adductor pollicis responses to 0.07 mg/kg was possible. Nevertheless, large errors are possible in this range of values, because small changes in twitch height correspond to large differences in logit values. Thus, dose-response data obtained here must be interpreted with consideration of these possible inaccuracies. However, the differences obtained in maximum blockade between the two muscles indicate that laryngeal adductor muscles are more resistant to the neuromuscular effect of vecuronium than is the adductor pollicis.

The results reported here are similar to those of a limited study involving five subjects in which electromyography of the vocal cords was recorded.§ Using vecuronium 0.06 mg/kg, onset was faster and intensity of blockade less at the vocal cords. The technique described in the present study has certain advantages over electromyography: no additional invasive procedure is required; the lungs can be ventilated mechanically instead of with jet ventilation *via* a cricothyroid puncture; end-tidal CO_2 tension can be monitored; and a measure of the force of contraction of the laryngeal muscles is obtained.

Among the muscle groups that have been studied thus

§ Gilly H, Redl G, Werba A, Streiner W, Draxler V, Spiss CK: Pharmacodynamics of vecuronium in two muscle groups: Vocal cords versus thenar neuromuscular blockade in man (abstract). ANESTHESIOLOGY 67:A614, 1987.

far, the adductors of the vocal cords appear to be the muscles most resistant to the neuromuscular effect of vecuronium. In a study involving the administration of the same doses of vecuronium,[5] the diaphragm was blocked 78% after 0.04 mg/kg, compared with 55% for the larynx in the present study. Adductor pollicis blockades (84 and 89%, respectively) were comparable. Recovery of the laryngeal muscles also seemed to be faster than that of the diaphragm. For example, after vecuronium 0.07 mg/kg, 75% T1 recovery was reached in 26 min for the diaphragm,[5] compared to 20 min for the larynx (table 3). Onset of paralysis at both the larynx and the diaphragm[5] was approximately 3 min.

It is impossible to determine, from this study, which laryngeal muscle, or which combination of muscles, contributes the most to glottic closure. The thyroarytenoid, lateral cricoarytenoid, and arytenoid muscles are supplied by the recurrent laryngeal nerve, and in this study all were most likely stimulated. Nevertheless, the end result probably is close to physiologically induced glottic closure. The contribution of the posterior cricoarytenoid muscle probably was negligible, because the site of stimulation was far away from the branches supplying this abductor muscle and the location of the measuring device favorable to adduction measurement.[6]

The reasons for the high resistance of the vocal cord adductors to the neuromuscular effect of vecuronium are unclear. The thyroarytenoid, and perhaps the other adductor muscles of the larynx, have fast contraction times.[10] Thus, they behave as fast-twitch muscle. Some experimental data suggest that fast muscles are more resistant to neuromuscular blockers than are slow muscles,[11] such as the adductor pollicis.[12] However, this hypothesis has not been verified in all cases.[13] The faster onset of vocal cord muscles may be related to blood flow.[14] In terms of kinetic–dynamic relationships, the k_{eo}, or rate constant of equilibration with effect compartment,[14] would be faster at the vocal cords than at the adductor pollicis.

Clinically, the current results suggest a sound basis for the recommendation that tracheal intubation be performed with large doses of vecuronium and that the optimum time for intubation be 3 min after administration of vecuronium. Because the ED_{95} was evaluated to be 0.08 mg/kg, this dose is likely to be associated with 95% paralysis in only half the patients, and predictable vocal cord paralysis in most patients to require as much as 0.12 to 0.15 mg/kg. If tracheal intubation is attempted after a shorter interval after induction of anesthesia, a larger dose may be needed. If the dose administered is insufficient to block vocal cord muscles, intubating conditions would depend on the degree of blockade achieved and the depth of anesthesia.

Monitoring the adductor pollicis response to determine onset of blockade and optimal time for tracheal intubation might be misleading. Because the adductor pollicis may be blocked with a dose insufficient to produce blockade of the muscles of the larynx, absence of a response at the adductor pollicis does not guarantee adequate intubating conditions. On the other hand, if a larger dose, sufficient to block laryngeal muscles, is given, onset of adductor pollicis blockade is likely to be longer than that of the vocal cords. In fact, in the 3–6-min range, laryngeal muscles recover while adductor pollicis blockade becomes more intense. It is possible that the orbicularis oculi, which is a fast-onset[5] resistant[3,5] muscle, is a better choice for monitoring onset.

Recovery of the vocal cord adductors occurs much faster than that of the adductor pollicis, suggesting that when adductor pollicis function is normal, the patient has the neuromuscular power to protect his or her airway. However, the competence of this reflex may be affected by other drugs, such as general anesthetics and opioids. Furthermore, this "laryngeal adductor sparing" effect of vecuronium does not imply that upper airway patency is ensured. Patency depends on the functional integrity of other muscles, such as the posterior cricoarytenoid,[15] genioglossus,[16] geniohyoid,[17] and masseter.[18] Among these, only the masseter has been studied with respect to its sensitivity to neuromuscular blocking drugs. Results indicate that its sensitivity to neuromuscular blocking drugs is either equal to or greater than that of the adductor pollicis.[19,20] Thus, the finding that laryngeal adductors are particularly resistant to the effect of vecuronium does not imply that other airway muscles, particularly those responsible for maintaining patency, behave similarly.

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