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Differential Effects of *d*-Tubocurarine on Inspiratory Muscles and Two Peripheral Muscle Groups in Anesthetized Man

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Differential sensitivities of muscle groups to non-depolarizing relaxants have been reported since the late 1940's. In most comparisons of peripheral versus respiratory muscle function, vital capacity, respiratory rate, tidal volume, minute ventilation, respiratory flow rates, or CO₂ response curves have been used as ventilatory indices.¹⁻⁷ Inspiratory pressure has also been used as an index of readiness for tracheal extubation in the postanesthetic period.⁸

In the present study it was decided to use inspiratory pressure, obtainable by a simple, noninvasive technique, to compare sensitivities to and recovery times from *d*-tubocurarine in respiratory and non-respiratory muscle groups.

METHODS AND MATERIALS

Sixteen patients, ASA 1 and 2, scheduled for elective operations on extremities, were studied. The study was approved by the Human Investigation Committee of our institution. Appropriate informed consent was obtained. Patients were premedicated with atropine. Induction of anesthesia was with thiopental, 4 mg/kg, and endotracheal intubation was facilitated with succinylcholine, 1 mg/kg. Anesthesia was maintained with N₂O-O₂ in equal volumes plus halothane. End-tidal halothane was measured with a Beckman LB-2 analyzer and kept at 0.75 per cent. Airway pressure was measured with a Statham venous strain gauge via a catheter in the endotracheal tube lumen. End-tidal CO₂ was measured with a Godart capnograph. Thumb force was measured with a Grass FT .03 force-displacement transducer and the ulnar nerve was

stimulated through 25-gauge subcutaneous needle electrodes with a Grass S-5 stimulator. Single stimuli of 0.1-msec duration and a voltage one and a half times that necessary to evoke maximal twitch were used. All data were recorded on a Grass polygraph.

After recovery from succinylcholine, the patients breathed spontaneously, and control determinations were made for inspiratory pressure and thumb twitch. Then *d*Tc was administered iv, 3 mg every 2 min, and measurements of thumb force and airway pressure were made. Occlusion of the airway was achieved by placing a clamp on an extended section of the breathing circuit. Occlusion was always at end expiration as determined by observing excursions of the airway pressure-recording pen. Every subject reached a plateau after four or five breaths, and this plateau was chosen as the inspiratory pressure point. The end point of *d*Tc administration was a 90 per cent reduction of this pressure. Ventilation was assisted or controlled as paralysis progressed to keep end-tidal P_{CO₂} at 5 per cent. Then spontaneous recoveries of inspiratory pressure and thumb twitch were recorded.

RESULTS

Figure 1 shows mean decay and recovery curves for the 16 subjects. The respiratory muscle curve lies significantly within the peripheral muscle curve. The ratios of *d*Tc doses for inspiratory pressure/peripheral muscle were 1.80 and 1.91 for 50 per cent and 10 per cent of control, respectively (table 1). Comparing recovery times revealed peripheral muscle/inspiratory pressure ratios of 2.10 and 1.91 for 50 per cent and 90 per cent recovery, respectively (table 2).

In four of the 16 patients facial muscle movement was measured with a mercury column strain gauge fixed with tape from the superciliary ridge to the cheek. The facial nerve was stimulated via 25-gauge subcutaneous needle electrodes using the same conditions used for stimulation of the ulnar nerve. In

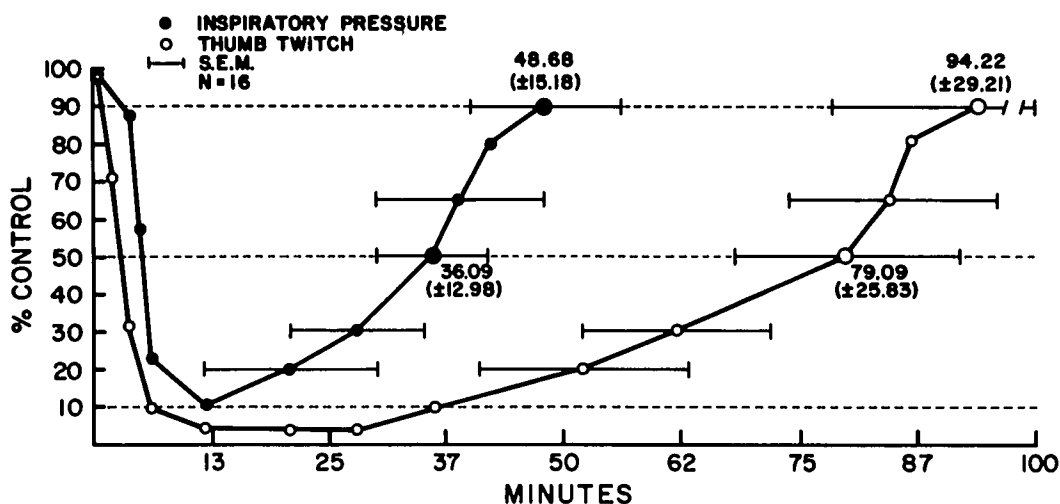
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FIG. 1. Decay and recovery curves for inspiratory pressure and thumb twitch. The vertical axis represents percentage of control and the horizontal axis represents time. Incremental doses of *d*Tc (3 mg/min) were administered until inspiratory force decreased to 10 per cent of control.



these subjects we found no statistically significant difference between thumb twitch and facial twitch responses.

DISCUSSION

This study shows clearly the differential effects of *d*Tc on ventilatory versus peripheral muscle. We found a wide range of sensitivities to this relaxant, which Foldes *et al.*⁴ and Katz⁹ also reported. Despite this range, we found consistencies in the ratios of doses necessary to produce fixed levels of depression. Nearly twice the dose of *d*Tc was needed to depress ventilatory musculature at both 50 and 90 percent.

Recovery times showed similar consistency, in that ventilatory musculature recovered about twice as rapidly as did peripheral musculature.

Although halothane has been shown to influence neuromuscular transmission,^{10,11} and anesthetic depth would certainly influence inspiratory efforts, maintenance of constant end-tidal halothane minimized this effect. Another factor influencing inspiratory efforts would be the subject's position on his CO₂ response

curve. This factor was minimized by constant end-tidal CO₂. The point in the ventilatory cycle at which occlusion occurred would also influence generated inspiratory pressure. Gal and Smith¹² recently demonstrated in awake curarized subjects that maximal voluntary airway pressure varied with lung volume. We felt that this variable was minimized by occluding at end exhalation or functional residual capacity. Our results correlate well with those of Gal and Smith. We found the peripheral musculature about twice as sensitive to *d*Tc, and they found 40 per cent depression of airway pressure when thumb twitch was 90 percent reduced.

Johansen *et al.*¹ studied the effects of *d*Tc on inspiratory pressure and grip strength in awake subjects. After 0.1–0.2 mg/kg, maximum mean depression of grip strength was 65 per cent. The corresponding depression of inspiratory pressure was 30 per cent, for a ratio of 2.16:1. Their ratio of times to 90 per cent recovery also was 2:1, that is, inspiratory pressure recovered twice as rapidly. These data also compare favorably with our 1.91 figures for ratios of both

TABLE 1. Mean Doses ± SD for Depression to 50 Per Cent and 10 Per Cent of Control Values for Inspiratory Pressure and Peripheral Muscle Twitch*

Depression	Mean Dose <i>d</i> Tc (mg/kg) Requirements		Ratio of Doses Inspiratory Pressure/ Peripheral Muscle
	Peripheral Muscle	Inspiratory Pressure	
50 per cent of control Range	.073 ± .025 .037–.132	.129 ± .051 .049–.240	1.80
10 per cent of control Range	.143 ± .037 .06–.198	.267 ± .074 .11–.35	1.91

* Ratios of doses for inspiratory pressure depression over peripheral muscle depression are in the right-hand column.

TABLE 2. Mean Times ± SD for Recovery to 50 Per Cent and 90 Per Cent of Control for Inspiratory Force and Peripheral Muscle Twitch*

Recovery to	Mean Time (Min)		Ratio of Times Peripheral Muscle/ Inspiratory Pressure
	Peripheral Muscle	Inspiratory Pressure	
50 per cent of control Range	79.09 ± 25.83 50–130	36.09 ± 12.98 20–60	2.10
90 per cent of control Range	94.22 ± 29.21 58–133	48.68 ± 15.18 22–75	1.91

* Ratios of times for peripheral muscle recovery over inspiratory pressure recovery are in the right-hand column.

doses to 90 per cent depression and recovery times to 10 per cent depression.

Our demonstration that the muscles of the hand are more sensitive to the effects of *d*-tubocurarine than is respiratory muscle is in keeping with the concept of "respiratory sparing." Inspiratory force is a valuable indicator in assessing recovery from neuromuscular blockade, because unlike spirometric tests, it is not affected by intrinsic pulmonary disease. It is essentially an isometric measurement, much like the test of grip strength, and provides a reproducible comparison of the two muscle groups.

The wide range of sensitivities to *d*Tc reaffirms the concept of using the drug in divided doses while monitoring blockade rather than in predetermined doses by weight. The consistent return of inspiratory force prior to peripheral strength indicates that adequate recovery as observed by conventional ulnar or facial nerve monitors implies good ventilatory muscle recovery as well.

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A Hazard of Double-orifice Epidural Catheters

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The abrupt occurrence of cardiovascular collapse during the course of continuous epidural anesthesia may be subsequent to inadvertent subarachnoid injection of local anesthetic due to the migration of the catheter tip into the subarachnoid space.¹ The following case report and laboratory investigation suggest that, in addition to catheter migration, catheter design and injection pressures are factors in the conversion of epidural anesthesia to subarachnoid anesthesia.

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REPORT OF A CASE

A 65-year-old Mexican-American woman was admitted for below-the-knee amputation and groin dissection for malignant melanoma of the right heel. She had a history of adult-onset diabetes mellitus controlled with 40 units of NPH insulin subcutaneously per day. Four months prior to admission she had had a left below-the-knee amputation with spinal anesthesia, without difficulty. Preoperative physical examination showed blood pressure 140/90 torr, pulse rate 80/min, weight 48 kg, and height 157 cm, and was otherwise unremarkable. Laboratory data, electrocardiogram and chest x-ray were all within normal limits.

The patient received 25 units of NPH insulin subcutaneously an hour preoperatively, with no other premedication. After her arrival in the operating room, electrocardiogram leads and blood pressure cuff were placed and intravenous infusion of 5 per cent dextrose in lactated Ringer's solution, 150 ml/hr, was started. With the patient in the lateral decubitus position, a Portex® double-orifice (orifices 180 degrees opposed 5 mm and 12 mm from the tip) epidural catheter was introduced 3 cm into the epidural space via a 17-gauge Tuohy needle placed in the L2-3 interspace. There was no flow of blood or