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

MICHAEL L. WYMORE, M.D.,* AND JOHN H. EISELE, M.D.†

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. Inspiratory pressure has also been used as an index of readiness for tracheal extubation in the postanesthetic period.

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-Ο₂ 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 dTc 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 dTc 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 dTc 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
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. and Katz 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, 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 CO$_2$ response curve. This factor was minimized by constant end-tidal CO$_2$. The point in the ventilatory cycle at which occlusion occurred would also influence generated inspiratory pressure. Gal and Smith 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. 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**

<table>
<thead>
<tr>
<th>Depression</th>
<th>Mean Dose $d$Tc (mg/kg) Requirements</th>
<th>Ratio of Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peripheral Muscle</td>
<td>Inspiratory Pressure</td>
</tr>
<tr>
<td>50 per cent of control</td>
<td>.075 ± .025</td>
<td>.129 ± .051</td>
</tr>
<tr>
<td>Range</td>
<td>.037–.132</td>
<td>.049–.240</td>
</tr>
<tr>
<td>10 per cent of control</td>
<td>.143 ± .037</td>
<td>.267 ± .074</td>
</tr>
<tr>
<td>Range</td>
<td>.06–.198</td>
<td>.11–.35</td>
</tr>
</tbody>
</table>

* 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**

<table>
<thead>
<tr>
<th>Recovery to</th>
<th>Mean Time (Min)</th>
<th>Ratio of Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Muscle</td>
<td>Inspiratory Pressure</td>
<td>Inspiratory Pressure/ Peripheral Muscle</td>
</tr>
<tr>
<td>50 per cent of control</td>
<td>36.09 ± 12.98</td>
<td>2.10</td>
</tr>
<tr>
<td>Range</td>
<td>50–130</td>
<td>20–60</td>
</tr>
<tr>
<td>90 per cent of control</td>
<td>48.68 ± 15.18</td>
<td>1.91</td>
</tr>
<tr>
<td>Range</td>
<td>58–133</td>
<td>22–75</td>
</tr>
</tbody>
</table>

* 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 con-
cept of “respiratory sparing.” Inspiratory force is a
valuable indicator in assessing recovery from neuro-
muscular 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 dTc 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 ade-
quate recovery as observed by conventional ulnar
or facial nerve monitors implies good ventilatory
muscle recovery as well.

REFERENCES
1. Johansen SH, Jørgensen M, Malbec H: Effect of tubo-
curarine on respiratory and nonrespiratory muscle power
2. Poulsen HH, Høns W: The effect of some curarizing drugs
in unanaesthetized man. I. d-Tubocurarine chloride, gal-
laminium iodide, decamethonium iodide, succinylcholine
iodide and its bis-monochlor-substituted derivative in single
curarizing drugs in man. I. Potency, duration of action,
and effects on vital capacity of d-tubocurarine, dimethyl-
d-tubocurarine, and decamethylen-bis (tri-methylam-
nonium bromide). J Pharmacol Exp Ther 98:318–329,
1950
muscle relaxants in unanaesthetized subjects. Anesthesiol-
ogy 22:230–236, 1961
5. Foldes FF, Monte AP, Brunn HM, Jr, et al: The influence of
exercise on the neuromuscular activity of relaxant drugs.
6. Walts LF, Levin N, Dillon JB: Assessment of recovery from
7. Doughty AG, Wylie WD: An assessment of Flaxedil (gallamine
disturbances in ventilation following the use of muscle
9. Katz RL: Comparison of electrical and mechanical recording of
spontaneous and evoked muscle activity. Anesthesiol-
ogy 26:204–211, 1965
pencuronium and d-tubocurarine-induced neuromuscular
blockades on alveolar concentrations of halothane and
muscular effects of Forane and halothane alone and in
combination with d-tubocurarine in man. Anesthesiology
35:38–42, 1971
12. Gal TJ, Smith TC: Partial paralysis with d-tubocurarine and
the ventilatory response to CO2: An example of respiratory
A Hazard of Double-orifice Epidural Catheters

C. F. Ward, M.D.,* Robert Osborne, M.D.,† Jonathan L. Benumof, M.D.,* Lawrence J. Saidman, M.D.‡

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.

*Assistant Professor of Anesthesiology.
†Resident.
‡Professor of Anesthesiology.

Received from the Department of Anesthesiology, University of
California Medical Center, San Diego, 225 West Dickinson Street,
San Diego, California 92103. Accepted for publication October 24,
1977.

Address reprint requests to Dr. Ward.

REPORT OF A CASE

A 65-year-old Mexican-American woman was admitted for
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 diffi-
culty. 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

0003-3022/78/0500—0362 $00.50 © The American Society of Anesthesiologists, Inc.