The Effect of Resting Muscle Tension on the Dose-effect Relationship of d-Tubocurarine: Does Preload Influence the Evoked EMG?

AARON F. KOPMAN, M.D.*

A recent paper from this department reported that the indirectly evoked mechanomyogram (MMG) of the adductor pollicis brevis and the integrated electromyogram (EMG) of the first dorsal interosseus may be used essentially interchangeably in determining the depth of nondepolarizing neuromuscular blockade. This study also suggested that, without a preload applied to the thumb, the EMG might underestimate the ED$_{95}$ of metocurine by between 15 and 20%. This latter result was surprising, because there is no obvious reason why changes in muscle tension should alter the evoked EMG. A potential weakness in the above investigation, however, was that EMG and MMG responses were recorded from different muscles.

Use of the electromyogram has not generally been associated with the simultaneous application of a preload to the muscle under study. If the presence or absence of resting tension does, in fact, effect the evoked EMG, the accuracy of much of the data obtained with the integrated EMG in the past might be open to some question. Because of the significance of this issue, we decided to repeat the above investigation in a more rigorous manner; EMG and MMG responses were both simultaneously recorded from the adductor pollicis muscle.

MATERIALS AND METHODS

Forty ASA 1–11, adult female patients (age range 18–65 yr) undergoing elective gynecological surgical procedures, for whom the administration of a muscle relaxant was indicated by the proposed surgery, were included in the study. All patients were free from neuromuscular disease and were within 15% of ideal body weight. The protocol was approved by our hospital’s Human Subject Review Committee. Patients were premedicated with diazepam 10 mg and glycopyrrrolate 0.2 mg approximately 90 min prior to surgery. Anesthesia was induced with thiopental sodium 4–5 mg/kg iv and maintained with inhalation of nitrous oxide and oxygen plus iv fentanyl. Endotracheal intubation was not performed until after the study period (<15 min from time of induction). Controlled ventilation via a mask was maintained during the test period. Two consecutively selected groups were studied.

Group 1 (EMG Only, n = 20). The indirectly evoked integrated compound action potential of the adductor pollicis muscle to supramaximal stimulation of the ulnar nerve was measured and recorded using a Datex™ 221
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**TABLE 1. Log-probit Analysis of Dose-response Relationships for d-tubocurarine**

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>EMG Only (no preload)*</th>
<th>EMG (Simultaneously Evoked)†</th>
<th>MMG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observations (n)</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Mean values of individual patients (±SE)</td>
<td>0.186 ± (.008)</td>
<td>0.208 ± (.007)</td>
<td>0.203 ± (.008)</td>
</tr>
<tr>
<td>ED50 (mg/kg)</td>
<td>0.363 ± (.011)‡</td>
<td>0.440 ± (.015)‡</td>
<td>0.419 ± (.014)</td>
</tr>
<tr>
<td>ED95 (mg/kg)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

* Group 1. † Group 2. ‡ P < 0.05.

NMT monitor. Supramaximal nerve stimulation was achieved using the nerve stimulator incorporated into the Datex™ unit (pulse width 100 μs, constant current, 0–70 ma range). The test hand was immobilized, but no resting tension was applied to the thumb. Stimulating and recording electrodes were 3M infant Red Dot™ electrodes. After anesthesia was induced and before any muscle relaxants were administered, control twitch height and train-of-four (T4/T1) fade ratio were established. Train-of-four stimulation was given every 20 s during the period of observation, and single twitch depression (height of first twitch in a train/control twitch) (T1/Tc) and train-of-four fade were continuously recorded.

A cumulative dose-response curve was determined by incremental administration of d-tubocurarine until twitch tension was depressed by at least 90%. The first dose administered was 0.15 mg/kg; incremental boluses ranging from 0.05 to 0.15 mg/kg were given when the evoked T1/Tc ratio was stable (±1%) for three consecutive trains. The size of each incremental dose was varied based on the response to the prior doses of relaxant. For example, if a cumulative dose of 0.5 mg/kg resulted in 86% twitch depression, then the final increment would be reduced to 0.5 mg/kg. At least three doses were administered to each patient.

Group 2 (EMG versus MMG, n = 20). Protocol in this group was identical to that in group 1 except that simultaneous measurement of the evoked isometric mechanical response of the ipsilateral adductor pollicis muscle was also recorded. Thumb preload was adjusted to between 250–350 g, and twitch tension was measured with a Grass FT-10D linear force transducer.

At the end of surgery, any residual paralysis was antagonized with neostigmine to an MMG T4/T1 ratio of at least 0.70. Simultaneous responses were examined in pairs by linear regression (least squares) analysis. Only individuals in whom both the MMG and EMG T1/Tc ratio returned to 1.0 ± 0.15 were included in the study.

The ED50 and ED95 for dTc (EMG in group 1, both EMG and MMG in group 2) were calculated by averaging the values for these parameters as determined by log-probit regression analysis of each individual patient. These mean values were then compared by one-way analysis of variance, and the Student-Newman-Keuls test for multiple comparisons. The simultaneously evoked EMG and MMG responses in group 2 were also compared using a paired Student's t test. Observed differences were considered significant when P = <0.05.

**RESULTS**

The potency of dTc as calculated from the simultaneously recorded MMG and integrated EMG of the adductor pollicis muscle agree very closely. The EMG derived ED95 of 0.44 mg/kg was higher than the ED95 as estimated by the MMG by only about 5%. This difference was not significant according to the Student-Newman-Keuls test; however, the paired Student's t test revealed a P value of <0.05. Despite its statistical significance, this variation is clinically meaningless. None of the estimated ED90 values were statistically different from each other.

Although the ED95 of 0.39 mg/kg found in group 1 (EMG, no preload) was not statistically different from the MMG value of 0.42, it was 12.5% less (P < 0.05) than that found in the EMG-preload group. This discrepancy is very similar to the 15% difference found in the estimated ED95 of metocurine when EMG responses from the first dorsal interosseous muscle were recorded in the presence or absence of resting tension.¹

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**TABLE 2. Dose-response Relationships for d-tubocurarine**

<table>
<thead>
<tr>
<th>ED 50 (mg/kg)</th>
<th>ED95 (mg/kg)</th>
<th>n*</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.185</td>
<td>0.449</td>
<td>36‡</td>
<td>2</td>
</tr>
<tr>
<td>0.250</td>
<td>0.510</td>
<td>52‡</td>
<td>3</td>
</tr>
<tr>
<td>0.250</td>
<td>0.520</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>0.254</td>
<td>0.539</td>
<td>10</td>
<td>2</td>
</tr>
</tbody>
</table>

All references refer to studies of mechanical response of the adductor pollicis muscle done under nitrous oxide-narcotic anesthesia. Unless otherwise noted (‡), studies cited are cumulative technique.

* Number of patients in series.
† Single-dose technique study.

¹ Downloaded From: http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931370/ on 06/19/2017
DISCUSSION

The results of this study demonstrate that the indirectly evoked response of the adductor pollicis muscle as measured by the integrated compound EMG is very similar to that recorded using traditional mechanical methods. The ED₉₅ of dTC as estimated by these two approaches differed by only 5% from each other (P > 0.05).

In our previous study of the dose-effect relationship of metocurine, we found that the presence or absence of resting tension on the thumb had a significant effect on the measured response of the first dorsal interosseous muscle.⁴ Adding a preload to the thumb increased the estimated ED₉₅ of metocurine by 18%. In this study of the dose-effect relationship of dTC, the effect of added preload to the adductor pollicis was very similar. The estimated ED₉₅ of dTC was higher by 14% in the group where resting tension was applied. This difference was significant at the P < 0.05 level. Therefore, the results of this study lend support to the observation that adding a preload to the muscle under study may affect the evoked EMG response.

However, if the ED₉₅ of dTC as measured by the MMG is taken as the “gold standard,” group 1 only underestimated the ED₉₅ by 9%, and this difference was not statistically significant. Consequently, it does not necessarily follow that EMG data obtained from the adductor pollicis in the absence of resting tension will overestimate sensitivity to nondepolarizing muscle relaxants. While it is still possible that this is the case, the intra-group variation in this study was such that no definitive answers to this question were obtained.

If, in fact, the EMG (in the absence of resting tension) underestimates the ED₉₅, is an error of 10–15% actually important? Individual sensitivity to nondepolarizing neuromuscular blockers are known to show considerable scatter. The range in values for the ED₉₅ of dTC in the MMG group was from 0.30 to 0.56 mg/kg. In view of this marked individual variation, it may be argued that to quibble about differences in potency of under 20% is unrewarding. While this position has some appeal, ultimately, I think it should be rejected. It is true that the Datex™ NMT unit may be used quite successfully and safely as a clinical tool in the absence of a preload to the muscles being monitored. However, at least for research purposes, there is no reason to accept an easily avoidable potential error.

The mechanism underlying the change in evoked EMG response to preload is undetermined. It may represent nothing more than a technical problem in recording the evoked action potential. In group 2, because the thumb was abducted under tension, the distance between recording electrode and muscle may have been reduced, resulting in a larger EMG signal. Thus, it is possible that this phenomenon may not be seen if needle rather than surface recording electrodes are employed. However, until further information on the effect of preload on the evoked integrated EMG is available, when the Datex NMT™ is employed as a research instrument, it may be prudent to apply a small preload to the muscle under investigation.

REFERENCES


Mixed Venous Oxygen Saturation during Thoracic Anesthesia

DANIEL M. THYS, M.D.,* EDMOND COHEN, M.D.,† JAMES B. EISENKRAFT, M.D.*

During anesthesia for pulmonary surgery, profound changes in oxygenation are often observed following collapse of the non-dependent lung.¹² The standard method by which oxygenation is assessed intraoperatively consists of intermittent analysis of arterial blood gases. Mixed venous oxygen saturation (SvO₂) can now be monitored continuously using a balloon-tipped, thermodilution, fiberoptic, pulmonary arterial catheter (PAC). The clinical usefulness of this measurement device has