Frequency Sweep Electromyogram and Voluntary Effort in Volunteers after d-Tubocurarine

Helmut R. Gerber, M.D.,* Sophus H. Johansen, M.D.,† J. Thomas Mortimer, Ph.D.,‡ Edmund Yodkowski, B.E.E.§

A new method for monitoring the effect of muscle relaxants on the myoneural junction was tested in unanesthetized volunteers. Evoked electromyographic responses to stimulation, sweeping exponentially from 1 to 100 Hz over 10 seconds, were recorded from the hand and abdominal muscles. d-Tubocurarine (dTc) was given intravenously in incremental doses until head lift was abolished. Thumb twitch tension, vital capacity, peak expiratory flow, maximal inspiratory force, and hand grip strength were recorded during partial paralysis and recovery. The frequency sweep electromyogram (FS-EMG) of the musculus rectus abdominis was more depressed than the FS-EMG of the musculus abductor digitii V at the time head lift was abolished. The abdominal muscle recovered faster from dTc paralysis than did the hand muscle. The latter failed to respond normally to the highest frequencies of stimulation during the entire period of observation lasting 72 minutes after dTc injection. At the time of maximal neuromuscular blockade, respiratory function showed less depression than the FS-EMG of the abdominal muscle. (Key words: Neuromuscular relaxants, d-tubocurarine; Neuromuscular transmission; Measurement techniques, electromyogram.)

NEUROMUSCULAR BLOCKADE is generally assessed in the awake patient by respiratory measurements, i.e., vital capacity and maximal inspiratory force, and by voluntary head-lift while in the supine position.

In anesthetized patients, neuromuscular transmission is usually evaluated by measuring the mechanical or electrical response of muscle following neural stimulation. Various patterns of stimulation are used, including a series of single twitches, a train of four pulses applied at 2 Hz, and tetanic stimuli at 30, 50 or 100 Hz. Most of these methods require a control reading from the intact myoneural junction, and they are often too painful to be used in conscious people.

We studied a monitoring method that measures the indirectly evoked electromyogram (EMG) in response to an exponential stimulation frequency sweep of 1–100 Hz in awake volunteers. Respiratory muscles are less sensitive to neuromuscular blockade than peripheral muscles in animals and man. Therefore, the electromyographic responses of hand and abdominal muscles of volunteers were compared with peripheral and respiratory muscle force during partial neuromuscular blockade with d-tubocurarine (dTc).

Methods

Seven healthy, informed, paid male volunteers, 21 to 32 years of age, were studied in the supine position. Three electrodes were placed in a hand muscle (musculus abductor digitii V), and three in an abdominal muscle (rectus abdominis). The electrodes were placed inside a 22-gauge hypodermic needle and inserted into the muscle through a lidocaine skin wheal. A small hook at the tip of the electrode allowed insertion of the electrode into the muscle and withdrawal of the needle without displacement of the electrodes. The electrodes were made of coiled stainless steel wire, approximately 45 μm thick, with a coil diameter of about 200 μm. For stimulation, singly coiled steel wire electrodes were used, and for recording, a doubly wound coiled electrode. The two stimulating electrodes were placed approximately 1.5 cm apart with the recording electrode midway between them. All electrodes were inserted at an angle of about 20–30 degrees relative to the skin surface and positioned so that they would run roughly parallel to the direction of muscle fibers. Care was taken to insure that the non-insulated region of the electrodes was well within the muscle body. The abdominal electrodes were placed about 2 cm off the midline, a little above the umbilicus. In the hand the electrodes were inserted through the skin at a point slightly proximal to the head of the fifth metacarpal bone and moved in a proximal direction toward the origin of the muscle.

The stimulus rate was increased exponentially from an initial value of one pulse per second to a final rate of 100 Hz during a 10-second period. In each subject the stimulus amplitude was adjusted to provide supramaximal stimulation. The exponential frequency sweep minimizes the fatigue that may result from repeated testing since only a small proportion of the stimulation period is at frequencies capable of inducing fatigue. The tests were repeated at intervals not less than 2 minutes apart. Animal experiments have shown that facilitation and fatigue
are kept minimal when rest periods of at least 2 minutes are provided between test runs. The stimulus consisted of a rectangular current pulse 100 microseconds long. The amplitude of the current pulse was variable from 0 to 20 mA and was adjusted for each subject to provide supramaximal stimulation. Animal experiments conducted by authors J.T.M. and E.Y. have demonstrated that the contribution of directly excited muscle fibers to the recorded compound action potential is minimal under these conditions. In these experiments the tibialis anterior muscle of the cat was stimulated as outlined and force measured by means of a transducer attached to the muscle tendon. The threshold for intramuscular stimulation was determined by observing the point at which muscle force was first detected and/or the level at which the compound action potential was first discernible. The animals were then curarized (.5 mg/kg) and the threshold measurements immediately repeated. At this level of curarization, the excitation measured is a result of direct muscle fiber stimulation. It was found that with 100-microsecond current impulses, the threshold in the curarized preparation was more than 20 mA.

Analysis of the neuromuscular block was achieved by processing the evoked compound muscle action potential as a function of stimulus frequency while the stimulation rate was increased exponentially from an initial rate of one pulse per second to a final frequency of 100 Hz. The stimulation periods were at least 2 minutes apart. The compound action potential recorded via the described bifilar coiled wire electrode was amplified, rectified, and its integral displayed on a strip chart recorder (Gould-Brush 220).

Thumb twitch tension in response to stimulation of the ulnar nerve was measured in the contralateral limb. The ulnar nerve was blocked at the level of the elbow by an injection of lidocaine. The nerve was then stimulated at the wrist using rigid needle electrodes with a rectangular current pulse (100 microseconds duration) delivered at a constant rate of 0.4 Hz. The stimulus amplitude was adjusted to provide supramaximal stimulation. The hand was fitted and strapped into a brace so that the entire hand (except for the thumb) and forearm were immobile. The force produced by adduction of the thumb (adductor pollicis) was recorded by means of a force transducer (Statham UC 4) and the amplitude of the response displayed on a strip chart recorder. The amplifier gain was adjusted to provide 8 units of deflection (10 units full scale) per control impulse.

Vital capacity (VC) and peak expiratory flow (PEF) were measured with the aid of a pulmonary function analyzer (National Cylinder Company) based on the principle of varying resistance with change in temperature of a heated wire located close to the mouthpiece. Maximum inspiratory force (MIF) was measured with a manometer reading from 0 to 120 cm H2O at a time when the nostrils were blocked by a clip. Hand grip strength was measured with a dynamometer made by the March Instrument Company.

d-Tubocurarine (Squibb) was administered intravenously in increments until zero time, i.e., the point at which head lift was abolished. This occurred after .16 mg/kg ± .01 SE (1.87 ± .08 mg/m2). The subjects were then allowed to recover spontaneously.

For the data analysis, points corresponding to the stimulation frequencies 2, 10, 50, and 100 Hz were selected from the frequency spectrum. The processed electromyographic recording can be expressed in several ways. Reporting the amplitude at a certain frequency in relation to the height of the control electromyographic response necessitates a control reading before neuromuscular blockers are administered. In analogy to the train-of-four, the use of the 1-Hz amplitude as reference point has the advantage that control readings are not necessary.

It was found that a response to the 1-Hz impulse of the sweep was well maintained in the partially blocked myoneural junction. Therefore, the amplitude (A) of the evoked electromyogram at any frequency (f) of stimulation sweeping from 1 to 100 Hz was expressed in relation to the amplitude of the 1-Hz response that started the stimulation cycle, A(f)/A (1 Hz). Thus, a ratio close to 1.0 indicates intact neuromuscular transmission. With increasing neuromuscular blockade, the ratio becomes substantially less than 1.0. Residual neuromuscular block by dTc was antagonized by the administration of .4 mg atropine and 1.0 mg neostigmine after the study period.

Results

At zero time all subjects experienced double vision and difficulty swallowing, but maintained
regular and spontaneous ventilation. A typical read-out of the processed electromyographic recordings is shown in figure 1. Before administration of \(dTc\), the evoked electromyogram maintained the amplitude of the 1-Hz response through the whole stimulation period of 10 seconds and the whole frequency spectrum to 100 Hz. With the onset of neuromuscular blockade, the amplitude at the high frequencies diminished first. With increasing neuromuscular block, the lower frequencies failed to elicit a full response, indicating that fewer muscle fibers were excited by indirect stimulation.

The peak depression of neuromuscular transmission occurred approximately 2 minutes later in the hand than in the abdomen. The peak depression in the abdomen coincided with the inability to lift the head, which persisted for an average of 7 minutes.

The evoked electromyographic responses of the hand and the abdomen during partial neuromuscular block and recovery are summarized in table 1. At zero time the abdominal muscles were more depressed than the hand muscles at all frequencies. The rate of recovery was faster in the abdominal muscles than in the hand. There was a marked difference between recoveries of the low-frequency response (< 10 Hz) and the high-frequency response (> 50 Hz) in hand and abdominal muscles. The evoked responses of hand and abdominal muscles returned within 20 minutes to approximately 80 per cent of the 1-Hz response for stimulation frequencies at and below 10 Hz. At and above 50 Hz the evoked EMG response returned in the hand to a maximum of 35%, compared with 61% in the abdomen.

At a time when the abdominal evoked EMG had recovered completely the high-frequency response of the hand was still depressed to 44% (50 Hz) and 17% (100 Hz) of the 1-Hz amplitude (table 2). At the end of observation periods that averaged 72 minutes after head lift had been abolished by the last dose of \(dTc\), the high-frequency response in the hand was still depressed to 82% (50 Hz) and 42% (100 Hz) of the 1-Hz amplitude. At the time of complete recovery of the abdominal EMG, hand-grip strength had recovered to 73% of control. At the end of the observation period, hand-grip strength had almost recovered (91% of control) at a time when the 100-Hz frequency response of the hand was still depressed by 58%.

The results of the study of respiratory muscle force and peripheral muscle force appear in table 3. Thumb twitch tension and respiratory modalities were depressed approximately to the same extent (60–70 per cent of control) at zero time, whereas hand-grip strength was markedly more depressed (25 per cent of control) at zero time.

The rates of recovery were similar for thumb twitch tension and respiratory modalities. Control values were reached after 20 minutes. At this time hand-grip strength was still depressed to about 52 per cent of control.

The exponential stimulation pattern employed in this study has negligible influence on the competency of the unblocked myoneural junction when the test runs are spaced at least 2 minutes apart. The frequency sweep technique provides a means of

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### Table 1. Frequency Sweep Electromyogram of M. Abductor Digi V (Hand) and M. Rectus Abdominis (Abd.)

<table>
<thead>
<tr>
<th></th>
<th>A (2 Hz) / A (1 Hz)</th>
<th>A (10 Hz) / A (1 Hz)</th>
<th>A (50 Hz) / A (1 Hz)</th>
<th>A (100 Hz) / A (1 Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>.69 ± .07*</td>
<td>.35 ± .06*</td>
<td>.59 ± .08*</td>
<td>.15 ± .05*</td>
</tr>
<tr>
<td>10 min</td>
<td>.83 ± .04**</td>
<td>.60 ± .10**</td>
<td>.75 ± .08*</td>
<td>.47 ± .13**</td>
</tr>
<tr>
<td>20 min</td>
<td>.92 ± .03*</td>
<td>.80 ± .08*</td>
<td>.82 ± .07*</td>
<td>.80 ± .07**</td>
</tr>
</tbody>
</table>

\(P\) =<.0005 \*<.0001 \*<.0001 \*<.0001 \*<.0001 \*<.0001 \*<.0001 \*<.0001

\(A(f)\) = amplitude of evoked electromyogram (EMG) at stimulation frequency \(f\).

\(A(1\text{ Hz})\) = amplitude of EMG at frequency 1 Hz.

For further explanation, see Methods.

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### Table 2. Hand-grip Strength and Evoked Electromyogram (EMG) of the Hand Muscle at the Point of Total Recovery of the Abdominal EMG (Mean Time 43 Minutes) and at the End of Observations (Mean Time 72 Minutes)

<table>
<thead>
<tr>
<th></th>
<th>Hand-grip Strength (Per Cent of Control)</th>
<th>EMG A (2 Hz) / A (1 Hz)</th>
<th>EMG A (10 Hz) / A (1 Hz)</th>
<th>EMG A (50 Hz) / A (1 Hz)</th>
<th>EMG A (100 Hz) / A (1 Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total abdominal recovery (43 min)</td>
<td>73</td>
<td>.99 ± .01</td>
<td>.86 ± .05</td>
<td>.44 ± .13</td>
<td>.17 ± .05</td>
</tr>
<tr>
<td>End of experiment (72 min)</td>
<td>91</td>
<td>.97 ± .01</td>
<td>.80 ± .05</td>
<td>.82 ± .17</td>
<td>.42 ± .14</td>
</tr>
</tbody>
</table>
TABLE 3. Recovery of Mechanical and Respiratory Modalities from Partial Neuromuscular Blockade, Per Cent of Control ± SE (Rounded to Full Numbers)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Hand-grip Strength</th>
<th>Twitch Tension</th>
<th>Inspiratory Force</th>
<th>Vital Capacity</th>
<th>Peak Expiratory Flow</th>
</tr>
</thead>
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<tr>
<td>0</td>
<td>25 ± 10</td>
<td>59 ± 4</td>
<td>58 ± 15</td>
<td>67 ± 5</td>
<td>73 ± 8</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.001</td>
<td>P &lt; 0.02</td>
</tr>
<tr>
<td>10</td>
<td>34 ± 10</td>
<td>80 ± 6</td>
<td>70 ± 8</td>
<td>90 ± 4</td>
<td>93 ± 3</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.20</td>
<td>P &lt; 0.005</td>
<td>P &lt; 0.10</td>
<td>P &lt; 0.05</td>
<td>P &lt; 0.025</td>
</tr>
<tr>
<td>20</td>
<td>52 ± 11</td>
<td>93 ± 3</td>
<td>88 ± 5</td>
<td>95 ± 3</td>
<td>95 ± 3</td>
</tr>
<tr>
<td></td>
<td>P &lt; 0.001</td>
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</table>

monitoring neuromuscular transmission across a broad range of stimulation rates. An exponential frequency sweep allows a greater proportion of the stimulation period to be spent at low frequencies while still monitoring the response to tetanic stimuli. After amplification, rectification and integration, the FS-EMG can be displayed as a curve, providing at a glance information about muscle responses to low-, intermediate- and high-frequency neural stimulation. For statistical analysis and to facilitate comparison with other published studies, we have analyzed only a few of the monitored frequency responses, i.e., 1, 2, 10, 50, and 100 Hz.

The two muscle groups tested were selected for the following reasons: m. abductor digiti V was chosen for the ease of access during monitoring in the clinical setting and as being representative of a limb muscle; m. rectus abdominis is an accessory muscle of respiration\(^{9,10}\) and is also a frequent target organ for surgical relaxation in abdominal surgery.

Investigations of differences in onset, degree and duration of nondepolarizing neuromuscular blocks have shown that the onset of paralysis and the degree are dependent on blood flow.\(^{11}\) In the present study a difference in perfusion of the muscles might contribute in part to more rapid and more profound depression of the abdominal electromyogram, compared with the electromyographic response in the hand muscle, and to the fact that the point of abolished head lift coincided with the peak depression of the abdominal electromyogram. Recently, Amaki and colleagues (personal communication), for example, also found faster onset of neuromuscular block in the rat diaphragm compared with a peripheral muscle. In another recent study comparison of respiratory musculature and thumb twitch tension in anesthetized patients revealed that the respiratory musculature is highly sensitive to dTc-induced block and has a different time course.\(^{12}\)

The dose needed for 75 per cent block of the respiratory musculature was .2 mg/kg, compared with .16 mg/kg in our study.

The difference in durations of drug effects in the hand and in abdominal muscles may be due in part to differences in the affinity constants of \(d\)-tubocurarine in the two groups of muscles. Another possible explanation for the faster recovery of respiratory muscles from neuromuscular blockade could be found in the repeated tetanic stimulation\(^{13}\) during respiration. At the point of maximal depression of the abdominal EMG, respiratory functions reached their lowest values, but no direct correlation could be found between the abdominal EMG and results of tests of respiratory function. In the hand, recovery of the 50-Hz frequency parallels the recovery of the hand-grip strength. The thumb twitch tension and respiratory functions appeared to recover together with the low-frequency response of the hand.

The concept of the margin of safety in neuromuscular transmission emphasizes the importance of determining the sensitivity of monitoring methods. Waud and Waud\(^{14}\) reported 75–90 per cent receptor occupancy when thumb twitch tension had recovered to control, 70–75 per cent receptor occupancy at sustained train-of-four and 50 per cent at sustained 100-Hz tetanus. The assessment of recovery from neuromuscular blockade in limb muscles will not give information directly comparable to the state of transmission of respiratory muscles, but since abdominal muscles (respiratory muscle) recover first, the use of a limb muscle for monitoring can be justified. Thus, Ali and co-workers, employing the same dose of \(d\)-tubocurarine (.16 mg/kg), have shown in volunteers that respiratory functions were quite acceptable at the 60 per cent train-of-four level.\(^{15}\)

The frequency sweep EMG contains information about low- and high-frequency stimulation of the myoneuronal junction. Low stimulation frequencies are important for the monitoring of neuromuscular blockade during anesthesia and in the immediate postoperative period. High-frequency stimuli and hand-grip strength may detect residual effects of muscle relaxants and other drugs interfering with neuromuscular transmission. Hand-grip strength and high-frequency responses in peripheral muscles were found to be depressed when respiratory functions and thumb twitch tension were back to normal. Similar results were obtained in a volunteer study by Rigg and co-workers comparing vital capacity and hand grip during partial neuromuscular blockade.\(^{16}\) Thus, hand-grip strength would be a...
good measure for clinical evaluation of postoperative patients, except that it requires a fully conscious and cooperative patient. The sweep frequency technique provides a means of detecting residual curarization without requiring patient cooperation. Whether and how residual curarization could affect patients after anesthesia and operation require further study.

References