Comparison of intubating conditions related to timed dosages and a nerve stimulator based on the measurement of acceleration using mivacurium

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A quantitative method of monitoring neuromuscular blockade has been recently introduced. It has been suggested, when using mivacurium, that a standardized passage of time be used for induction. The purpose of this study was to determine whether a difference existed in intubating conditions when using mivacurium between a timed-dose technique and the ParaGraph® (Vital Signs, Inc., Totowa, New Jersey).

In this prospective, experimental, clinical trial, 40 patients were randomized into two groups. Standardized induction sequences were used for both groups. A standardized rating tool was used to grade each intubation. Intubation commenced in the ParaGraph group when the monitor read one twitch. Intubation in the timed-dose group occurred 90 seconds after the first dose of mivacurium. The difference in intubating conditions score and time to intubation was tested by the Mann-Whitney-Wilcoxon test.

The ParaGraph group had superior intubating conditions when compared with the timed-dose group (P = .0001). Of the ParaGraph group, 100% had good to excellent intubating conditions, and 85% of the timed-dose group had fair to excellent intubating conditions. Time to intubation was longer in the ParaGraph group, with a mean of 216 seconds compared with 121 seconds in the timed-dose group.

The variable time to onset of mivacurium indicates that a timed-dose technique may yield less than optimal intubating conditions despite manufacturer recommendations.

Key words: Intubation, mivacurium, piezoelectric sensor, timed dose.

Introduction
Since Griffith and Johnson introduced curare into clinical anesthesia in 1942,1 the use of nondepolarizing muscle relaxants has become an important component of anesthetic management. This has introduced problems of monitoring neuromuscular blockade. Visual and tactile methods of assessing twitch response and, in particular, the train-of-four ratio are subjective, and experience does not improve the ability to accurately assess the train-of-four ratio.2

The ParaGraph® (Vital Signs, Inc., Totowa, New Jersey) is a new quantitative neuromuscular blockade monitor that uses the concept of acceleromyography.

 Acceleromyography is based on Newton's Second Law; if mass remains constant, force will vary directly with acceleration. An electrode is placed over the ulnar nerve, in the wrist area, a piezoelectric sensor is placed on the thumb to measure the...
response of the adductor pollicis, and the ulnar nerve is stimulated. The force and acceleration of the thumb movement is sensed by the piezoelectric sensor, and the results are displayed on a liquid crystal display screen. This method of monitoring neuromuscular blockade has been found to have a close correlation to forced-displacement transducer and to be more sensitive than manual train-of-four monitoring but not as sensitive as the mechanomyograph. Studies have found that vecuronium has a more rapid onset and recovery of neuromuscular blockade in the larynx and the diaphragm when compared to the adductor pollicis. It has been found that when two times the ED$_{95}$ of mivacurium was given, 95% twitch amplitude depression at the orbicularis oculi occurred 3 minutes sooner than at the adductor pollicis.

Ali et al found a timed-dose technique, while using mivacurium, had good to excellent intubating conditions in 93% of the subjects at 1.5 minutes after the first dose. Since this study, the manufacturers of mivacurium have suggested that a timed-dose technique should be used with induction of anesthesia and not a nerve stimulator.

The 40 patients were randomized into two groups. Standardized induction sequences were used for both groups. Intubation commenced in the ParaGraph group when the monitor read one twitch. Intubation in the timed-dose group occurred 90 seconds after the first dose of mivacurium.

An intubating rating tool was used for this study and consisted of five categories (Tables I and II). The five categories were jaw mobility, mask ventilation, vocal cord exposure, vocal cord position, and movement. Points are assigned to each category and then added for overall intubating conditions. This tool has been used in other published studies.

A quantitative neuromuscular blockade monitor, the ParaGraph, was used on all patients in the ParaGraph group. The time to intubation was measured using a stopwatch.

All patients received medications as deemed appropriate by the surgeon and/or anesthesia provider (e.g., antibiotics and histamine H$_2$-blockers). If the medications were known to interfere with neuromuscular blockade or the neuromuscular junction, the patient was excluded from the study. Subjects received up to 4 mg of midazolam preoperatively or immediately before induction of anesthesia. After standard monitoring was initiated for

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<table>
<thead>
<tr>
<th>Jaw mobility</th>
<th>Mask ventilation</th>
<th>Vocal cord exposure</th>
<th>Vocal cord position</th>
<th>Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mobile, 1 point</td>
<td>Easy, 1 point</td>
<td>Vocal cord and arytenoids completely visible, 1 point</td>
<td>Open, 1 point</td>
<td>None, 1 point</td>
</tr>
<tr>
<td>Partly mobile, 2 points</td>
<td>Difficult, 2 points</td>
<td>Vocal cord and arytenoids partially visible, 2 points</td>
<td>Mid-position, 2 points</td>
<td>1-2-coughs, 2 points</td>
</tr>
<tr>
<td>Immobile, 3 points</td>
<td>Impossible, 3 points</td>
<td>Vocal cords and arytenoids not visible, 3 points</td>
<td>Closed, 3 points</td>
<td>Persistent coughing, 3 points</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Purposeful movement, 4 points</td>
</tr>
</tbody>
</table>
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subjects in the ParaGraph group, a peripheral temperature was taken with the Mon-a-therm® (Mallinckrodt Medical Inc., St. Louis, Missouri) skin temperature probe to ensure peripheral temperature was 32.0°C or greater. The patients breathed pure oxygen, and anesthesia was induced with fentanyl, up to 2.0 µg/kg and propofol, 1.5 to 2.0 mg/kg. Once lid reflex was lost, mivacurium 0.15 mg/kg was given, and in the ParaGraph group, train-of-four monitoring was started every 10 seconds. Mask ventilation then commenced with oxygen and 1% to 2% isoflurane for 30 seconds, after which an additional 0.10 mg/kg of mivacurium was given. Mask ventilation continued with oxygen and 1% to 2% isoflurane for an additional 30 seconds and then an additional 0.5 mg/kg propofol. Mask ventilation occurred for an additional 30 seconds, and in the timed-dose group, the subjects were intubated. The ParaGraph group was intubated when the train-of-four count read one twitch or less.

**Results**

Three potential subjects were excluded from this study for the following reasons: induction protocol was violated, 90% neuromuscular blockade was not achieved, and an unforeseen anatomical abnormality was noted. This left 17 subjects in the ParaGraph group and 20 subjects in the timed-dose group. The power analysis was performed of this sample size to find a difference of 1.01 in total intubating scores between the two groups. It was found to have a power of 0.978 at an alpha of 0.05.

Homogeneity between the two groups of subjects was examined. Gender, ASA classification, and Mallampati classification were examined by chi-square analysis. None were found to be significant ($P > .05$). Weight did not differ between the two groups ($P > .05$, t test). The mean ±SD age of the ParaGraph group was 29.88 ± 9.46 years and of the timed-dose group, 37.35 ± 11.26 years ($P < .05$, t test).

In the ParaGraph group, 76% of the subjects had excellent intubating conditions, 24% fair, and 0% poor. In the timed-dose group, 30% of the subjects had excellent intubating conditions, 55% fair, and 15% poor (Figure 1).

The quality of intubation data was analyzed using the Mann-Whitney-Wilcoxon test. The differences in overall intubating conditions between the two groups were statistically significant ($P = .0001$, Figure 2). The ParaGraph group had a mean ±SD score of 5.29 ± 0.59, and the timed-dose group had a mean ±SD score of 6.3 ± 1.08.

Three categories of the intubating rating tool were studied individually and showed that vocal cord position and vocal cord exposure were not statistically significant between the two groups. The ParaGraph group had 15 subjects that had no movement and 2 subjects with 1 or 2 coughs with intubation; the timed-dose group had 7 subjects with no movement, 7 subjects with 1 or 2 coughs with intubation, and 6 subjects with more than 2 coughs or persistent coughing with intubation ($P = .003$).

There was a significant difference between the two groups in the time to intubation ($P = .003$, Figure 3). The ParaGraph group had a range of time to intubation, based on 90% blockade at the adduc-
tor pollicis, of 134 to 334 seconds with a mean ±SD of 216 ± 56.53 seconds. The timed-dose group, based on the passage of time, had a range of 109 to 144 seconds with a mean ±SD of 121 ± 9.53 seconds.

**Discussion**

Use of the ParaGraph, when using mivacurium, was superior, compared with using a timed-dose approach, in assuring optimal intubating conditions. Past studies have found that 95% twitch depression occurred in 3 minutes at the orbicularis oculi, which correlates better with the muscles of the larynx than at the adductor pollicis.13

Despite controversies concerning the onset of muscle relaxants at various muscle groups, it appears that 90% neuromuscular blockade at the adductor pollicis correlates with relaxation of the muscles of the airway when using mivacurium. Furthermore, mivacurium appears to be quite variable in onset based on 90% blockade of the adductor pollicis; thus a timed-dose technique when using mivacurium may yield less than optimal intubating conditions.

**REFERENCES**

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