AN EVALUATION OF PRIMING WITH VECURONIUM

M. SOSIS, A. STINER, G. E. LARIJANI AND A. T. MARR

Recently, a technique for facilitating rapid tracheal intubation — with the aid of non-depolarizing neuromuscular blocking drugs — has been described by Schwarz and colleagues (1985) using vecuronium. This method (priming) consists of the administration of a small dose of non-depolarizing blocker before induction, allowing sufficient time for the drug to reach the receptors and then the administration of a second larger dose after induction of anaesthesia to facilitate intubation. A suitable priming dose should allow the patient to maintain adequate ventilation and protect his airway. It should be well tolerated. In situations where suxamethonium is contraindicated (Gronert and They, 1975; Durant and Katz, 1982) this technique, if confirmed, would be a major advance.

This study was designed to compare the efficacy of priming with vecuronium against suxamethonium, and a single bolus dose of vecuronium.

PATIENTS AND METHODS

Fifty adult patients (ASA class I and II) free from neuromuscular diseases, and receiving no medication affecting sensitivity to neuromuscular blocking drugs took part in this investigation, which was approved by the Institutional Review Board. All patients gave informed written consent. Patients with anatomical conditions that would make tracheal intubation difficult were excluded.

SUMMARY

Priming with vecuronium was evaluated in three groups of patients. Group 1 (n = 10) received tubocurarine 0.05 mg kg⁻¹, group 2 (n = 19) received physiological saline and group 3 (n = 21) received vecuronium 0.012 mg kg⁻¹. After 4 min maximum inspiratory pressure was measured. Anaesthesia was induced with thio-pentone 6-8 mg kg⁻¹ and controlled ventilation with nitrous oxide and oxygen via a face mask instituted. The ulnar nerve was stimulated at the wrist. At 5 min group 1 patients received suxamethonium 1.5 mg kg⁻¹, group 2 received vecuronium 0.072 mg kg⁻¹, and group 3 received vecuronium 0.060 mg kg⁻¹. Intubation was accomplished at 6.5 min in all patients in group 1, 89% in group 2 and 90% in group 3. Patients in group 1 had no twitch response to stimulation at the time of intubation. Mean T4:T1 ratios at 6.5 min were 0.82 in group 2 and 0.61 in group 3 (P < 0.05). Intubating conditions were excellent in all group 1 patients, and in 53% and 67% of groups 2 and 3, respectively. Two patients in group 3 did not tolerate the priming dose and many had subjective complaints. Four group 3 patients could not sustain head lift and five showed decreased inspiratory pressure. Priming did not improve intubating conditions when compared with a single bolus technique and was not well tolerated.

In a randomized, double-blind manner the patients were assigned to one of the following treatments given in a standard volume: group 1 (n = 10) tubocurarine 0.05 mg kg⁻¹; group 2 (n = 19) physiological saline; group 3 (n = 21) vecuronium 0.012 mg kg⁻¹.

After 4 min each patient was asked to lift his head for 5 s and maximum inspiratory pressure was measured to assess whether the patient could
PRIMING WITH VECURONIUM

Table I. Scoring of intubating conditions

<table>
<thead>
<tr>
<th>Class</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>Easy and no reaction</td>
</tr>
<tr>
<td>Good</td>
<td>Slight vocal cord movement, jaw incompletely relaxed</td>
</tr>
<tr>
<td>Fair</td>
<td>Vocal and movement present, moderate reaction</td>
</tr>
<tr>
<td>Impossible</td>
<td>Intubation impossible without additional time</td>
</tr>
</tbody>
</table>

Thiopentone 6–8 mg kg⁻¹ was administered 4.5 min after the first injection. The lungs were ventilated with nitrous oxide and oxygen via a face mask. At 5 min, group 1 patients received suxamethonium 1.5 mg kg⁻¹, group 2 received vecuronium 0.072 mg kg⁻¹ and group 3 received vecuronium 0.060 mg kg⁻¹, again in a standard volume.

After the administration of the thiopentone, a DigiStim II nerve stimulator (Neuro Technology, Inc., Houston, Texas) was used for train-of-four stimulation of the ulnar nerve at the wrist using supramaximal impulses of 0.2 ms duration at 2 Hz through subcutaneous needles. The resulting thumb twitch was measured using a Grass FT03C force displacement transducer and recorded on paper with a Grass Polygraph. At 6.5 min tracheal intubation was attempted by an experienced anaesthetist. Conditions for intubation were graded on the scale listed in table I. The train-of-four ratio was noted at 6.5 min, as was the time of maximal neuromuscular blockade. The twitch tension was within the range of the transducer used under these circumstances (Freund and Merati, 1973).

Multivariate analysis of variance, followed by Duncan’s multiple range test and Fischer’s exact probability test were performed to detect any significant differences in dependent variables between the groups. The critical level of significance chosen was \( P < 0.05 \). All results are expressed as mean ± SD.

Results

The results of the study are summarized in tables II and III. There were no significant differences between the groups in terms of age, weight or sex. All the patients in groups 1 and 2 could sustain a 5-s head lift before induction. In group 3, 19% could not sustain the head lift. This difference did not achieve significance.

Maximum inspiratory pressure decreased by 30 cm H₂O or more in 24% of patients in group 3. No patient in groups 1 and 2 showed a decrease in maximum inspiratory pressure.

Intubation was successful in all patients in group 1 at 6.5 min, in 89% of patients in group 2 and in 90% of the patients in group 3. Intubation conditions were “excellent” in all patients in group 1, and in 53% and 67% of those in groups 2 and 3, respectively. They were rated as “good” in 21% of those in group 2 and 24% in group 3. In 16% of the patients in group 2, intubating conditions were rated as “fair”.

At 6.5 min the mean train-of-four ratios were 0.82 ± 0.14 in group 2 and 0.61 ± 0.28 in group 3. This difference was significant. Both T1 and T4 were zero in group 1. The time to maximal blockade was 7.8 ± 0.1 min in group 1, 11.2 ± 1.5 min in group 2 and 10.6 ± 1.5 min in group 3.

Table II. The effects of tubocurarine, vecuronium or saline on maximum inspiratory pressure and ability to perform 5-s head lift. Significant difference from vecuronium: \( *P < 0.05 \)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose (mg kg⁻¹)</th>
<th>Successful intubation (%)</th>
<th>T4/T1</th>
<th>Maximal blockade (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubocurarine</td>
<td>0.05</td>
<td>100</td>
<td>—</td>
<td>7.8 ± 0.1</td>
</tr>
<tr>
<td>Saline</td>
<td>—</td>
<td>100</td>
<td>0*</td>
<td>11.2 ± 1.5</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>0.012</td>
<td>90</td>
<td>0.61 ± 0.28*</td>
<td>10.6 ± 1.5</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>0.012 + 0.060</td>
<td>89</td>
<td>0.82 ± 0.14</td>
<td>11.2 ± 1.5</td>
</tr>
</tbody>
</table>

Table III. The effects of suxamethonium and vecuronium given either as a bolus or in divided doses 5 min apart on intubation, T4/T1 at attempted intubation and time to maximal blockade (mean ± SD). Significant difference from vecuronium 0.072 mg kg⁻¹: \( *P < 0.05 \); significant difference from both vecuronium groups: \( P < 0.05 \)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose (mg kg⁻¹)</th>
<th>Successful intubation (%)</th>
<th>T4/T1</th>
<th>Maximal blockade (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suxamethonium</td>
<td>1.5</td>
<td>100</td>
<td>—</td>
<td>7.8 ± 0.1</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>0.072</td>
<td>89</td>
<td>0.61 ± 0.28*</td>
<td>10.6 ± 1.5</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>0.012 + 0.060</td>
<td>90</td>
<td>0.82 ± 0.14</td>
<td>11.2 ± 1.5</td>
</tr>
</tbody>
</table>
23 March 2018

Two patients in group 3 became agitated and complained of ventilatory distress soon after receiving their priming dose. Anaesthesia was induced immediately in one. Most patients in group 3 had severe ptosis shortly after the priming dose and many patients found the experience unpleasant and required considerable reassurance.

**DISCUSSION**

Vecuronium is a non-depolarizing neuromuscular blocking drug with a duration of action between those of suxamethonium and pancuronium (Miller et al., 1984) in standard doses. Attempts to use vecuronium in place of suxamethonium for tracheal intubation have shown that, even at a dose of 0.2 mg kg\(^{-1}\), the time to reach 100\% neuromuscular blockage is longer than with suxamethonium 1.5 mg kg\(^{-1}\) (Bencini and Newton, 1984).

Anaesthetists have long known that small doses of non-depolarizing blockers, as are used to prevent post-suxamethonium myalgia, are generally tolerated by awake patients, although occasional adverse reactions have been reported (Rogoff, Lippman and Walts, 1974; Engbaek and Viby-Mogensen, 1984).

Paton and Waud (1967) have shown that at least 70\% of the receptors at the neuromuscular junction must be occupied before depression of the single twitch will occur, although tetanic fade will occur at lower levels of receptor occupancy. In an attempt to speed the onset of non-depolarizing drugs, priming has been advocated (Foldes, 1984; Doherty et al., 1985; Mehta et al., 1985; Schwartz et al., 1985).

In a pilot study, we attempted to determine the maximum priming dose that would be tolerated by awake, unpremedicated patients as determined by ability to sustain 5-s head lift. We found that 30\% of patients receiving vecuronium 0.015 mg kg\(^{-1}\), as suggested by Foldes (1984) and Schwarz and colleagues (1985), could not tolerate this dose. This is hardly surprising, since this is the ED\(_{50}\) of vecuronium (Fisher et al., 1982).

Brand and colleagues (1977) have demonstrated the importance of head lift and inspiratory pressure in assessing recovery from neuromuscular blockade. Viby-Mogensen, Jorgensen and Ording (1979), Pavlin, Holle and Schoene (1982), and Lennmarken and Lofstrom (1984) have stressed the usefulness of head lift as a sign that the trachea can be extubated and the patient left with little supervision. The present study has shown that the incidence of inability to sustain 5-s head lift was reduced to 19\% by decreasing the dose of vecuronium to 0.012 mg kg\(^{-1}\). However, at this dose, 24\% of our patients showed decreases of at least 30 cm H\(_2\)O in maximum inspiratory pressure.

Krieg and colleagues (1980) showed that vecuronium 0.072 mg kg\(^{-1}\) produced intubating conditions rated as “good” in six of 12 patients and “excellent” in the remaining six at 2 min after injection. Consequently, at 90 s, vecuronium 0.072 mg kg\(^{-1}\) would yield sub-optimal intubating conditions. Therefore, any improvement conferred by priming on intubating conditions would be clearly seen.

Our results, using vecuronium 0.012 mg kg\(^{-1}\) given 5 min before 0.06 mg kg\(^{-1}\), showed no improvement in intubating conditions, and a slightly lower train-of-four ratio when compared with a bolus of 0.072 mg kg\(^{-1}\). We disagree with Schwarz and colleagues (1985) that the “divided dose method of administration compensates for the relatively slow onset of action of vecuronium (and)...provides excellent conditions for tracheal intubation just as rapidly as SCh” (suxamethonium).

We are surprised that the 10 premedicated awake patients studied by Schwarz and colleagues (1985) who received vecuronium 0.015 mg kg\(^{-1}\) “experienced no discomfort during the 3–4 minutes that elapsed until the administration of thiopental.” They reported a train-of-four ratio of 0.77 ± 0.03 (SEM) 5 min after a priming dose of vecuronium 0.015 mg kg\(^{-1}\). They did not list the range of values found and we speculate that some of their patients would have had ratios considered too low for awake patients. Their group of 17 patients who received vecuronium 0.015 mg kg\(^{-1}\) showed twitch tensions averaging 84.7\% of control, demonstrating that the “margin of safety” (Paton and Waud, 1967) had been exceeded.

Engbaek and colleagues (1985) noted train-of-four ratios of 0.57, 0.58, 0.59 and 0.82 and considerable subjective symptoms in four patients who received vecuronium 0.015 mg kg\(^{-1}\). They concluded that doses larger than 0.010 mg kg\(^{-1}\), the ED\(_{10}\) (Fisher et al., 1982), are not well tolerated by awake patients and they reported a patient in whom 0.005 mg kg\(^{-1}\) caused a dangerous degree of paralysis.
We agree with Schwarz and colleagues (1985) that all patients receiving a priming dose should be watched carefully and that anaesthesia should be induced rapidly if patient intolerance occurs. This is in marked contrast to the administration of a small dose of a non-depolarizer before suxamethonium, since the 0.05-mg kg⁻¹ dose administered to group 1 patients represents less than the ED₁₀₀ of tubocurarine (Donlon et al., 1980). We cannot agree with Schwarz and colleagues (1985) that a marked reaction to a priming dose in an awake patient is a useful sign. Extreme sensitivity to neuromuscular blocking drugs can be determined with a twitch monitor after the patient is asleep and the airway secured.

Katz (1967) and Pelikan, Tether and Unna (1953) have noted great variability in the response to tubocurarine. If non-depolarizing drugs are given to awake patients, a suitably small dose must be chosen to avoid patient discomfort and, more importantly, the risk of aspiration (Musich and Walts, 1986). For vecuronium this dose should certainly be no greater than 0.010 mg kg⁻¹. However, even the small improvement in T₄/T₁ noted here is expected to be decreased if the priming dose is diminished.

In summary, this study has shown that priming with vecuronium produced no improvement in intubating conditions when compared with a single bolus technique. Priming is complicated, time consuming and, more significantly, may alarm the patients and conceivably put them at risk of aspiration.

REFERENCES