Atracurium or Vecuronium for Rapid Sequence Endotracheal Intubation

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In the clinical situation that mandates a rapid sequence induction of anesthesia and endotracheal intubation, there is currently no ideal substitute for succinylcholine (SCh) when its use is contraindicated. Neuromuscular blockade will occur sooner if the intubating dose of a nondepolarizing drug is preceded by a small, subparalyzing initial dose (priming principle). However, this priming dose could alarm patients should they develop partial paralysis while still awake; further, paralysis may be incomplete when laryngoscopy is attempted.$^1,3$ High-dose pancuronium, 0.15–0.20 mg/kg, (or other long-duration, nondepolarizing relaxants) produces a prolonged (anticipated 3–5 h) paralysis with accentuated autonomic side effects.$^4$ Recently, vecuronium was used in a dose of 0.28 mg/kg (although not for endotracheal intubation) without observed harmful side effects.$^5$ This prompted our interest in examining the newer shorter acting relaxants, vecuronium and atracurium, in higher doses to determine if they could produce paralysis as quickly as it is produced with SCh, but without undue side effects or marked duration of action. The usual recommended doses of atracurium and vecuronium for endotracheal intubation approximate 0.5 mg/kg and 0.1 mg/kg, respectively; these doses require 2.5–3.5 min to produce suitable conditions for endotracheal intubation.$^6$ We proposed to decrease the onset time by increasing the dose. We recognized that anticipated doses were considerably beyond the ED$_{95}$ range; therefore, we expanded the dose ranges gradually in pilot studies to minimize risk.

**MATERIALS AND METHODS**

All patients were scheduled to undergo elective orthopedic surgery and were classified as ASA I or II without apparent neuromuscular, renal, or hepatic disease. Initially, appropriate intubating dosages of vecuronium and atracurium were determined in pilot studies. Successive patients received increasing quantities of one of the relaxants until their tracheas could be intubated easily within 60 s without significant side effects. Side effects regarded as significant were wheezing or hypotension that was marked or resistant to therapy or other alterations in vital signs. These pilot studies resulted in the selection of doses of atracurium of 1.5 mg/kg and vecuronium of 0.25 mg/kg, or about six times the ED$_{95}$ for each drug.$^6$ The study was approved by the institutional review board.

Forty-six patients received either atracurium (n = 26) or vecuronium (n = 20). The age range was from 16 to 80 yr, and the weight ranged from 56 to 118 kg. No premedication was used. Preinduction monitoring included precordial stethoscope, electrocardiogram, and automated blood pressure (every min). Because neither a force-displacement transducer or recorder was available for the initial phase of the atracurium study, assessment of neuromuscular activity of the initial 19 patients given atracurium was based on visual observation of the response to train-of-four stimulation of the ulnar nerve.$^7$ This was stimulated at the wrist through surface electrodes by a nerve stimulator delivering square wave pulses, supramaximal voltage, 0.2 ms duration. Subsequently, for all patients given vecuronium and the remaining seven patients given atracurium, the indirect twitch tension at 1 Hz of the adductor pollicis muscle was quantitated by a transducer (Grass FT10®) and recorded by a polygraph.

In patients with transducer–polygraph data, we recorded per cent twitch depression at 60 s, onset time for paralysis (time to 95% twitch depression), and recovery (time to return of two twitches in the train-of-four, n = 3). Recovery was more difficult to quantitate because it occurred during the surgical procedure, after the patient's arm position may have been changed or the arm had been draped away from view. In 29 patients, we were able to observe visually the train-of-four to determine relative recovery. Recovery in three patients was recorded. Clinical duration of the neuromuscular block was defined as the interval from injection of muscle relaxant to the observed recovery of two twitches in the train-of-four.

After breathing oxygen for 3–5 min, anesthesia was induced with thiopental, 3–5 mg/kg iv. One to 3 min later, when twitch tension stabilized, the bolus dose of muscle relaxant was injected over 5 s via a stopcock located...
at the cannula. Laryngoscopy and endotracheal intubation were performed 60 s later in every patient.

Intubation conditions were scored as follows: 3—excellent (jaw relaxed, vocal cords open, and no bucking); 2—satisfactory (jaw relaxed, slight movement of cords, and no bucking); 1—fair (less than favorable, but intubation possible); and 0—poor (impossible to intubate).

Results are expressed as mean ± SD. Chi-square analysis compared intubation results between atracurium and vecuronium. Comparisons within and between groups utilized paired and unpaired t tests respectively. P < 0.05 was considered significant for statistical conclusions.

RESULTS

Both muscle relaxants produced adequate (excellent to satisfactory) conditions for endotracheal intubation within 60 s following the bolus injection of 1.5 mg/kg atracurium or 0.25 mg/kg vecuronium as shown in table 1. These results are not significantly different.

Five of seven patients given atracurium and nine of 20 given vecuronium had 95% twitch depression at 60 s, which is the time laryngoscopy and endotracheal intubation were performed. Patients not 95% blocked had mean twitch depressions of 70% (atracurium) and 68% (vecuronium) (table 2). The onset time (time to 95% twitch depression) after atracurium was similar to that for vecuronium, 56 ± 20 versus 64 ± 19 s, respectively. The clinical duration of blockade, defined as the time interval from injection of muscle relaxant to the first visible response to the second of the T4 stimuli, was not different between the two groups, 71 ± 16 min for atracurium (n = 21) and 83 ± 27 min for vecuronium (n = 11). Clinical duration, at times brief, was never prolonged (atracurium 37–102 min; vecuronium 32–110 min) (table 2).

Preanesthetic heart rates were similar (atracurium 83 ± 12 beats/min, vecuronium 80 ± 12 beats/min). The maximal increase in heart rate following endotracheal intubation was significantly greater in patients given atracurium, 30 ± 17 versus 16 ± 14 beats/min in patients given vecuronium. Preanesthetic mean arterial pressures were virtually identical in both groups (atracurium 104 ± 8 mmHg, vecuronium 104 ± 9 mmHg). Postintubation mean arterial pressure in the atracurium group significantly decreased, 22 ± 15 mmHg; in the vecuronium group, postintubation mean arterial blood pressure significantly increased, 15 ± 15 mmHg. Mean arterial blood pressure decreased in only one patient given vecuronium, 14 mmHg. Atracurium produced hypotension (decrease of >20%) in 11 of 26 patients (42%)—blood pressure decreased 24% to 42% below preinduction levels within the first 60 s. Seven of these patients responded to endotracheal intubation with immediate return of arterial

### Table 1. Intubation Score 60 s Following Atracurium or Vecuronium*

<table>
<thead>
<tr>
<th>Rating</th>
<th>Score</th>
<th>Atracurium N = 26 (%)</th>
<th>Vecuronium N = 20 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>3</td>
<td>62</td>
<td>75</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>2</td>
<td>38</td>
<td>25</td>
</tr>
<tr>
<td>Fair</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Results not significantly different.

blood pressure to preinduction levels; arterial blood pressure in the remaining four patients did not recover with intubation, but did so after a small dose (7.5 mg) of meperidine.

### Table 2. Muscle Paralysis After Bolus Doses of Atracurium or Vecuronium*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Atracurium</th>
<th>Vecuronium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Depression of twitch tension at 60 s (%) (of patients not achieving 95% block)</td>
<td>70 ± 4</td>
</tr>
<tr>
<td></td>
<td>Onset time (s) to 95% twitch depression</td>
<td>56 ± 20</td>
</tr>
<tr>
<td></td>
<td>Duration of clinical blockade (min) T2/T4†</td>
<td>71 ± 16</td>
</tr>
<tr>
<td></td>
<td>Range of duration (min)†</td>
<td>37–102</td>
</tr>
</tbody>
</table>

Mean ± SD
Number of patients in parentheses.

* Results not significantly different.
† Clinical duration of blockade defined as the visually observed first return of the second twitch in a train-of-four (n = 21, atracurium; n = 8, vecuronium) and clinical duration recorded by polygraph record (n = 3, vecuronium).

DISCUSSION

We should first comment on the human use of drug doses far beyond those generally recommended, and which, therefore, could be associated with a higher incidence of adverse reactions. We had believed for some time that there was no satisfactory solution to an uncommon clinical problem—when Sch is contraindicated, what is the best alternative relaxant when rapid sequence induction—endotracheal intubation is necessary? As discussed elsewhere in this paper, high-dose pancuronium, the priming principle, or other methods were considered unsatisfactory alternatives. The safety of cautious, careful administration of doses of muscle relaxant much greater than those usually recommended had been proven in sev-
eral studies. The results have demonstrated that the muscle relaxants in these doses could be expected to have a longer duration, and side effects consistent with the known autonomic actions of these drugs could occur. Our clinical experience with pancuronium in doses of 0.15–0.2 mg/kg (when specifically indicated) supported these conclusions, in that these doses were associated with paralysis of 3–5 h duration and pronounced tachycardia.

Because initial studies and experiences with vecuronium and atracurium had demonstrated some unusual and desirable properties, we had ample reason to believe that one or both of these agents might be considerably more efficacious than high-dose pancuronium or other methods in this unique clinical situation. While we recognized that atracurium had a greater incidence of side effects than vecuronium and that these could be more common with the use of higher doses, we also knew that data gathered previously during specific, controlled clinical situations might not be directly applicable to the unique situation that we identified. Therefore, we investigated both drugs and established the selected doses by means of a pilot study in which we gradually increased doses in consecutive patients. We emphasize that the patients for this study were carefully selected and managed, including an evaluation of potential airway problems and ease of intubation. Administration of such higher doses of these drugs to less-fit patients demands careful preanesthetic evaluation of hepatic, renal, musculoskeletal, and cardiovascular function.

We should further comment that the manufacturer’s guidelines for specific drug use are informational only; they are restricted by the Food and Drug Administration (FDA) to those situations well defined by adequate and controlled trials. However, the FDA specifically does not limit the use of drugs to those situations included in the manufacturer’s guidelines. Undefined usage has been called “unapproved use” by some; however, the FDA describes this as “unlabeled application”—appropriate in those instances in which rational usage reflects certain special situations not included in the official labeling.

Use of a large bolus dose is a known, effective method to speed the apparent onset of a nondepolarizing agent. For atracurium and vecuronium, this rapid onset does not seem to be associated with markedly prolonged paralysis, as the longest duration was 102 and 110 min, respectively, as estimated by the first visualization (n = 29) or recording (n = 3) of the second twitch in a train-of-four. Therefore, when SC is contraindicated and rapid laryngoscopy–intubation is necessary, atracurium and vecuronium may be used in increased dosages to facilitate rapid endotracheal intubation without greatly prolonging duration. When the second twitch in a train-of-four returns, reversal of muscle paralysis by pharmacologic means should be feasible; therefore, recovery from atracurium 1.5 mg/kg or vecuronium 0.25 mg/kg could be complete within 110 min and should not result in the prolonged paralysis seen when pancuronium is used in these clinical situations. Although the visual train-of-four has recently been criticized with regard to accuracy, quantification of block appears to be more accurate when one evaluates the number of responses in the train-of-four (as we did) rather than fade.

Our findings of differences in cardiovascular effects are consistent with previous reports. Patients given atracurium had an increase in heart rate of 30 ± 17 beats/min with a decrease in arterial blood pressure of 22 ± 15 mmHg, while those given vecuronium had an increase in heart rate of 16 ± 14 beats/min with an increase in mean arterial blood pressure of 15 ± 15 mmHg. Because laryngoscopy and endotracheal intubation after thiopental constitute a major stimulus during light anesthesia and are generally associated with tachycardia and hypertension, and because large doses (0.28 mg/kg) of vecuronium result in minimal cardiovascular changes, those changes noted with vecuronium in the present study can presumably be attributed to the intubation stimuli rather than to the drug. Atracurium more than counteracted the laryngoscopy-related hypertension and exaggerated the response in heart rate. The more pronounced tachycardia was likely a reflex compensation for the hypotension. While atracurium decreased the arterial systolic blood pressure on several occasions by as much as 40%, this hypotension was brief and responded to appropriate therapy.

It is apparent from the quantitative onset data with both drugs and from visual train-of-four responses during intubation with atracurium that adequate intubating conditions can be achieved when limb neuromuscular blockade is incomplete. Adequate endotracheal intubating conditions are dependent on depth of anesthesia, skill of the endoscopist, and muscle relaxation and can be present at only 40–70% inhibition of twitch tension. Thus, it is difficult to evaluate the relative merit of muscle relaxants for rapid induction–endotracheal intubation based only on an intubation scale. We presume that differences in onset in various patients are due to differences in muscle blood flow and relaxant binding between central (abdomen, thorax, neck, and larynx) and peripheral (limb) muscle groups. Laryngoscopy and endotracheal intubation can be successfully accomplished before abolition of the peripheral twitch if the dose is increased enough to suppress quickly the transmission at central muscle receptor sites.

In summary, vecuronium 0.25 mg/kg provides complete paralysis within approximately 1 min; this is of relatively limited duration (<110 min). Mild hypertension
and tachycardia occur during endotracheal intubation, but these do not appear to be drug related. Atracurium 1.5 mg/kg also provides rapid, total paralysis of limited duration, but in association with moderate hypotension and tachycardia. We conclude that vecuronium may be preferred for situations in which Sch is contraindicated and in which rapid paralysis is mandatory.

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Facial nerve paralysis developing after general anesthesia has been reported.1-4 An unusual case is described in which unilateral facial paresis in association with Heerfordt’s syndrome developed after general anesthesia.

REPORT OF A CASE

A 34-yr-old woman was admitted for colposcopy and cervical biopsy after a cervical smear revealed cervical dysplasia. She had a 3-yr history of biopsy-proven sarcoidosis with bilateral lower extremity weakness due to involvement of the lumbar spinal cord. Two years before her current admission she had developed bilateral uveitis, which responded to a 10-day course of high-dose prednisone therapy. She did not receive any further steroid treatment or other medications. She denied experiencing any ocular pain, otalgia, hearing loss, or previous episodes of facial nerve weakness or paroxysmal swelling. Preoperative chest roentgenogram and electrocardiogram were normal.

Diazepam, 10 mg orally, was given 2 h preoperatively. General anesthesia was induced with 275 mg thiopental iv. Anesthesia was maintained with a mixture of oxygen 3 l/min, nitrous oxide 6 l/min, and halothane. An oral airway was not used. The face mask was held lightly, and excessive pressure at the ramus of the mandible was not required. Anesthesia was maintained for 45 min.

After returning to the ward, the patient complained of increased difficulty in talking, dribbling of saliva and food, and an inability to move the lower left lip. Examination revealed asymmetry of movement of the lower lip with inability to purse the lips, as in whistling. This indicated paralysis of the muscles innervated by the marginal mandibular branch of the facial nerve. Taste sensation of the anterior two-thirds of the tongue was intact, as was motor function in the remaining area of distribution of the facial nerve. There were no other deficits of cranial or peripheral nerve function.

A provisional diagnosis of iatrogenic facial palsy as the result of compression of the marginal mandibular branch near the angle of the jaw was made, and the therapeutic goal was, initially, to await spontaneous remission. However, on the second postoperative day, the patient complained of photophobia and mistiness of vision. Ophthalmologic examination revealed anterior uveitis with keratin precipitates on the posterior cornea. There was no evidence of parotid gland swelling or tenderness but an occasional evening increase in temperature (oral) of between 99.5 and 100° F occurred. The diagnosis was revised to that of Heerfordt’s syndrome, and therapy with oral prednisone (80 mg/day, reducing over 10 days) and hydrocortisone eye drops was initiated. Remission of symptoms occurred gradually over 8 weeks, after which time normal function had returned.

DISCUSSION

The incidence of nerve injuries following general anesthesia has been quoted in two large studies as 0.14% and