Vecuronium: Effect on Intracranial Pressure and Hemodynamics in Neurosurgical Patients

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Pharmacologically induced paralysis is a valuable adjunct in the anesthetic management of neurosurgical patients. However, some currently employed neuromuscular blocking agents have significant undesirable effects on intracranial pressure (ICP).

Vecuronium has an intermediate duration of action with minimal hemodynamic side effects in humans.1 Animal studies suggest that vecuronium does not increase ICP.2 To determine whether similar safety exists in humans, we investigated the influence of vecuronium on both ICP and hemodynamics in patients with brain tumors.

METHODS AND MATERIALS

The subjects were ten consecutive patients undergoing elective craniotomy for tumor resection. The patients ranged in age from 47–75 yr, were free of significant concurrent cardiopulmonary disease, and had preoperative CT scans which revealed supratentorial tumors ≥ 3 cm diameter. All patients had either significant cerebral edema or a shift of midline structures, and all received a preoperative course of corticosteroids and anticonvulsants. Seven patients received glycopyrrolate 0.2 mg im and small doses (less than 0.1 mg/kg) of morphine sulfate im prior to arrival in the operating room. The study protocol was approved by our Human Investigation Committee, and informed consent for the procedures was obtained.

On arrival in the operating suite, a 20-gauge radial artery catheter and a subarachnoid pressure bolt were placed under local anesthesia. The subarachnoid bolt was situated over the frontal region on the side contralateral to the intracranial mass. All pressures were continuously transduced and recorded with the zero reference point at the external auditory meatus. Patency and proper function of the subarachnoid bolt were verified by observation of respiratory and cardiac oscillations in the ICP waveform.

With patients in the supine, 15° head-up position, which position was maintained throughout the study period, anesthesia was induced with thiopental 6 mg/kg iv, and endotracheal intubation was performed after an additional dose of thiopental 4 mg/kg iv and succinylcholine 1 mg/kg iv. Anesthesia was maintained with 70% nitrous oxide in oxygen, and ventilation was controlled to produce normocarbia. The constancy of controlled ventilation was monitored with breath-to-breath end-tidal CO2 measurement.

Recording of neuromuscular function was begun immediately after the initial dose of thiopental. Monitoring was performed with a force transducer (Grass FT-10) measuring adductor pollicis twitch tension in response to supramaximal ulnar nerve stimulation at 0.15 Hz delivered for a duration of 0.15 ms via 25 gauge subcutaneously placed needles. Following complete resolution of prior relaxant effects and after a 5-min period of stable ICP and arterial pressure, vecuronium 0.14 mg/kg iv was administered as a bolus. Constant controlled ventilation was continued for 10 min after vecuronium administration, while ICP, heart rate, and arterial blood pressure were recorded and external stimuli were avoided. Arterial blood gas for gas analysis was obtained 1–3 min before and after vecuronium. Values for mean arterial pressure (MAP = diastolic pressure + ½ pulse pressure) and cerebral perfusion pressure (CPP = MAP – ICP) were calculated. Data were analyzed using a general linear model procedure for two-way analysis of variance and Scheffe’s test for multiple comparisons. All values are the mean for the group ± the standard error of the mean. P < 0.05 was considered significant.

RESULTS

The findings of the preoperative head CT scans are shown in table 1. All patients had CT findings of significant cerebral edema or shift in midline structures.

Vecuronium produced 100% neuromuscular blockade in 107 s ± 11 SE. In all cases, 100% blockade oc-
Table 1. Age, CT Characteristics, and Intracranial Compliance in Ten Patients Who Subsequently Received Vecuronium, 0.14 mg/kg iv

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Age (yr)</th>
<th>Tumor Diameter (cm)</th>
<th>Cerebral Edema (0-3)</th>
<th>Midline Shift (mm)</th>
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<tr>
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<td>6</td>
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<tr>
<td>10</td>
<td>67</td>
<td>5</td>
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*0 = No edema; 3 = edema throughout ipsilateral hemisphere.

Vecuronium has the potential to release histamine\(^{11,12}\) and reduce mean arterial pressure.\(^{11,12}\) Furthermore, laudanosine, a metabolite of atracurium, elicits EEG evidence of arousal following cumulative atracurium doses as low as 1 mg/kg in dogs.\(^{13}\) Pancuronium does not increase ICP,\(^{14,15}\) but its attendant cardiovascular stimulation\(^{7}\) suggests the need for caution when used in patients with intracranial vascular pathology or severe abnormalities of autoregulation.

The use of succinylcholine in neurosurgical anesthesia has been controversial.\(^{16-18}\) Some studies have associated succinylcholine with increases in ICP\(^{14,15,19,20}\) or cerebrospinal fluid pressure,\(^{21,22}\) while others have

**DISCUSSION**

Intracranial hypertension and impairment of cerebrovascular autoregulation are common sequelae of a variety of neurosurgical diseases, including brain tumors.\(^3\) Optimal anesthetic management should include the use of neuromuscular blocking agents that are devoid of direct intracranial or significant hemodynamic effects at doses adequate for endotracheal intubation. D-tubocurarine increases ICP in both animals\(^3\) and man,\(^5\) possible secondary to histamine-induced cerebrovascular vasodilation.\(^6\) D-tubocurarine may lead to reductions in mean arterial pressure,\(^7\) which, in concert with elevated ICP, may jeopardize cerebral perfusion.

Animal investigation with atracurium\(^8\) has demonstrated no effect on ICP, and recent studies in man\(^9,10\) indicate that atracurium does not result in significant ICP changes in neurosurgical patients. However, atracurium has the potential to release histamine\(^{11,12}\) and reduce mean arterial pressure.\(^{11,12}\) Furthermore, laudanosine, a metabolite of atracurium, elicits EEG evidence of arousal following cumulative atracurium doses as low as 1 mg/kg in dogs.\(^{13}\) Pancuronium does not increase ICP,\(^{14,15}\) but its attendant cardiovascular stimulation\(^{7}\) suggests the need for caution when used in patients with intracranial vascular pathology or severe abnormalities of autoregulation.

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**FIG. 1.** Intracranial pressure (ICP, mmHg ± SE) following vecuronium 0.14 mg/kg. \(\ast P < 0.05\) compared to value at time 0.

**FIG. 2.** Mean arterial pressure (MAP, mmHg ± SE) following vecuronium 0.14 mg/kg. \(\ast P < 0.05\) compared to value at time 0.
demonstrated no effect.\(^8\) Interpretation and comparison of studies has been rendered difficult by interspecies variability, study design, and presence or absence of intracranial pathology. Recent evidence\(^9\) indicates that succinylcholine can induce marked ICP increases in some, but not all, patients with intracranial mass lesions. The decision to administer succinylcholine when ICP is not monitored must continue to be weighed against the possibility that conditions characterized by reduced intracranial compliance may be aggravated when succinylcholine is given.

The decreases in arterial and intracranial pressures observed in this study were unexpected. The dose of vecuronium used has not been reported to cause significant changes in arterial blood pressure in healthy adults,\(^1\) and it is unlikely that vecuronium directly affects cerebral blood volume or some other component of the intracranial contents. Rather, we suspect that vecuronium-induced paralysis reduced ICP simply by increasing abdominal and chest wall compliance and decreasing the transmission of airway pressure to the cerebrospinal fluid. The decrease in arterial blood pressure may have reflected attenuation of the hemodynamic response to endotracheal intubation, although our records indicated apparently stable arterial and intracranial pressures in the 10–15 min between intubation and the time when vecuronium was given.

A positive correlation between intraoperative increases in ICP and the extent of edema surrounding brain tumors has been reported,\(^2\) and the changes in ICP also were found to be closely associated with simultaneous changes in arterial blood pressure.\(^3\) In the present study, the majority of patients presented with large amounts of preoperative brain edema, making them particularly vulnerable to hemodynamically induced changes in ICP. Given this patient population, it is not surprising that ICP decreased in concert with MAP, without significant change in CPP, following vecuronium. The important fact is, however, that no increase in ICP occurred, despite the presence of sizeable intracranial mass lesions.

In summary, we observed decreases in ICP and MAP after vecuronium 0.14 mg/kg without significant changes in CPP in ten patients with brain tumors. Vecuronium appears to be a particularly advantageous muscle relaxant for patients in whom preexisting intracranial pathology might be exacerbated by histamine release or increases in systemic arterial blood pressure.

REFERENCES

Introducer Sheath Malfunction Producing Insidious Air Embolism

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Venous air embolism from the use of catheter introducer sheaths which were not self-sealing has led to the use of self-sealing sheaths. Despite use of a sheath with this safety feature, we encountered an unusual presentation of probable venous air embolism (VAE) which led to pulmonary edema. We describe herein the mechanism of self-sealing valve malfunction and resultant air entrainment.

CASE REPORT

A 64-year-old man underwent retroperitoneal lymph node dissection. Induction and maintenance of general anesthesia were uneventful. An 8.5 F side-arm introducer sheath (Walrus, Medical Parameters, Inc., Woburn, MA) was placed in the right internal jugular vein for central venous access. As had occurred during a previous laparotomy, peritoneal traction led to sinus arrest, with 2–4 s pauses. Therefore, a consultant cardiologist placed a 6 F bipolar pacing wire (USCI Division, C. R. Bard, Inc, Billerica, MA) through the sheath assembly. Although the pacing wire could not be passed into the right ventricle, it did allow effective atrial pacing, and was used intermittently throughout the procedure. At the conclusion of operation, neuromuscular blockade was reversed, and the trachea was extubated in the operating room.

In the recovey room, the patient was alert, with normal vital signs, and breathing comfortably in the semi-sitting position. Approximately 3 h later, a systolic arterial blood pressure of 90 mmHg was noted, and was treated by return to the supine position and iv administration of 300 ml of lactated Ringer’s solution. Sinus rhythm continued at 75 bpm. Hypotension again occurred, and was accompanied by an increase in tidal volume and respiratory rate. The patient was placed in the head-down position and given more iv fluid. The pulse oximeter was placed, revealing an arterial oxygen saturation (Sao2) of 85% while breathing oxygen via face mask. PaO2 was 33 mmHg, pH 7.27, and Paco2 43 mmHg. Electrocardiogram (ECG) and chest radiograph were unchanged from their preoperative appearances. Arterial blood pressure rose to 110/70 mmHg, and cardiac rhythm remained sinus. Central venous pressure (CVP) was below 5 cm H2O. An endotracheal tube was placed and conventional mechanical ventilation was begun, with Fio2 of 1.0, positive end expiratory pressure (PEEP) = 5 cm H2O. Arterial blood gases were then Paco2 85 mmHg, pH 7.36, Paco2 43 mmHg.

Intermittent hypotension ensued, responding to iv fluids and a dopamine infusion. At this point, a screw cap on the introducer sheath was noted to be missing, with fluid leaking around the pacing wire. Sheath and pacing wire were removed and replaced with a new sheath. A pulmonary artery catheter was inserted several hours later. Initial measurements were pulmonary artery (PA) pressure of 30/12 mmHg, pulmonary artery wedge (PAW) pressure of 12 mmHg, cardiac output of 5.5 L/min, and systemic vascular resistance of 750 dynes sec cm⁻⁵. A chest radiograph taken 3 h after the initial episode showed diffuse pulmonary edema without cardiomegaly.

Mechanical ventilation was maintained over the next 3 days, during which time the FiO2 was reduced from 1.0 to 0.5, and PEEP from 12 cm H2O to 5 cm H2O, while maintaining PaO2 greater than 70 mmHg. The patient remained hemodynamically stable, and the iv dopamine infusion was discontinued within 48 h. Serial ECGs and creatine phosphokinase values gave no suggestion of myocardial infarction, and PAW pressures remained below 15 mmHg. The trachea was extubated on the third postoperative day, by which time the chest radio-