Letter to the Editor

To the Editor

Vecuronium induced prolonged paralysis in two pediatric intensive care patients

Neuromuscular blocking drugs (NMBD) are widely used to facilitate endotracheal intubation in intensive care units. These drugs are known to be useful especially in children with seizures, traumatic head injury, and respiratory failure.[1-4] However, recently published reports give information about patients who had prolonged muscle weakness after discontinuation of NMBDs.[3,4] These reports point out that the prolonged paralysis extends beyond the weaning period, necessitates rehabilitation, and increases the hospitalization period in most adult, and a few pediatric, critically ill patients. Although NMBD have been thought to be responsible for prolonged paralysis in those patients, critical illness neuropathy, infections, steroid myopathy, and other drugs should be considered in the differential diagnosis.[4-9] We report two patients with spontaneously resolved prolonged paralysis attributed to vecuronium therapy in our pediatric intensive care unit.

Patient 1: A two-month-old girl who was mechanically ventilated for respiratory failure due to *Klebsiella pneumoniae* pneumonia in our pediatric intensive care unit. She had been operated on for anomalous origin of left coronary artery from the pulmonary artery that was reimplanted to the aorta. She was admitted to our unit with pneumonia the second day after heart surgery. We applied vecuronium infusion to achieve neuromuscular blockage. Midazolam infusion was also given for sedation. Neurological examination was unremarkable. She received high-dose corticosteroid therapy (2 mg/kg/day, prednisolone, 14 days) for bronchial hyperreactivity.

Vecuronium was given at a dose of 0.1 mg/kg/hour, for 26 days (total dose was 374.4 mg). At the time of vecuronium cessation her neurological examination revealed hypotonicity, absence of active movements of head and extremities, and absent deep tendon reflexes (DTR). Her DTR, extremity and head movements returned to normal at 5, 15, and 21 days after cessation of vecuronium, respectively. Creatinine kinase was 52 IU/L(0-170). Electromyogram and muscle biopsy could not be performed. She had sufficient respiratory effort and was extubated 13 days after stopping of vecuronium infusion. The patient is 18 months old now, and has no neurologic problems.

Patient 2: A four-year-old boy was mechanically ventilated for respiratory failure due to *Ralstonia pickettii* pneumonia in our pediatric intensive care unit. He had acute lymphoblastic leukemia and had been followed up for six months. He had severe neutropenia because of chemotherapy. Neurological examination was normal. He was administered fentanyl (1μg/kg/hour) for sedation and analgesia during the intubation period. Vecuronium infusion was given at a dose of 0.1 mg/kg/hour, for four days (total dose was 192 mg). At the time of the cessation of vecuronium his neurological examination revealed hypotonicity, and absence of active extremity movements and DTR. Creatinine kinase was 23 IU/L(0-170). Electromyogram and muscle biopsy could not be performed. His DTR and extremity movements returned to normal three days after discontinuation of vecuronium. He had sufficient respiratory effort and was easily extubated. He returned to normal daily activities without neurological deficit only seven days after vecuronium cessation.

Prolonged paralysis has been reported in patients managed in intensive care units.[1,2,5-7] Currently available literature consists of only case reports. No randomized trials are available, making it difficult to draw definite conclusions about underlying mechanisms. Prolonged paralysis attributed to NMBD may be related to associated factors, such as multi organ failure especially renal/hepatic, concomitant drugs (mainly aminoglycosides and corticosteroids), acid-base, electrolyte disturbances and atrophy as a result of non-use of muscles. These factors act by altering NMBD clearance and/or potentiating the neuromuscular junction.[3,7-10] The presence of hypokalemia, respiratory acidosis, hypermagnesemia and hypothermia and the administration of too many antibiotics can result in failure of reversal or the recurrence of blockage due to NMBD. The most common antibiotics blamed for prolonged NMBD effect are aminoglycosides, tetracyclines, lincomycin, and polymyxin. Numerous other pharmacologic agents potentiate the effects of NMBD; local anesthetics, calcium channel blockers, nitroglycerine, high-dose corticosteroids, furosemide, and alkylating cytotoxic agents.[2-5] We consider that prednisolone could have contributed to the prolonged effect of vecuronium in Patient 1. The safe dose of NMBD may vary from patient to patient, drug medication and also dependent concomitant drugs and conditions.

In conclusion, we have to use NMBD for intubation and mechanical ventilated patients in pediatric intensive care units. However, these drugs have some morbidity in long term use. Neuromuscular blocking drugs, such as vecuronium, should be stopped when patients recover, to prevent prolonged paralysis.

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To the Editor

Re: Exacerbation of Pre-existing Epilepsy by Mild Head Injury

Tai PC, Gross DW. Can J Neurol Sci 2004; 31:394-397.

Drs. Tai and Gross recently reported an exacerbation of pre-existing epilepsy in a series of patients following mild injury to the brain. The authors lay claim to a causal connection by way of cerebral insult rather than the effects of stress.

Unfortunately there was no assessment of seizure frequency in a group of control individuals receiving injuries other than to the brain. The authors suggest that because the increase in seizure frequency was prolonged following the brain injury, it is unlikely that the increase was solely due to stress. However, an adjustment reaction following injury may be prolonged for a period of years, notably in those designated as having post-traumatic stress disorder.[1] Neuronal plasticity changes may take place in the limbic circuitry of chronically stressed individuals regardless of injury or type of injury.[2]

It is possible that, unwittingly, Drs. Tai and Gross may have included two, or even three, injured individuals without brain trauma in their series of five, namely those without a documented blow to the head. The authors assumed there was brain injury solely as a result of deceleration. However, brain injury without head contact in adults is so rare that it is almost never seen in a clinical setting in civilian life.[3]

The authors may be right in supporting a direct relationship between exacerbation of seizure disorder and a minor injury – regardless of whether or not there was trauma to the brain.

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1. Yehuda R. Post-traumatic stress disorder. N Engl J Med 2002; 346: 108-130.
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Response

Exacerbation of Pre-existing Epilepsy by Mild Head Injury

Tai PC, Gross DW. Can J Neurol Sci 2004; 31:394-397.

While we had considered the possible role of stress, none of our patients met DSM-IV-TR criteria for post-traumatic stress disorder[1] and, therefore, it remains our opinion that the most likely explanation for seizure exacerbation was head trauma. As our series was retrospective, some accidents occurred years before presentation. Based on the nature of the accidents, we suspect some degree of head trauma likely was present in all patients. We presented this series because we were struck by the temporal relationship between minor accidents and exacerbation of seizures in epileptic patients. Further study is required to ascertain whether what has previously been considered trivial head injury can provoke seizures in epilepsy patients.

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1. 309.81 Posttraumatic Stress Disorder. In: American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. 4th ed. Washington, DC: American Psychiatric Association 2000:463-468.

To the Editor

Re: Comparison of Monitoring Techniques for Intraoperative Cerebral Ischemia.

DW Rowed, DA Houlden, LM Burkholder, AB Taylor. Can J Neurol Sci 2004;31(3):347-356.

The methods and results of this article do not warrant its conclusion that somatosensory evoked potentials (SEPs) are more reliable than EEG to detect cerebral ischemia. Bilateral median SEPs and four-channel EEG (F3-C3', T3-C3', F4-C4', T4-C4') were monitored in 156 carotid endarterectomies. However, multi-channel recording is fundamental to EEG and 16-channel monitoring is adviseable.[1,2] The EEG was measured from intermittent two-second epochs, but requires a longer time-base for proper analysis.[1] Significant amplitude change was defined as a >50% reduction for SEPs and a >75% reduction of “all activity” for EEG. The reference for the EEG criterion states that major changes "consist of attenuation of all activity by at least 75% and/or a twofold or more increase of ≤ 1 Hz delta activity",[1] but increased delta was ignored and blunted by 1 Hz low frequency filtering. Moderate ischemic EEG changes were also ignored. Finally, the disproportionately high EEG technical failure rate of 5% is contrary to previous experience.[1,2] Fundamentally, SEPs were compared to suboptimal EEG.

No patient with preservation of both modalities at the end of monitoring suffered an intraoperative stroke. Two patients had congruent SEP/EEG deterioration restored after shunting. Two patients suffered intraoperative stroke. One had congruent persistent deterioration of both tests. The other had persistent SEP but “no significant” EEG changes. This single critical case forms the entire basis for the authors' contention that SEP monitoring is superior. Disturbingly, EEG waveforms are not provided and the deficits and imaging results are not described. The reader cannot determine the validity of the EEG interpretation or the lesion's location. If the infarct was deep subcortical, then the EEG may have been unaltered. If it was cortical, then the EEG technique was likely inadequate because a proper EEG should be altered and accepting such an unexpected result requires more proof than that provided.

Furthermore, one patient had significant EEG deterioration reversed after shunting but did not have a significant SEP change. Waveforms are again not provided, but this could have been an example of ischemia detected and reversed by EEG