Recovery from Neuromuscular Blockade: How Much is Enough?

by Cynthia A. Lien, MD

The use of nondepolarizing neuromuscular blocking agents as an adjunct to general anesthesia remains quite common. While some might argue against the frequent use of nondepolarizing neuromuscular blocking agents because of the patient safety dangers of residual weakness after reversal, others would say that these medications have been important in the growth and development of anesthesia and surgery. To quote Dr. Foldes, "The first use of Ômuscle relaxants' not only revolutionized the practice of anesthesia but also started the modern era of surgery and made possible the explosive development of cardiothoracic, neurologic, and organ transplant surgery."[1]

In spite of the frequent use of nondepolarizers, however, ideal dosing and monitoring remain controversial. In the 1970s Ali [2, 3] described a train-of-four ratio of 0.60 as being indicative of adequate recovery of neuromuscular strength. With this train-of-four ratio patients have, on average, a vital capacity of 55 ml/kg, a negative inspiratory force of 70 cm H2O and a peak expiratory flow of 95% control values. This degree of recovery should allow patients to cough and maintain a patent airway.

Our ability to detect residual neuromuscular block in the clinical setting, though, is limited. Clinicians can determine the adequacy of return of neuromuscular function through clinical tests and/or monitoring of neuromuscular function with a nerve stimulator. The clinical tests that have been recommended as being good indicators of inadequate recovery of neuromuscular strength include the head lift, leg lift and hand grip.[4] These tests, though, can be performed over a relatively wide range of train-of-four ratios in otherwise healthy volunteers.[5] With train-of-four ratios as low as 0.50 head lift and leg lift can be sustained in some individuals.

In terms of nerve stimulation, the train-of-four ratio is commonly used to determine adequacy of return of neuromuscular function. Clinicians cannot, however, regardless of their level of expertise reliably detect anything less than 60% fade in the train-of-four ratio.[6] Double burst stimulation of the ulnar nerve may improve the clinician's ability to detect more subtle degrees of neuromuscular block.[7] It has been reported to allow detection of 40% fade between the first and the second response but is less well tolerated by patients than train-of-four stimulation.[8] The use of monitors of neuromuscular blockade still does not eliminate the admission of extubated patients to the postanesthesia care unit with unacceptably high residual levels of neuromuscular blockade.[9-12]

Detection of residual neuromuscular block is important because it may have a whole host of clinical implications. We have long known that precurarization, which can decrease the train-of-four ratio to as low as 0.63, may cause difficulty breathing and swallowing as well as decreases in inspiratory force and peak expiratory flow rate. Even a decrease in the train-of-four ratio to 0.85 following precurarization is associated with general discomfort, malaise, ptosis, and blurred vision.[13,14] While this information has been available for a long time, it was generally argued that onset of block is different from

recovery of neuromuscular function. More recently, though, Kopman 5 found that, in volunteers recovering from mivacurium-induced neuromuscular block, a train-of-four ratio of 0.7 to 0.75 was associated with diplopia, decreased grip strength, inability to sit up without assistance, marked facial weakness and difficulty with swallowing and speaking. Even with a train-of-four ratio of 0.90, volunteers had significant visual disturbances such as diplopia and difficulty tracking objects.

Other more recent studies in volunteers have shown that train-of-four ratios of 0.6 and 0.7 are associated with decreased upper esophageal tone and a decrease in the coordination of the esophageal musculature during swallowing.15,16 Fluoroscopic study of these individuals while swallowing demonstrated significant pharyngeal dysfunction resulting in misdirected swallowing leading to a four- to five-fold increase in the risk of aspiration. With train-of-four recovery to 0.90, esophageal tone and pharyngeal coordination returned towards baseline.

As recently described by Eriksson, in addition to the effects of residual neuromuscular block on respiratory function and esophageal coordination, nondepolarizing neuromuscular blocking agents interfere with hypoxic ventilatory control.17 In vitro, while application of acetylcholine to the carotid body results in hyperventilation, application of anticholinergics eliminated the increase in neuronal activity of the carotid body sinus nerve that otherwise occurs with hypoxia. In awake volunteers who have received atracurium, vecuronium, or pancuronium, with a train-of-four ratio of 0.70, the hypoxic ventilatory drive is significantly reduced by, on average, 30%.

The question then is: does any of this impact on clinical outcome? A recent prospective, randomized, blinded study indicates that residual neuromuscular block following administration of pancuronium is associated with an increased incidence of postoperative pulmonary complications.18 Several factors need to be considered when choosing and dosing nondepolarizing muscle relaxants. The surgical patient population is becoming increasingly elderly. Advanced age has been shown, with the majority of muscle relaxants, to decrease their clearance. The patient population is more debilitated than many years ago, when ill patients were not candidates for elective surgery. The presence of concomitant disease, such as hepatic or renal dysfunction, will slow the elimination of the majority of relaxants from the body. Furthermore, anesthetics are becoming shorter acting. With the increasing use of agents such as remifentanil, desflurane, sevoflurane, and propofol, patients are fully alert more rapidly. Therefore, they are more likely to be cognizant of the unpleasant effects of residual neuromuscular block. Finally, surgery is increasingly being done on an ambulatory basis. Patients are expected to be sufficiently recovered from an anesthetic to walk out of the hospital and function at home.

Because complications are preventable with sufficient care and attention, it should not be residual neuromuscular blockade that increases the morbidity associated with a general anesthetic. It should not be residual neuromuscular blockade that keeps ambulatory patients in the hospital longer. Finally, it should not be residual neuromuscular blockade that leads patients to be dissatisfied with their anesthetic care.

These recent studies in patients and volunteers indicate that the "bar" for an acceptable level of recovery of neuromuscular function should be raised to a train-of-four ratio of > 0.90. With this degree of recovery, patients would be better able to protect their airways, would have normal respiratory function, and would feel better. They would likely have fewer complications related to surgery and anesthesia. Furthermore, if clinicians are striving for this more complete degree of recovery, they would be less likely to extubate a patient's trachea at a train-of-four ratio of < 0.60.

Outcome studies examining the effect of residual neuromuscular block on patients are obviously warranted. While these agents have been in use for many years, clinical practice has changed and the patient population has changed. The time may have come to modify our use of the nondepolarizing relaxants so as to increase the likelihood of the desired safe patient outcome.

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