Prolonged Paralysis and Apnea After Receiving a Neuromuscular Blocking Agent: What Nurses Should Know

By Kathryn S. Jaramillo, RN, BSN, Elizabeth Scruth, RN, MN, MPH, CCNS, CCRN, and Eugene Cheng, MD

Abstract  After receiving mivacurium, a short-acting neuromuscular blocking agent used for intubation before surgery, a patient experienced prolonged paralysis and prolonged apnea that required ventilator support. Although this complication is rare, all critical care nurses should be aware of it so they can be competent in managing and providing holistic and comprehensive nursing care to the patient and the patient’s family. Although this complication has been documented in the anesthesia literature, it has received little mention in critical care nursing journals. (American Journal of Critical Care. 2009;18:592,588-591)

This case report describes a patient who had prolonged paralysis and apnea after receiving mivacurium, a neuromuscular blocking agent (NMBA), for endotracheal intubation before surgery. This rare perioperative complication occurs in patients with plasma cholinesterase (pseudocholinesterase) deficiency. Most reported cases of prolonged paralysis are in patients receiving succinylcholine. In this case report, we discuss the use of both depolarizing and nondepolarizing muscle relaxants that undergo metabolism by plasma cholinesterase and the following critical care nursing issues: providing competent care for patients receiving NMBAs, management of acute prolonged paralysis and apnea, management of suspected plasma cholinesterase deficiency, strategies for prevention and patient safety, and future objectives for research.

Case Report  A 56-year-old woman with a below-the-knee amputation of the right lower extremity was readmitted to the hospital for treatment of a 1-week-old stump that was dehisced and infected due to injury. Her medical history included chronic kidney disease treated with peritoneal dialysis, congestive heart failure, hypertension, neuropathy, peripheral vascular disease, diabetes, and malnourishment. The plan...
of care on this admission was antibiotic therapy and surgical debridement of her infected wound. The patient’s amputation had been done without problems with her under spinal anesthesia and intravenous sedation. No history of personal or family problems with anesthesia was reported. The induction of anesthesia started with preoxygenation followed by intravenous administration of 20 mg etomidate and 20 mg mivacurium. Endotracheal intubation was accomplished without incident. Sevoflurane was started for maintenance anesthesia in a nitrous oxide and oxygen mixture. The patient also received 1500 µg alfentanil and 1 mg midazolam intravenously. Intraoperative monitoring included non-invasive monitoring of blood pressure, electrocardiography, measurement of body temperature, peripheral nerve stimulation, pulse oximetry, oxygen analysis, and measurement of end-tidal carbon dioxide.

After induction and the start of maintenance anesthesia, the train of four (TOF) delivered by the peripheral nerve stimulator was 0 out of 4 twitches, indicating complete paralysis or 100% blockage of the acetylcholine receptors at the motor end plate. Because the patient’s TOF did not return as expected and neuromuscular blockade could not be reversed, the surgical procedure was deferred and the patient was transferred to the intensive care unit (ICU) still intubated and mechanically ventilated for recovery from anesthesia. The prolonged paralysis was assumed to be due to plasma cholinesterase deficiency that resulted in extremely slow metabolism of mivacurium. By day 3, the patient’s paralysis had completely resolved and she was successfully extubated. However, because she still required surgical debridement, the patient was returned to the operating room on day 5 after admission. Anesthesia and surgery were completed without complications. Rocuronium was used for neuromuscular blockade.

### Discussion

Prolonged paralysis associated with the use of succinylcholine or mivacurium is rare. However, if prolonged paralysis does occur, the patient is usually admitted to the ICU for extended intubation and mechanical ventilation. Succinylcholine and mivacurium are NMBAs of choice when only a very short period of paralysis is needed. Recovery from succinylcholine paralysis starts within 2 to 3 minutes, and recovery from mivacurium paralysis begins within approximately 5 to 10 minutes. Because of their rapid metabolism by plasma cholinesterase, both of these drugs have a short duration of action compared with other commonly used NMBAs. When paralysis is significantly prolonged for either of these drugs, a problem with plasma cholinesterase should be suspected.

A plasma cholinesterase deficiency or abnormality is attributed to a wide range of genetic and environmental influences, including genetic inheritance of an atypical allele, an acquired state of deficiency due to a pathological condition, or an iatrogenic deficiency as a result of drug interaction, overdose, or chemical exposure. A collaborative effort is required to review the case, interpret test results, determine the root cause of the event, and determine the source of plasma cholinesterase abnormality or deficiency.

### Monitoring Effects of NMBAs

Nurses caring for patients receiving NMBAs such as mivacurium or succinylcholine should know the indications, mechanism of action (depolarizing or nondepolarizing), duration of action, safe management, and how to evaluate drug effects (see Table). Nurses should be competent in operating a peripheral nerve stimulator to measure TOF, which indicates the patient’s degree of neuromuscular blockade.

Because the patient is paralyzed, failure to move cannot be interpreted as meaning that the patient is comfortable. Actually, immobility itself is a potential cause of pain and discomfort. Sudden onset of pain is usually accompanied by temporary increases in physiological and behavioral responses. Therefore, sudden increases in blood pressure, heart rate, tearing, and/or diaphoresis should warrant further assessment and treatment of potential sources of pain, anxiety, or stress. Although researchers in other studies have found that heart rate and blood pressure changes are not always reliable indicators of patients’ level of comfort, nurses should still ensure that their paralyzed patients receive scheduled doses of analgesics and sedatives such as fentanyl and midazolam as empiric therapy for both pain.

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### Recovery from succinylcholine and mivacurium paralysis should occur within minutes.
Furthermore, nurses should exhibit strong communication skills to provide comfort, reassurance, and emotional support. Nurses should also provide interventions to protect paralyzed patients from the risks of corneal abrasion, skin breakdown or pressure ulcers, development of ventilator-associated pneumonia, and impaired functional mobility after extubation. Last, nurses must evaluate patients for full recovery from residual neuromuscular paralysis before extubation. Before extubation, patients should have a 4 of 4 TOF, a score of at least -1 or 0 on the Richmond Agitation Sedation Scale, good strength, and the ability to hold both legs off the bed for at least 5 seconds.8,9,15

Prolonged paralysis and apnea due to mivacurium, which is a nondepolarizing NMBA with paralyzing effects that resolve with plasma cholinesterase hydrolysis, will no longer be an issue because the drug is no longer being manufactured. However, in the future, if other nondepolarizing NMAs that are dependent on plasma cholinesterase metabolism are produced, nurses should be prepared to provide the same care as for patients with prolonged neuromuscular blockade from succinylcholine. In addition, nurses should be alert to correcting electrolyte imbalances. Abnormalities in potassium, magnesium, or calcium levels can contribute to the impaired function of plasma cholinesterase.2

At this time, the reversal of paralysis due to succinylcholine or mivacurium by using drugs that inhibit plasma cholinesterase and are also used for nondepolarizing NMBAs that are not dependent on plasma cholinesterase for metabolism is not recommended because of the potential for intensified neuromuscular blockade. Furthermore, residual blockade may be only several hours long, and exposure of patients to muscarinic side effects of increased acetylcholine levels such as bradycardia, excessive oral and pulmonary secretions, and vomiting may not be warranted.1,5,16 Use of fresh frozen plasma to reverse paralysis is questionable because the reversal from the small amount of plasma cholinesterase contained in fresh frozen plasma is usually transient and multiple units may be required to keep the paralysis adequately reversed.2 Whether or not reversal of paralysis is attempted, the primary plan of

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<th>Nursing skill</th>
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| **Know effects of neuromuscular blocking agents** | Depolarizing neuromuscular blocking agents (eg, succinylcholine)  
- Drug directly attaches to the postsynaptic acetylcholine receptor at the motor end plate, causing persistent depolarization of motor end plate. Drug effects wear off as plasma cholinesterase enzyme rapidly hydrolyzes the drug. No reversal agent exists.  
Nondepolarizing neuromuscular blocking agents (eg, mivacurium)  
- Drug blocks the acetylcholine receptor and prevents binding to the postsynaptic acetylcholine receptor. Drug prevents depolarization of plasma membrane of motor end plate and muscle contraction. Effects wear off after the drug is hydrolyzed. |
| **Use peripheral nerve stimulator** | Quantify train of 4 to determine degree of blockade:  
4 twitches = 0%-75% blockade  
3 twitches = 80% blockade  
2 twitches = 85% blockade  
1 twitch = 90% blockade  
0 twitch = 100% blockade |
| **Administer sedative/amnestic** | Reduce the patient’s anxiety, stress, fear, or loss of physical function during paralysis |
| **Assess resolution of neuromuscular blockade, sedation, and readiness for extubation** | Anticipate risk of residual neuromuscular blockade, poor muscle strength, and premature extubation. Assess for the following: score of at least -1 or 0 on Richmond Agitation Sedation Scale, return of gag/cough reflex, ability to lift head off the pillow for ≥ 5 seconds, ability to lift both legs off the bed for ≥ 5 seconds, ability to maintain bilateral hand grips for ≥ 5 seconds, consistent and adequate tidal volumes and respiratory rate on ventilator pressure settings. |
| **Recognize abnormal results of laboratory tests** | Obtain venous blood sample 24 hours after administration of neuromuscular blocking agent to quantify plasma cholinesterase level and dibucaine inhibition number. Low plasma cholinesterase level means decreased ability to hydrolyze succinylcholine or mivacurium. A decreased dibucaine inhibition number (<80%) indicates the presence of an abnormal plasma level of cholinesterase. A genetic consultation should be considered. |
| **Take steps to prevent complications and to ensure patients’ safety** | Conduct thorough preoperative assessments, flag medical records that indicate adverse reaction to any medication, especially anesthetics. Provide interventions to prevent skin breakdown, decrease risk for ventilator-associated pneumonia, and avoid impaired functional mobility after extubation. Implement teaching plan for patient to be knowledgeable about implications of plasma cholinesterase deficiency. |
During paralysis, lack of movement cannot be interpreted as the patient being comfortable.

Low plasma cholinesterase level cause decreased ability to hydrolyze succinylcholine or mivacurium.

care is to protect the airway with an endotracheal tube and ventilator support until adequate spontaneous breathing is regained.

Whenever a patient has prolonged paralysis or apnea after receiving an NMBA that is metabolized by plasma cholinesterase, it is important to obtain a venous blood sample from the patient at least 24 hours after the NMBA was administered to measure plasma cholinesterase level and determine the dibucaine inhibition number.7-10,17 A low level of plasma cholinesterase means decreased ability to hydrolyze succinylcholine or mivacurium. A dibucaine inhibition number less than 80% indicates the presence of an abnormal or potentially dysfunctional plasma cholinesterase enzyme, and referral for genetic testing should be considered. Because plasma cholinesterase deficiency is attributed to many genetic and environmental influences, a collaborative approach is required to interpret test results and manage patients’ care.17

Our patient had a very low plasma cholinesterase count (715 IU/L; reference range, 2673-6592 IU/L) and a borderline normal dibucaine inhibition number (80.6%; reference range, 81.6%-88.3%). These findings indicate that the patient’s prolonged paralysis after mivacurium was more likely due to an acquired deficiency in plasma cholinesterase that was probably a result of poor nutrition with poor hepatic synthesis of plasma cholinesterase. In addition, the patient’s borderline low-normal dibucaine inhibition number suggests that she may have inherited an atypical allele that manifested itself as a dysfunctional or inadequate plasma cholinesterase enzyme only because of external factors such as malnourishment and potential adverse drug interactions. If her dibucaine inhibition number had been 30% to 70%, it would have been more likely that the patient had 1 normal gene allele and 1 abnormal gene allele for plasma cholinesterase. If the dibucaine inhibition number had been less than 30%, the individual most likely would have had 2 abnormal gene alleles for plasma cholinesterase. Because the patient’s dibucaine number was on the low side of the normal range, genetic testing was not indicated. However, if the patient or the patient’s family is concerned, a counseling session with a collaborative team can provide the information necessary to help the patient determine the implications, benefits, risks, and costs of participating in genetic testing.1,8-10

Nurses should recognize and report an abnormal dibucaine inhibition number and plasma cholinesterase levels. Additionally, nurses should not hesitate to discuss referral for genetic consultation when the dibucaine inhibition number is less than 80%. Furthermore, to prevent a recurrence, the patient’s medical record should be flagged with a note about an adverse reaction to succinylcholine or mivacurium. Discharge teaching for the patient should focus on the adverse reaction to the specific NMBA with recommendations to wear a medical-alert bracelet and to be sure to tell anesthesiologists and surgeons of this condition before any surgeries. Patients with plasma cholinesterase deficiency are at risk for toxic effects from other drugs that undergo plasma cholinesterase metabolism such as tetracaine, procaine, and cocaine.2

No evidence is currently available to support the routine practice of genetic screening for deficiency in plasma cholinesterase in order to predict an individual’s response to NMBA such as succinylcholine or mivacurium. To better understand the pharmacogenomics of this enzyme deficiency, consulting with a medical geneticist with experience in pharmacogenomics would be especially useful. Currently, population linkage studies have revealed more than 10 different genetic variants related to plasma cholinesterase deficiency and more than 25 different phenotypes or variations in the way that plasma cholinesterase deficiency can be expressed. Much more research is needed on the function of plasma cholinesterase and its impact on drug therapy. Future pharmacogenomic research could help develop individualized anesthetics as well as drug therapy for medical illnesses with optimal effect and minimal adverse drug reactions.17-25

ACKNOWLEDGMENT
This study was done at Kaiser Permanente Medical Center, San Jose, California.

FINANCIAL DISCLOSURES
None reported.

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Am J Crit Care 2009;18 592-588 10.4037/ajcc2009572
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