

Postoperative Residual Curarization: A Case Report

Clay Freeman, CRNA, DNP

Abstract

An elderly frail male patient with a history of liver disease presented for a laparoscopic ablation of a liver mass. Nondepolarizing neuromuscular blockade agents were used to maintain a train-of-four count of 1 to 2 twitches throughout the surgery. At the conclusion of the operation the patient's neuromuscular blockade was assessed via train-of-four at the corrugator supercilii, and the patient was given neuromuscular blockade reversal agents. Approximately 10 minutes after his arrival to the recovery unit, the patient presented with symptoms suggestive of postoperative residual curarization. This case report demonstrates the importance of objective assessment strategies when evaluating neuromuscular blockade. Monitoring twitches at the adductor pollicis at the end of surgery gives the practitioner better evidence of a more complete neuromuscular blockade recovery. The dosing and timing of neuromuscular blockade reversal agents should be especially prudent to ensure adequate patient recovery and safety postoperatively.

INTRODUCTION

A 67-year-old male was admitted with chronic hepatitis C and signs of cirrhosis. He presented with pitting edema scored as a plus one and mild jaundice. During an ultrasound screening and hepatic evaluation, a 1-cm mass on the liver was discovered. Initial clinical assessment and diagnostic imaging indicated suspicion for hepatocellular carcinoma with possible arterial and venous involvement. A laparoscopic ultrasound-guided biopsy and radiofrequency ablation of his liver lesion was planned after overnight observation. The procedure was planned to be converted to an open laparotomy if necessary intraoperatively.

In addition to chronic hepatitis C, the patient's history was significant for hypertension, hyperlipidemia, and coronary artery disease. His overall body habitus was considered frail with a height of 175 cm, weight of 71 kg, and body mass index of 23. Home medications included lisinopril, aspirin, amlodipine, atenolol, and simvastatin. He denied any history of a stroke, but mild ataxia was present along with an unsteady gait related to hip dysfunction. He had used a walker for ambulation for the past several years and lived at home by himself. He displayed general weakness but stated that he was able to complete his activities of daily living without assistance. He had a prior history of heavy alcohol abuse for "many years" but denied current alcohol intake, with his last use approximately 5 years ago. He maintained a 20-pack-year smoking history. He denied any shortness of breath or difficulty breathing, although he stated that he did have a chronic cough. The patient's lung sounds were clear to auscultation. His oxygen saturation was 94% on room air in the preoperative holding area.

Past surgical history included an uneventful triple-vessel coronary artery bypass graft surgery in 2001 with no chest pain since that time and a laparoscopic cholecystectomy, which was also uneventful and free of anesthetic complication. Previous anesthesia records from these procedures were not available. The patient's current liver function tests indicated hepatic damage as demonstrated by the following values: alanine aminotransferase (ALT), 100 U/L; aspartate aminotransferase (AST), 91 U/L; and partial thromboplastin time (pTT), 14.9 s. Laboratory values prior to surgery included the following: hemoglobin, 13.7 g/dL; hematocrit, 40.2%; platelets, 288,000; and international normalized ratio, 1.2. The patient had no known drug allergies.

CASE SUMMARY

The patient was brought into the operating room and assisted onto the operating table, standard monitors were applied, and preoxygenation with 100% oxygen was initiated. A standard induction sequence with intravenous (IV) fentanyl 100 mcg, lidocaine 100 mg, propofol 130 mg, and rocuronium 50 mg was performed through the patient's existing 20-gauge peripheral IV line. Mask ventilation was easily accomplished with an oral airway in place. Intubation with a size 8.0 endotracheal tube was achieved with direct laryngoscopy grade 1 view. Sevoflurane was titrated to an end tidal concentration of 2.0%. A 16-gauge IV line was placed following induction and connected to a hot line with a fluid warmer. A peripheral nerve stimulator (PNS) was utilized to assess neuromuscular blockade (NMB) throughout the procedure. Vecuronium at a dose of 0.5 to 1 mg was administered approximately every 20 to 30 minutes upon recognition of a train-of-four (TOF) count at 2 or 3 with the goal to maintain 1 to 2 twitches on TOF.

The surgical procedure was initiated and proceeded without incident. The patient's vital signs remained stable throughout the procedure and ventilation was adequately achieved with a volume control mode, tidal volume of 500, rate of 12, 50% fraction of inspired oxygen (FiO_2), and positive end expiratory pressure of 5 cmH_2O . A total of 11 mg of vecuronium, 7 mg of morphine, and 200 mcg fentanyl were given during the 3-hour case, with the last dose of 1 mg vecuronium given 1.5 hours before surgical closure.

Upon closure of the 5 laparoscopic incisions, twitches were assessed at 2 twitches out of 4 at the corrugator supercilii muscle. A reversal of NMB, 2 mg neostigmine along with 0.4 mg glycopyrrolate, was administered. The patient began to initiate respirations and was taken off the ventilator. He was able to maintain adequate tidal volumes at this time. Morphine 2 mg was then slowly titrated intravenously to achieve a respiratory rate of 10 to 12 breaths per minute. Sevoflurane was discontinued and shortly thereafter the patient was extubated awake after observing the patient was able to sustain a head lift of greater than 5 s upon command. The patient was then transported to the post-anesthesia care unit (PACU) without oxygen. His vital signs upon arrival were as follows: blood pressure, 166/79 mmHg; heart rate, 95 in sinus rhythm; 100% oxygen saturation; respiratory rate, 17; and temperature, 36.6°C per external monitor. The patient was awake and following commands without signs of distress. He denied any pain or other complaints at the time of arrival to the PACU.

Approximately 10 minutes later, the nurse anesthetist, the resident nurse anesthetist, and an anesthesiologist were paged to the PACU to evaluate the patient. He appeared to be having difficulty breathing and swallowing, with overall anxiety. His blood pressure was 210/110 mmHg with tachycardia of 120 beats per minute. He was unable to verbalize but nodded appropriately when asked if he was short of breath. His breath sounds were diminished bilaterally on auscultation. His oxygen saturation remained greater than 92%. Respirations were then assisted at a rate of approximately 20 breaths per minute with a self-inflating resuscitator and 100% FiO_2 . Labetalol 10 mg was given intravenously to decrease his blood pressure. An additional dose of NMB reversal, 2 mg neostigmine and 0.4 mg glycopyrrolate, was administered. After approximately 5 minutes of assisted

ventilation, the patient demonstrated significant improvement in respirations. His vital signs returned to baseline and he was able to breathe effectively on his own. A 12-lead electrocardiogram and chest x-ray were ordered and the findings were unremarkable for acute events. The patient was later discharged to the intensive care unit, as planned preoperatively. Upon assessment the next day, the patient denied any concerns or complaints of anesthetic complications. The patient was discharged several days later without further incidents. He was seen in the clinic 1 week later with no reports of significant events throughout his hospitalization.

REVIEW OF THE CURRENT EVIDENCE

Residual paralysis from NMB is a serious and underrecognized problem postoperatively. Historically, residual paralysis has been identified as postoperative residual curarization (PORC) since it was first noticed after the use of curare. The occurrence of PORC remains under-estimated among practitioners.¹ Indeed, the decision to use reversal agents after NMB varies among international communities and even individual practitioners.¹ Much of the debate is likely due to the high degree of variability in monitoring for the degree of NMB. A number of ways exist to measure NMB but none are more prevalent than the PNS.^{1,2} However, the use of the PNS intraoperatively has not demonstrated a decreased incidence of PORC when compared with more subjective measures such as a patient-sustained head lift.²⁻⁴

Important in the use of the PNS is how it is utilized and how the results are interpreted by the provider. The different sites used for TOF monitoring produce variable results.⁵⁻⁹ The corrugator supercilii muscle and adductor pollicis muscle are 2 frequently monitored sites. The corrugator supercilii muscle demonstrates a recovery time comparable with that of the diaphragm.^{5,7,8} The adductor pollicis has a more delayed recovery time than that of the corrugator supercilii muscle.^{2,5,6} The adductor pollicis is in fact one of the muscles that is part of the last group of muscles to recover from NMB.^{5,7}

Interpretation of TOF is also a crucial aspect in evaluating the degree of neuromuscular recovery. A TOF ratio of at least 0.7 was previously believed to be an acceptable criterion for determining patient readiness for extubation.^{1,2,4,6} However, several studies have evaluated whether this criterion is satisfactory enough to avoid adverse events in the postoperative recovery period. Further evaluation has demonstrated a TOF value of 0.9 or greater to be preferable to lessen the likelihood of respiratory compromise in patients who received NMB.³⁻⁶ This is best appreciated in the demonstration that even healthy volunteers complain of some difficulty breathing with a TOF ratio of 0.7 and even up to 0.9.^{3-5,7,8} Although the diaphragm is functional at a TOF of 0.7, some of the upper airway and esophageal muscles remain weak.^{3-5,10} Such aspects predispose the patient to increased risk of aspiration, airway obstruction, atelectasis, pneumonia, and hypoxia.^{3,7} Complicating matters when determining adequate reversal is the realization that many of the subjective measures still demonstrate some degree of NMB.² Subjective criteria such as a sustained head lift, purposeful hand grip, and adequate patient tidal volumes can still be present with a TOF ratio of 0.5.^{4-6,8}

The use of NMB antagonism also remains debated owing to

mixed understandings of neuromuscular blocking agents and NMB antagonists. The occurrence of PORC has been assumed to have decreased in part due to the addition of intermediate-acting paralytics such as rocuronium and cisatracurium.^{11,12} Upon experimentation, however, studies have not revealed this to be true.^{4,5} Differences in incidences of PORC are seen only when long-acting paralytics such as pancuronium are compared with paralytics like vecuronium, which is intermediate-acting.^{11,12} Evidence suggests that practitioners are also underestimating the time necessary for full recovery after a single dose of an intermediate-acting agent.^{1,5,12} Residual muscle weakness of clinical significance may continue for more than 2 hours.^{1,3,5} Understanding recovery time is especially prudent when considering the sometimes unpredictable nature of steroid-based neuromuscular blocking agents.^{1,5}

Reversal agents exert their effects by increasing acetylcholine at the neuromuscular junction and inhibiting cholinesterase, thereby indirectly competing with neuromuscular blocking agents. Reversal agents are most effective when given at 2 twitches or greater.^{3,4,12} Giving neostigmine before the patient has 2 twitches can result in delayed recovery and incidence of PORC.^{3,4,12}

DISCUSSION

How to best reverse the neuromuscular blocked patient is clearly a subjective decision at this time.^{1,7,8} The NMB in the present case report was monitored, maintained, and reversed according to typical practices by anesthesia providers. The criteria used to determine readiness for extubation are also considered typical within the anesthesia community.^{1,7,8} Our patient demonstrated what appeared to be an adequate count of twitches on TOF prior to administration of the reversal agent. Afterward, a TOF count of 4 twitches was achieved and the patient was extubated awake after a sustained head lift was confirmed. Spontaneous ventilation tidal volumes were around 5 mL/kg. However, the patient presented evidence of PORC in the PACU. Assessment of patient vital signs, respiratory rate, and pupillary size decreased suspicion of respiratory compromise due to opioids or benzodiazepines. Although visual assessments are not conclusive, differential diagnoses were quickly reduced to likely PORC. The identification of PORC was reinforced by patient improvement 5 minutes after administration of a repeat dose of neostigmine. The patient's improvement in motor function correlated with the onset time of the reversal effects of neostigmine. The patient again showed clinical signs of adequate recovery (sustained head lift to command, adequate tidal volumes, ability to cough) and was extubated.

Considering what appeared to be a typical anesthetic case utilizing NMB, reflection on this case discloses the limitations in current practices. More specific and detailed assessment may have prevented this scenario of PORC. The site of monitoring for twitches can demonstrate a noticeable difference in measured outcomes. This patient's twitches were examined at the corrugator supercilii muscle. A more appropriate evaluation should be made by moving the PNS to the ulnar nerve and monitoring the adductor pollicis muscle at the conclusion of surgery, because the adductor pollicis is one of the last muscle groups to recover from NMB. Monitoring at sites that recover more quickly puts the patient at greater risk for PORC. The patient may still be

compromised in respiratory function even when he or she can sustain a head lift of greater than 5 s.^{4,7,8} It is also preferable if a patient's motor function has spontaneously returned with greater than 2 twitches on TOF count before a NMB antagonist is administered. Additionally, dosing NMB antagonism on the basis of the degree of neuromuscular recovery is of critical importance to avoid PORC. Upon recovery of 2 TOF twitches, an ideal dose of neostigmine is 0.05 mg/kg.^{4,5} With these doses in mind, the patient in this case was optimally antagonized only after his second administration of neostigmine in the PACU. All these measures are especially pertinent in high-risk patients. The patients who are likely to recover neuromuscular function more slowly than anticipated are the elderly, the obese, and those with kidney or liver malfunction.^{1,12} With respect to the patient's age, history, and the procedure being performed, a high degree of awareness for possible PORC should be suspected.

Much can also be gained in the understanding of residual NMB across the entire anesthesia practice from studying scenarios such as these and what the literature suggests. The American Association of Nurse Anesthetists standard V states, "When neuromuscular blocking agents are administered, monitor neuromuscular response to assess depth of blockade and degree of recovery."⁷ While the literature does not suggest an increased incidence of PORC whether neuromuscular monitoring is used or not,^{4,5} standards set forth by professional organizations are encouraged. Clearly more teaching and discussion are needed across the entire anesthesia practice to decrease the disparity among practitioners. Such disparities include appropriate neuromuscular monitoring, the interpretation of monitoring results, length of time until spontaneous NMB recovery, and timing of reversal agents. Understanding these facets is vital to improving patient care and increasing the quality of anesthesia care. PORC is a true risk for post-anesthetic patients that can result in delayed recovery, increased morbidity, and increased risks of aspiration and other adverse respiratory events. These risks should demonstrate to anesthesia practitioners that appropriate care of patients is also about ensuring appropriate postoperative recovery.

REFERENCES

1. Hukill SF, Griffin SL. *Current Attitudes Related to the Use of Reversal Agents After Pharmacologic Neuromuscular Blockade* [master's thesis]. St. Louis, MO: Webster University; 2008.
2. Plaud B. Neuromuscular monitoring, residual blockade, and reversal: time for re-evaluation of our clinical practice. *Can J Anaesth*. 2013;60(7):634-640. <http://dx.doi.org/10.1007/s12630-013-9952-4>.
3. Kopman AF. Neuromuscular monitoring: old issues, new controversies. *J Crit Care*. 2009;24(1):11-20. <http://dx.doi.org/10.1016/j.jcrc.2008.02.008>.
4. Kopman AF, Eikermann M. Antagonism of non-depolarising neuromuscular block: current practice. *Anaesthesia*. 2009;64:22-30. <http://dx.doi.org/10.1111/j.1365-2044.2008.05867.x>.
5. Hemmerling TM, Le N. Brief review: Neuromuscular monitoring: an update for the clinician. *Can J Anaesth*. 2007;54(1):58-72. <http://dx.doi.org/10.1007/BF03021901>.
6. Donati F. Residual paralysis: a real problem or did we invent a new disease? *Can J Anaesth*. 2013;60(7):714-729. <http://dx.doi.org/10.1007/s12630-013-9932-8>.
7. Murphy GS, Brull SJ. Residual neuromuscular block: lessons unlearned. Part I: definitions, incidence, and adverse physiologic effects of residual neuromuscular block. *Anesth Anal*. 2010;111(1):120-128.
8. Brull SJ, Murphy GS. Residual neuromuscular block: lessons unlearned. Part II: methods to reduce the risk of residual weakness. *Anesth Anal*. 2010;111(1):129-140.
9. Welliver MD, Jones WH. Interdisciplinary intraoperative communication and collaboration needed for optimal neuromuscular blockade management. *J Anaesth Clin Pharm*. 2014;30(3):442-443. <http://dx.doi.org/10.4103/0970-9185.137300>.
10. Neft M, Quarashi JA, Greenier E. A closer look at the standards for nurse anesthesia practice. *AANA J*. 2013;81:92-96.
11. Hunter J. Antagonising neuromuscular block at the end of surgery. *BMJ*. 2012 Oct 15;345:e6666. doi: 10.1136/bmj.e6666.
12. Lee PJ, MacLennan A, Naughton NN, O'Reilly M. An analysis of reintubations from a quality assurance database of 152,000 cases. *J Clin Anesth*. 2003;15(8):575-581. <http://dx.doi.org/10.1016/j.jclinane.2003.03.006>.