

Neuromuscular Blocking Agents: Reducing Associated Wrong-Drug Errors

ABSTRACT

Neuromuscular blocking agents (NMBAs) are commonly used to paralyze skeletal muscles during surgery conducted under general anesthesia and for patients requiring intubation for airway management. These medications are used in emergency departments, intensive care units, interventional radiology areas, and even medical and surgical units. NMBAs render patients unable to move or breathe and are considered high-alert drugs because misuse can lead to catastrophic injuries or death, especially when administered to patients who are not properly ventilated. Between June 2004 and March 2009, Pennsylvania healthcare facilities submitted 154 event reports that mentioned medication errors involving the use of NMBAs. Analysis reveals that the most common medication error event types associated with this class of medications were wrong-drug errors (37%) followed by wrong-dose/overdosage errors (16.2%). Further analysis showed that 47.4% of the intended medications were not NMBAs, including cases in which the patient was harmed. Strategies to address these problems include limiting access to NMBAs, segregating NMBAs from other medications, sequestering and affixing warning labels to vials of NMBAs stocked in the pharmacy, and requiring independent double checks before dispensing and administering NMBAs. (Pa Patient Saf Advis 2009 Dec;6[4]:109-14.)

Neuromuscular blocking agents (NMBAs) are commonly used to relax skeletal muscles during surgery conducted under general anesthesia. These agents are also used in emergency departments (EDs), intensive care units (ICUs), interventional radiology areas, and even medical and surgical units for patients requiring intubation for airway management.¹

NMBAs produce their effect at the neuromuscular junction by interacting with acetylcholine either by depolarizing the motor end plate or by competing with acetylcholine for binding sites on the motor end plate. This interaction prevents motor transmission, which then prevents patient movement. After a patient is administered a dose of NMBA, progressive paralysis develops, initially affecting the smaller muscle groups (e.g., face, hands). Paralysis then progresses to the medium to large muscles (e.g., mouth, extremities, torso) until all the muscle groups are paralyzed and respiration ceases. It is crucial for healthcare practitioners to remember that NMBAs *do not affect* a patient's level of consciousness, pain, or anxiety. These medications simply render the patient unable to move or breathe.² NMBAs are considered high-alert drugs because misuse can lead to catastrophic injuries or death, especially when they are erroneously

given to patients who are not properly ventilated. Therefore, this class of medications should only be administered by staff with experience in maintaining an adequate airway and respiratory support in facilities where intubation can readily be performed, oxygen can be administered, and respiratory support can be provided.

Due to the potentially devastating effects from the misadministration of NMBAs, clinical analysts reviewed medication error reports submitted to the Pennsylvania Patient Safety Authority in which an NMBA was listed as the medication prescribed or medication administered, as well as medication error reports in which an NMBA was mentioned in the description of the event.

A Look at the Numbers

Pennsylvania healthcare facilities submitted 154 event reports through the Authority's reporting system from June 2004 to June 8, 2009, that mentioned medication errors involving the use of NMBAs. Further breakdown by harm score, which is adapted from the National Coordinating Council for Medication Error Reporting and Prevention harm index,³ shows that 77.9% (n = 120) of the events reached the patient (harm index = C to I) and 9.1% (n = 14) of the events were indicated by the facility as resulting in harm to the patient (see Table 1), which is nearly 13 times greater when compared to *all* medication errors reported to the Authority (0.7%) in that time period. A review of medication errors submitted to the U.S. Pharmacopeia MedMarx® program in 2006 shows that 51% (n = 332) of errors reached the patient (categories C to I), and 9.4% (n = 61) resulted in some level of patient harm (categories E to I).¹

Analysis of the reported ages of the patient involved in medication errors with NMBAs reveals that more than 17% (n = 27) of the reports involved pediatric patients (see Table 2). The care areas most often cited in these reports include the ED (13.6%, n = 21) and the operating room (OR) (12.3%, n = 19). (See Table 3.)

The predominant medication error event types associated with this class of medications (see Table 4) were wrong-drug errors (37%, n = 57) followed by wrong-dose/overdosage errors (16.2%, n = 25). A 2006 MedMarx study that looked at 599 MEDMARX records involving NMBAs in which at least 1 type of error was identified, with a total of 648 types of errors selected (more than 1 type of error was involved in some cases), showed that "improper dose/quantity" (28.2%) followed by "unauthorized/wrong drug" (27.7%) were the most common types of errors involving the use of NMBAs.¹

Table 1. Reports Involving Neuromuscular Blocking Agents Grouped by Harm Score (N = 154)

HARM SCORE	TOTAL	% OF TOTAL REPORTS (N = 154)
A. Circumstances that could cause adverse events.	7	4.6%
B. An event occurred, but it did not reach the individual.	27	17.5%
C. An event occurred that reached the individual but did not cause harm.	55	35.7%
D. An event occurred that required monitoring to confirm that it resulted in no harm.	51	33.1%
E. An event occurred that contributed to or resulted in temporary harm and required treatment or intervention.	11	7.1%
F. An event occurred that contributed to or resulted in temporary harm and required initial or prolonged hospitalization.	2	1.3%
G. An event occurred that contributed to or resulted in permanent harm.	0	0%
H. An event occurred that resulted in a near-death event.	1	0.7%
I. An event occurred that contributed to or resulted in death.	0	0%

Wrong-Drug Errors Involving NMBAs

Analysis of Authority reports focused on the predominant event type for this class of medication, as well as potentially the most devastating: wrong-drug errors. If an NMBA is given in error to a patient who is not intubated, the respiratory muscles may be paralyzed, potentially leading to serious harm or death. Analysis of the medications reported in the “prescribed medication” field (i.e., the intended medication the patient was to receive) showed that 47.4% (n = 27) of the intended medications were not NMBAs and included a variety of medications. There were six cases in which the NMBA vecuronium was administered instead of the intended antibiotic cefazolin; all of these cases resulted in harm to the patient. Table 5 lists the intended (i.e., prescribed) medications involved in wrong-drug reports. It is important to note that 80.7% of the wrong-drug errors reached the patient (n = 46) and 22.8% (n = 13) resulted in harm to the patient. When looking at all wrong-drug medication errors during the reporting period under analysis, 64% (14,070 reports of 21,826 wrong-drug errors) reached patients, but only 0.93% (202 reports of 21,826 wrong-drug errors) resulted in harm.

Wrong-drug medication errors reported to the Authority include the following:

A patient was admitted for a planned surgery. While in holding area of the OR prior to surgery, anesthesia staff started an IV [intravenous] infusion and administered what they thought was midazolam [Versed®] 1.6 mg IV. The patient immediately began flailing and reaching up to her face, and she became apneic. Ambu bag ventilation was initiated, and pulse ox was placed and was 90%. The patient was taken to the OR to be ventilated and monitored until patient awoke (approximately five minutes). The patient described being awake and paralyzed with vivid recollection.

A trauma patient was admitted to the ED. The ED physician was planning to intubate the patient, and the nurse brought in the requested medications for the intubation [midazolam, fentanyl, and succinylcholine]. The succinylcholine had been drawn up in a syringe and labeled. The physician decided not to intubate. An order was given to the nurse to give fentanyl for pain. The nurse picked up the syringe and administered 1 mL when she realized it was succinylcholine. The physician was in attendance and intubated the patient. The patient would have been intubated prior to flight. Intubation occurred earlier than planned.

In the literature, other cases appear in which NMBAs have been inadvertently administered to patients who were not receiving proper ventilatory assistance. While some of those errors have occurred in the OR, most have taken place in EDs, interventional radiology departments, ICUs, and other medical, surgical, and psychiatric units.⁴

Contributing Factors to Wrong-Drug Errors

Many wrong-drug errors can be attributed to one or more common contributing factors.

Unsafe storage. Unsafe, unnecessary, and unexpected availability of NMBAs contribute to drug mix-ups. In some cases, patient care area refrigerators have been inadvertently stocked with NMBAs. In other reports, vials of NMBAs have been placed into adjacent or, at times, the wrong storage areas (i.e., anesthesia kits, automated dispensing cabinets [ADCs]) where the drug was previously not stocked. An example of a storage-related event reported to the Authority is as follows:

A patient had a cesarean section and a healthy baby was delivered. The physician ordered IV Ancef® 2 gm prior to closing. The CRNA [certified nurse anesthetist] obtained [and administered] the medication

from the anesthesia kit that he thought was Ancef, but the patient developed respiratory insufficiency and the CRNA noted that he had administered vecuronium not Ancef. The CRNA attempted to reverse the medication two times and was unsuccessful. The patient was then given anesthesia to enable intubation. The patient was sent to the ICU for recovery and monitoring.

In 2002, the Institute for Safe Medication Practices (ISMP) published a case in which atracurium was administered subcutaneously instead of hepatitis B vaccine to seven infants.⁵ The infants developed respiratory distress within 30 minutes. Five infants recovered, one sustained permanent injury, and another died. NMBAs had never been available as part of the floor stock in the nursery. For convenience, an anesthesiologist from a nearby OR had placed the vial of atracurium in the unit refrigerator near vaccine vials of similar appearance.

According to the 2006 MedMarx report, a physician removed vials of midazolam and rocuronium from a medication cart in the OR, labeled two empty syringes with the respective drug names, and was interrupted while drawing up the two different drugs into the syringes.¹ When he returned, he administered the content of one of the syringes to his patient in the preoperative holding area. Shortly after, the physician was called away to answer a page. On his return, he found the patient unresponsive. The patient was resuscitated, given neostigmine to reverse the respiratory paralysis, intubated, and administered oxygen. It was later determined that the physician had administered the syringe containing rocuronium instead of the intended midazolam.

Similar product labeling and packaging. Vials of NMBAs have been confused with look-alike vials of products (e.g., normal saline, heparin, vaccines), especially when both are stored in the refrigerator. One example involving similar manufacturer labeling, as well as storage issues, submitted to the Authority is as follows:

A patient was scheduled for an open reduction internal fixation for a fracture of the left hand. The patient had sedation and nerve block of the extremity. One gram of Ancef was ordered prior to start of surgery. After the Ancef was administered by the CRNA, the patient said he felt short of breath. The anesthesiologist came into the room at the time that the patient complained of being short of breath. The patient was immediately ventilated, anesthetized, and intubated. The surgery procedure was completed, and the patient was extubated and taken to the postanesthesia care unit with no sequelae. After the surgery was completed, a review of the trash and needle box led the anesthesiologist and the CRNA to believe that vecuronium (which was located next to Ancef in anesthesia cart) had been administered rather than Ancef (both require reconstituting and are similar shape vials).

Table 2. Patient Age Groups Associated with Reports Involving Neuromuscular Blocking Agents (N = 154)

AGE GROUP	TOTAL	% OF TOTAL REPORTS (N = 154)
Younger than 17	27	17.5%
17 to 64	80	52%
65 or older	35	22.7%
Unknown	12	7.8%

Table 3. Predominant Care Areas Involved in Medication Errors Involving Neuromuscular Blocking Agents (n = 120)

UNIT	TOTAL	% OF TOTAL REPORTS (N = 154)
Emergency department	21	13.6%
Operating room	19	12.3%
Pediatric intensive care unit (ICU)	15	9.7%
Anesthesia	15	9.7%
Pharmacy	10	6.5%
Medical/surgical ICU	9	5.8%
Medical ICU	9	5.8%
Neonatal ICU	8	5.2%
Cardiac ICU	8	5.2%
Surgical ICU	6	3.9%

Other cases have been reported in the literature. For example, a number of nurses mistakenly reconstituted measles and Bacillus Calmette-Guérin vaccines with pancuronium, instead of sodium chloride, and administered the vaccines to healthy infants. One infant died after experiencing seizures and respiratory arrest. The pancuronium vial looked very similar to a vial of the correct diluent (i.e., sodium chloride injection).⁶

In another example, an ED nurse administered pancuronium instead of influenza vaccine to several patients. The vials were the same size, and the labels were quite similar. The look-alike vials had been stored next to each other in the refrigerator. The patients experienced dyspnea and respiratory depression but, fortunately, sustained no permanent injuries.⁷

Look-alike drug names. Wrong-drug errors have occurred due to similarities in the drug names. Reports submitted to the Authority include the following:

Narcan® 0.5 mg was ordered, and the nurse prepared Norcuron®, which was caught and not given. In follow-up to the event, labels were placed on the medication drawers indicting both the generic and brand name.

Norcuron 10 mg was ordered verbally. The first nurse asked another nurse to obtain the medication from the automated dispensing cabinet. The second nurse repeated back “Narcan 10 mg” and the first nurse stated, “yes.” The second nurse handed 5 x 2 mg syringes to the first nurse. Narcan was given by the first nurse.

Table 4. Predominant Medication Error Event Types Associated with Neuromuscular Blocking Agents (n = 120)

EVENT TYPE	NUMBER	% OF TOTAL REPORTS (N = 154)
Wrong drug	57	37%
Wrong dose/overdosage	25	16.2%
Prescription/refill delayed	7	4.5%
Wrong technique	6	3.9%
Extra dose	6	3.9%
Other	19	12.3%

Table 5. Intended (Prescribed) Medications Involved in Wrong-Drug Medication Error Reports (n = 57)

MEDICATIONS PRESCRIBED	TOTAL	% OF WRONG-DRUG ERRORS (n = 57)
Vecuronium (Norcuron®)*	7	12.3%
Neostigmine (Prostigmin®)*	7	12.3%
Succinylcholine (Anectine®; Quelicin®)*	6	10.5%
Cefazolin (Ancef®)	6	10.5%
Midazolam (Versed®)	5	8.8%
Phenylephrine (Neo-Synephrine®)	4	7%
Rocuronium (Zemuron®)*	3	5.3%
Cisatracurium (Nimbex®)*	3	5.3%
Fentanyl	3	5.3%
Pancuronium Bromide®*	2	3.5%
Etomidate (Amidate®)	2	3.5%
Propofol (Diprivan®)	2	3.5%
Diltiazem (Cardizem®)	1	1.8%
Glycopyrrolate	1	1.8%
Naloxone (Narcan®)	1	1.8%
Mivacurium (Mivacron®)*	1	1.8%
Acetazolamide	1	1.8%
Norepinephrine (Levophed®)	1	1.8%
No drug listed	1	1.8%

* Medications that are neuromuscular blocking agents

Similar cases have been reported to ISMP involving mix-ups between the proprietary names Narcan (naloxone) and Norcuron (vecuronium). In one case, a pharmacist misheard a verbal order and dispensed the NMBA Norcuron when the opioid antagonist Narcan 1 mg IV was ordered. The patient experienced respiratory arrest and required intubation. In another case, a nurse transcribed a verbal order for Narcan as “1 amp Narcan,” but a pharmacist misread the handwritten transcription as “1 amp Norcuron.” When Norcuron was dispensed, another nurse thought Norcuron was the generic name for Narcan and administered it to the patient, who immediately stopped breathing. The patient was successfully resuscitated. In the third case, a physician wrote “Narcan 1 amp IV.” An ICU nurse tried to obtain the drug from an automated dispensing module where drugs were listed by their generic names. She confused Narcan with Norcuron. She asked a colleague, “What is the generic name for Norcuron?” When her coworker said vecuronium, she removed the NMBA from the cabinet and gave the patient an unknown quantity from the 10 mg vial. The patient experienced respiratory and cardiac arrest but was resuscitated, placed on mechanical ventilation, and transferred to the ICU.⁸

In an example involving look-alike generic drug names, a physician prescribed vancomycin 1.5 g IV every 12 hours for a patient, which the nurse transcribed correctly onto the medication administration record. However, the pharmacist misread the faxed copy of the handwritten order and entered vecuronium into the pharmacy computer. A technician prepared the 1.5 g dose in 250 mL using 15 vials (100 mg/10 mL) of vecuronium. The checking pharmacist did not recognize the error, so the bag was dispensed to the unit. Fortunately, the technician had affixed a vivid alert sticker stating, “Neuromuscular blocker, patient must be intubated” to the bag, which the nurse noticed, thereby averting a serious medication error.⁶

Unlabeled syringes. NMBAs have been accidentally administered when syringes containing the drug were either unlabeled or mislabeled. Although Pennsylvania facilities have not submitted reports specifically mentioning unlabeled syringes with NMBAs to the Authority, one example of a mislabeled syringe is as follows:

The anesthesiologist thought he was administering Versed. The syringe had a label that indicated it was Versed. There was a second label underneath that indicated it was rocuronium. The patient was unable to speak for three to five minutes, and the anesthesiologist recognized that the wrong drug was given to the patient. This was reversed and the patient responded without any problem

One example of an unlabeled-syringe-related error reported in the literature occurred in an ED. Commercially prefilled saline flush syringes were not available, so nurses prepared a supply of syringes

each day from multidose vials. Vecuronium had been prepared for a trauma patient in the ED, but it was not used. The syringe was not labeled and was inadvertently placed with the saline flush syringes. The syringe containing vecuronium was later used to flush the IV line of an alert three-year-old child. The child became flaccid, and respiratory efforts ceased. She was quickly intubated and ventilated, so permanent harm was averted.⁹

Risk Reduction Strategies

To reduce the risk of harm from NMBAs, consider multiple strategies, including both high- (e.g., limiting access to NMBAs) and low-leverage (e.g., increasing awareness) strategies. These strategies include the following (listed high to low):^{1,4,10}

Limit access. Based on the results of the 2004 ISMP Medication Safety Self-Assessment, NMBAs were available as floor stock outside the OR in 80% of participating hospitals; 59% of respondents said that when available outside the OR, these drugs were not sequestered from other floor stock items or labeled with auxiliary warnings.⁶ When possible, dispense NMBAs from the pharmacy as prescribed for patients. Allow floor stock of these agents only in the OR, ED, and critical care units where patients can be properly ventilated and monitored.

Segregate storage. When NMBAs must be available as floor stock, have pharmacy assemble the vials in a distinct, sealed box with warnings affixed as noted below. Sequester the boxes in both refrigerated and nonrefrigerated locations.

Warning labels. Affix fluorescent red labels that note: “Warning: Paralyzing Agent—Causes Respiratory Arrest” on each vial, syringe, bag, and storage box of NMBAs.

Safeguard storage in the pharmacy. Sequester and affix warning labels to vials of NMBAs stocked in the pharmacy. Be sure they do not obscure the vial label in any way.

Standardize prescribing. Include the need for ventilation support during and after administration as well as a protocol that stipulates automatic discontinuation of these agents after extubation and removal from a ventilator. Never accept orders to continue medications upon patient transfer.

Computer reminders. Build alerts in the pharmacy computer to verify the patient’s location when NMBAs are entered. If the patient is not in a critical care unit, ED, OR, or invasive procedure area, question the order and verify ventilatory assistance before dispensing the drug. If possible, establish computerized crosschecking of the patient’s location when entering NMBAs. Cautionary messages should also appear on ADC screens when applicable. Consider a pop-up box that asks, “Is the patient being ventilated?”

Redundancies. Consider an independent double check of these medications before dispensing and

administering. Ensure the medication is checked against the original order.

Supervision during initial administration. Require bedside attendance of a licensed practitioner who has experience with intubation and airway management during initial administration of an NMBA.

Prompt removal of discontinued products. Place vials, bags, and syringes of NMBAs in a sequestered bin for immediate pharmacy pickup after the patient has been extubated or the drug has been discontinued.

Increase awareness. Educate staff about the risk of serious errors with these high-alert drugs. Provide staff with a list of both generic and brand names for all NMBAs available at the facility.

Communication of orders. Always refer to NMBAs as “paralyzing agents” rather than muscle relaxants. Orders should not be written “prn for agitation” but more specifically as part of an intubation procedure or to maintain a specific level of paralysis while the patient is on a ventilator only.

Notes

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4. Institute for Safe Medication Practices. Paralyzed by mistakes: preventing errors with neuromuscular blocking agents. *ISMP Med Saf Alert* 2005 Sep 22;10(19):1-3.
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9. Paparella S. The danger of neuromuscular blocking agents. *J Emerg Nurs* 2004 Jun;30(3):250-2.
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Self-Assessment Questions

The following questions about this article may be useful for internal education and assessment. You may use the following examples or come up with your own.

1. All of the following are true about neuromuscular blocking agents (NMBAs) EXCEPT:
 - a. They are commonly used to relax skeletal muscles during surgery conducted under general anesthesia.
 - b. They can be given to patients who are not properly ventilated.
 - c. They should only be administered by staff with experience in maintaining an adequate airway and respiratory support.
 - d. They are often used in emergency departments, intensive care units, and interventional radiology areas.
 - e. They interact with acetylcholine to prevent motor transmission, which then prevents patient movement.
2. The most commonly reported type of medication error event types associated with NMBAs are _____.
 - a. wrong-technique errors
 - b. extra-dose errors
 - c. wrong-drug errors
 - d. wrong-dose/overdosage errors
 - e. prescription/refill delayed errors
3. Wrong-drug errors associated with the use of NMBAs can be attributed to all of the following factors EXCEPT:
 - a. Patient care area refrigerators stocked with NMBAs
 - b. Confusion with look-alike vials
 - c. Similarities in the drug names (i.e., look-alike drug names)
 - d. Syringes containing the drug were either unlabeled or mislabeled.
4. Which of the following is the most effective strategy to reduce the risk of harm from NMBAs?
 - a. Apply warning labels to vials, syringes, and/or bags of NMBAs.
 - b. Educate staff about the risk of serious errors with NMBAs.
 - c. Conduct independent double checks of NMBAs before dispensing and administering.
 - d. Limit access to NMBAs by *only* storing them in care areas where patients can be properly ventilated and monitored.
 - e. Build alerts in the pharmacy computer to verify the patient's location when NMBAs are entered.
5. A patient had a cesarean section and a healthy baby was delivered. The physician ordered IV Ancef® 2 gm prior to closing. The certified registered nurse anesthetist (CRNA) obtained and administered a medication from the anesthesia kit that he thought was Ancef. The patient developed respiratory insufficiency, and the CRNA noted that he had administered vecuronium, a NMBA, not Ancef.

Select the most effective strategy to prevent this event from reoccurring?

 - a. Remove NMBAs from anesthesia kits in the labor and delivery unit.
 - b. Affix fluorescent red labels that note: "Warning: Paralyzing Agent—Causes Respiratory Arrest" on each vial of NMBA.
 - c. Build alerts in the pharmacy computer to verify the patient's location when NMBAs are entered.
 - d. Require an independent double check of NMBAs when retrieving and before administering the medication.
 - e. Educate staff about the risk of serious errors with these NMBAs.

PENNSYLVANIA PATIENT SAFETY ADVISORY

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