

Neuromuscular blocking agents: Enhancing safety by reducing the risk of accidental administration

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Abstract

Neuromuscular blocking agents (NMBAs) are often found as ward stock in critical care units to ensure their availability in case of urgent need. The unintentional administration of an NMBA to a non-intubated and non-ventilated patient can result in severe permanent injury or death. Incidents involving mix-ups with NMBAs have occurred within and outside of critical care units. Case reports are highlighted with the intent to increase practitioner awareness of situations that could lead to similar errors and to promote changes in the critical care environment in order to enhance medication safety with NMBAs.

Background

Neuromuscular blocking agents (NMBAs) are considered high-alert drugs: "...drugs that bear a heightened risk of causing significant patient harm when they are used in error." (ISMP, 2005). Focusing on high-alert medications is a good starting point to assess and enhance safety in medication use processes (prescribing, transcription, dispensing, administration, and monitoring). NMBA guidelines identifying the potential adverse events associated with use of these medications (e.g., prolonged recovery and acute quadriplegic myopathy syndrome [AQMS]) have been discussed (American College of Critical Care Medicine of the Society of Critical Care Medicine [ACCM], American Society of Health-System Pharmacists [AHSC], American College of Chest Physicians [ACCP], 2002; Murray et al., 2002). This article shares reports of adverse events, resulting from medication incidents where NMBAs were inadvertently administered, for the purpose of learning and taking action to implement medication system safeguards.

NMBAs are commonly found in critical care unit stock for indications requiring respiratory and skeletal muscle paralysis in circumstances such as to manage increased intracranial pressure, or to manage critically ill patients by decreasing oxygen consumption when other therapies have failed (ACCM et al., 2002; Murray et al., 2002). (Refer to Table One for a sample list of neuromuscular blocking agents available in Canada.)

In cases where NMBAs have been inadvertently administered to non-intubated, non-ventilated patients, incidents have resulted in death or severe permanent harm (ISMP, 2006; Phillips & Williams, 2006). Regardless of

where NMBA medication incidents occur, they can provide valuable lessons for enhancing NMBA safety. The following cases are provided to increase awareness of potential system-based failures.

Reports of inadvertent administration of neuromuscular blocking agents

Critical care unit

"Pancuronium [requiring refrigeration] ...was misplaced among heparin flush stock. A nurse inadvertently administered 5 mL of the neuromuscular blocking agent instead of heparin... The patient, who was in the intensive care unit, experienced the effects of the pancuronium administration, but recovered after 10 hours on a respirator." (United States Pharmacopeia [USP], 2000, p. 2).

"A ventilated ICU patient was receiving vecuronium and a potassium chloride infusion. After the patient was extubated, vecuronium was discontinued. The infusion bag containing vecuronium remained in the room and was mistaken to be potassium chloride. Soon after the medication was started, the patient arrested, requiring intubation and ventilation for six hours." (ISMP, 2006, p. 1).

"The names NARCAN (naloxone) and NORCURON (vecuronium) look alike when orders are handwritten and sound alike when orders are transmitted verbally. We have been alerted to three cases where patients in respiratory distress from opiate overdoses needed Narcan, but inadvertently received Norcuron, a neuromuscular blocker ... 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 mentally confused Narcan with Norcuron. She asked a colleague, 'What is the generic name for Norcuron?' When her coworker said vecuronium, she removed the neuromuscular blocking agent from the cabinet and gave the patient an unknown quantity from the 10 mg vial. The

Table One: Sample list of neuromuscular blocking agents available in Canada

Generic Name	Common Trade Name
atracurium	Tracrium
cisatracurium	Nimbex
mivacurium	Mivacron
pancuronium	Pavulon
succinylcholine†	Quelicin†
tubocurarine	Tubarine
vecuronium	Norcuron
† Depolarizing neuromuscular blocking agent.	

patient experienced respiratory and cardiac arrest, but was resuscitated, placed on mechanical ventilation, and transferred to ICU.” (ISMP, 1998, p. 1).

Operating room

“... respiratory compromise suddenly developed in a patient undergoing a minor surgical procedure requiring only local anesthesia and sedation. Immediate interventions included intubation and ventilatory support. The patient required ventilation for approximately 10 minutes. The anesthesiologist later surmised that... atracurium might have been administered to the patient instead of the intended midazolam... the atracurium and midazolam vials were both 10 mL in size and located adjacent to each other... Practitioners at this hospital were presumably accustomed to having the neuromuscular blocker in the smaller 5 mL vial and the midazolam in a 10 mL vial... the substitution of rocuronium (a commonly used neuromuscular blocker in a 5 mL vial) with atracurium (10 mL vial)... in the anesthesia drug cart due to a national (manufacturer) shortage [was also identified as a contributing factor].” (ISMP Canada, 2004, p. 1).

“... the inadvertent administration of rocuronium from an unlabelled pre-filled syringe... The intended drug was a sedative. The patient was successfully resuscitated after suffering a respiratory arrest.” (ISMP Canada, 2004, p. 1).

Emergency department

“... in a pediatric emergency department (ED) where vecuronium was administered to an alert three-year-old child who was not ventilator-supported. In this case, commercially prepared, prefilled saline syringes were not available in the ED, so nurses drew up supplies of saline flush syringes from multiple-dose vials, labelling them by hand. Prior to the child’s admission, vecuronium syringes had been prepared for another patient. An unused syringe of vecuronium, hand-labelled similarly to the saline syringes, somehow found its way into the saline supplies. As a result, the syringe containing vecuronium was mistakenly used to flush the child’s IV line. The child became frightened and



Figure One: Examples of the variety of vial caps and closures of NMBAs in Canada. (Used with permission from ISMP Canada.)

flaccid. All respiratory efforts ceased, and he was quickly intubated and ventilated... The child was treated supportively and sustained no serious harm.” (ISMP, 1999, August 25, p.1).

“A nurse, intending to select epoetin alpha (Procrit) from the medication refrigerator, mistakenly chose a vial of pancuronium. The nurse realized her error as she was preparing the dose and corrected her mistake. Tragically, this near miss was not reported, and a co-worker later prepared and administered an inadvertent dose of pancuronium from the same refrigerator.” (Paparella, 2004, p. 251).

“A trauma patient was admitted to the ED for stabilization before transfer to a local trauma centre. The physician gave a verbal order for vecuronium and midazolam, and intubated the patient after the medications had been administered. He then mistakenly entered electronic orders for these medications onto an oncology patient’s record. While this patient’s nurse was taking a break, another ED nurse administered medications to the oncology patient without recognizing that vecuronium would paralyze the respiratory muscles. After she left the room, the patient arrested. The ED team responded, but the patient could not be resuscitated.” (ISMP, 2005, September 22, p. 2).

“An emergency room physician treating a combative patient ordered a neuromuscular blocker (vecuronium, Norcuron®) without first assuring the patient was appropriately ventilated. The patient, who was not intubated, received the drug and developed respiratory arrest. The patient suffered an anoxic insult.” (ISMP, 1996, p. 2).

General medical/surgical patient care areas

“...an order to ‘continue same meds’ upon transfer from a critical care unit has led to continued use (sometimes fatal) of neuromuscular blocking agents for restless, but extubated patients.” (ISMP, 2000, p. 1).

“Unknown to pharmacy, an anesthesiologist had ordered trial supplies of mivacurium from a drug representative. When the product was delivered to the pharmacy, it was stocked next to look-alike bags of metronidazole. Both solutions were encased in foil wrappers. Believing metronidazole was the only product in foil wrappers in the pharmacy, a technician labelled several mivacurium bags as metronidazole... four patients received mivacurium instead of metronidazole; all experienced respiratory arrest. One patient died, another was seriously injured, and two recovered.” (ISMP, 2005, September 22, p. 2).

“...cisatracurium infusion had been delivered by accident to a medical unit along with three bags of antibiotics. A nurse had verified that the first three bags in the stacked pile of piggybacks were the prescribed antibiotics, but she was interrupted before checking the fourth bag, which contained cisatracurium. When she returned to the medication room, the nurse glanced at the yellow label, similar to the other labels on the antibiotics, and administered the

neuromuscular blocking agent, believing it was an antibiotic. The patient experienced a respiratory arrest and required ventilation for a few hours.” (ISMP, September 22, 2005, p.1).

“Atracurium was administered subcutaneously instead of hepatitis B vaccine to seven infants. The infants developed respiratory distress within 30 minutes. Five infants recovered, one sustained permanent injury, and another died. Neuromuscular blocking agents had never been available as 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.” (ISMP, 2005, September 22, p. 2).

Contributing factors

Multiple contributing factors often underlie medication incidents with NMBAs (i.e., inadvertent administration). For example, confirmation bias can cause a health care professional to read a label or select a drug product and “see” what they expect to see, rather than what is actually selected. Lack of differentiation between NMBAs and other medications (refer to Figure One), look-alike packaging and labelling, and unexpected changes to labelling or packaging (e.g., in cases of drug shortage or when a product is purchased from an alternate manufacturer) can contribute to confirmation bias and predispose to human error.

ISMP Canada, as part of the Canadian Medication Incident Reporting and Prevention System (CMIRPS), has been involved in a national collaboration with multiple stakeholders to identify and promote improvements to the packaging and labelling of medications to better distinguish them (ISMP Canada, 2005, October 30). NMBAs were identified as an important starting point. Agreement regarding the ideal features for packaging and labelling of neuromuscular blocking agents, some of which have already been implemented in the United States, are summarized in Table Two. Some of the participating Canadian manufacturers already have select features incorporated into their labelling and others are evaluating the feasibility of incorporating some or all of these (ISMP Canada, 2006).

Distinctive packaging and labelling are key safety features, but are only part of the solution. Contributing factors to the occurrence of NMBA medication incidents can also include: storage and access to these drugs outside of specialty areas, lack of an independent double check by a pharmacist prior to dispensing, not segregating NMBA storage (in patient care areas as well as in pharmacy), miscommunication, lack of readily available information at point of care, lack of practitioner knowledge, failure to discontinue/remove NMBAs from patient rooms or from medication administration records before patient transfer from critical care, and look-alike/sound-alike medication names.

Prevention strategies

Medication systems and processes need to be continuously assessed and enhanced in order to reduce error potential. Some examples of safety recommendations and prevention strategies to promote safer use of NMBAs are outlined below. It may be helpful to consider the *Hierarchy of Effectiveness* when developing and implementing safety solutions, where the most effective have been identified as those “...high-leverage error prevention tools that are designed to fix the system, not just people, whenever possible.” (ISMP, 1999, June 2, p. 1).

Restrict access

Restrict floor stock of NMBAs to critical care, the operating room and the emergency department, where patients can be mechanically ventilated and monitored (Cohen, 2007; ISMP, 1999; ISMP, 2005; ISMP, 2006; ISMP Canada, 2005, April; Paparella, 2004; Phillips & Williams, 2006).

Segregate storage

Segregate NMBAs from all other medications in all areas they are stored (Cohen, 2007; ISMP, 1999; ISMP, 2005; ISMP, 2006; ISMP Canada, 2005; Paparella, 2004; Phillips & Williams, 2006).

If *intubation kits* or *anesthesia kits* containing NMBAs must be kept in areas outside of the operating room, seal the kits to restrict access until the time of intubation (Phillips & Williams, 2006).

Remove NMBAs from a patient’s room as soon as they are discontinued, and dispose of them promptly. Do not return unopened vials to stock. Return vials to pharmacy immediately or place them into a return bin that is sequestered (Cohen, 2007; ISMP, 1999; ISMP, 2005; ISMP, 2006; ISMP Canada, 2002; Paparella, 2004).

Apply warning labels

Have pharmacy:

- affix clearly visible warning labels, such as “Warning: Paralyzing Agent – Causes Respiratory Arrest”, on each vial, syringe, admixed intravenous (IV) bag, and storage box

Table Two: Ideal features of neuromuscular blocking agent labelling and packaging include (ISMP Canada, 2006):

Red cap with white lettering: “Paralyzing agent” or “Warning: Paralyzing Agent”

Red ferrule with white lettering: “Paralyzing agent”

Red lettering on the product label: “Paralyzing agent” or “Warning: Paralyzing Agent”

Peel-off label, using the colour scheme and content information recognized by the ASA/CAS recommended standards, for application to a prepared syringe (ASA = American Society of Anesthesiologists [www.asahq.org]; CAS = Canadian Anesthesiologists’ Society [www.cas.ca])

Space on the product label for bar-code application

of NMBAAs (including those stocked in pharmacy) (Cohen, 2007; ISMP, 1996; ISMP, 1999; ISMP, 2005; ISMP, 2006; ISMP Canada, 2002; ISMP Canada, 2005). Ensure that the labels are placed without obscuring important information (Cohen, 2007).

- communicate changes in manufacturer, packaging, and labelling to frontline staff (e.g., where a product shortage requires a medication substitute or a change in supplier) (ISMP Canada, 2004; ISMP Canada, 2005).
- consider including preprinted drug name labels and warning labels where NMBAAs are stored, for use by practitioners who administer NMBAAs (ISMP Canada, 2004).

Computerize and automate

Work towards implementing computerization of the medication use process at the point of care (e.g., bar-coding, computerized physician order entry [CPOE]) in an effort to automate manual independent double check processes (ISMP, 1999; ISMP, 2005; ISMP, 2006).

Work to implement or optimize built-in clinical alerts. For example, an on-screen pop-up box that states “Ensure patient is intubated and ventilated” whenever an NMBA is selected for removal from an automated dispensing cabinet (Cohen, 2007; ISMP, 2006; Paparella, 2004).

Use single-item access drawers for storage of NMBAAs in an automated dispensing cabinet (Paparella, 2004; Phillips & Williams, 2006).

Standardize prescribing

Establish and use standard order sets (preprinted, computerized) for NMBAAs to prevent misinterpretation of handwritten orders. Include the need for full ventilation support during and after administration and a protocol stipulating automatic discontinuation of NMBAAs after extubation or on removal of full ventilator support (e.g., patient is now required to trigger the ventilator) (Cohen, 2007; ISMP, 2005; ISMP, 2006).

NMBAAs should never be referred to as “muscle relaxants” (Cohen, 2007; Phillips & Williams, 2006).

Do not accept orders such as “Resume the same medications” upon discharge from critical care (Cohen, 2007; ISMP, 2005; ISMP, 2006).

Do not accept indications such as “prn for agitation” (Cohen, 2007; ISMP, 2005; ISMP, 2006; Phillips & Williams, 2006).

Educate and inform

Share this article to increase staff awareness of medication incidents that have occurred with NMBAAs, including the need to:

- label medication syringes, even when only one product is to be administered (ISMP Canada, 2004); and
- report medication incidents, near misses, and potentially hazardous conditions to prompt medication safety improvements.

Provide up-to-date drug information readily available to practitioners at various points in the medication use process (including having generic and trade names) of NMBAs available.

Summary

Inadvertent administration of neuromuscular blocking agents can be fatal. It is well-known that “to err is human”. Critical care practitioners are encouraged to take this opportunity to learn from organizations that have experienced paralyzing incidents involving NMBAs. Assess potential areas of risk related to the stock and use of these agents in your own practice, in your critical care unit, and in your organization as a whole. Design and implement safeguards to enhance system safety. Awareness of hazards associated with the use of NMBAs and of strategies for safer use can reduce the potential for harmful events to occur with these medications. ☘

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ISMP Canada gratefully acknowledges the valuable lessons learned and information reported by professionals in the Canadian health care community that can then be shared to enhance medication system safety. All ISMP Canada Safety bulletins are available from <http://www.ismp-canada.org/ISMPSafetyBulletins.htm>

ISMP Canada is a national voluntary medication incident and ‘near miss’ reporting program founded for the purpose of sharing the learning experiences from medication errors. Implementation of preventative strategies and system safeguards to decrease the risk for error-induced injury and thereby promote medication safety in healthcare is our collaborative goal.

Medication Incidents (including near misses) can be reported to ISMP Canada:

(i) through the website

http://www.ismp-canada.org/err_report.htm or

(ii) by phone: 416-733-3131 or toll free: 1-866-544-7672.

ISMP Canada can also be contacted by e-mail: cmirps@ismp-canada.org.

ISMP Canada guarantees confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications.

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