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ISMP Canada Safety Bulletin

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Neuromuscular Blocking Agents: Sustaining Packaging Improvements over Time

Neuromuscular blocking agents, also known as paralyzing agents, are high-alert medications. They paralyze muscle function by blocking the connection between nerves and muscles. Notably, the muscles that are essential for breathing become paralyzed in patients who receive these medications—these patients need to be immediately ventilated. Serious injuries and deaths have occurred with substitution errors involving these drugs.[1-4] Incidents involving inadvertent administration of neuromuscular blocking agents and recommendations for prevention of error have been highlighted in previous issues of the ISMP Canada Safety Bulletin.[1,2] The purpose of the current bulletin is to affirm the progress that has been made in the packaging and labelling of these drugs, in an effort to sustain key safety improvements.

Background

In 2006, ISMP Canada convened a meeting of representatives of Canadian manufacturers of neuromuscular blocking agents. The intent was to collaborate in identifying opportunities to reduce the risk for accidental administration of a neuromuscular blocking agent because of a product mix-up.[5]

The pharmaceutical representatives agreed upon several ideal packaging and labelling features for neuromuscular blocking agents to help differentiate them from all other drugs:[5]

- red cap with white lettering: "Paralyzing Agent" or "Warning: Paralyzing Agent"
- red ferrule (metal seal) 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 recommended in standards for labels to be applied to prepared syringes, as set out by the Canadian Anesthesiologists' Society (CAS; www.cas.ca) and the American Society of Anesthesiologists (ASA; www.asahq.org)
- space on the product label for application of a bar code

Figure 1. Examples of closures on vials of neuromuscular blocking agents currently available in Canada. Although the colour may vary (see "Note about Colour" on next page), all neuromuscular blocking agents currently available in Canada have a warning on the cap and/or ferrule.

- development of a universal symbol for neuromuscular blocking agents, intended for global use (placement of this symbol [e.g., on the label] to be determined)
- review of potential benefit of using TALLman lettering for generic names of neuromuscular blocking agents

Current Status

Significant progress has been made, such that all neuromuscular blocking agents on the Canadian market now carry a warning on the cap and/or ferrule (refer to Figure 1 for examples).

Note about Colour

Although stakeholders agreed on use of a red* cap and ferrule, not all neuromuscular blocking agents currently available in Canada use a red colour for the cap or ferrule. Variations include the following:

- use of a transparent cap that reveals the warning on the ferrule
- use of a colour other than red for the cap and/or ferrule

Method for Review of Incident Data

Searches of the ISMP Canada and National System for Incident Reporting (NSIR)† databases were conducted. The searches were structured to identify incidents reported to ISMP Canada between February 28, 2006, and May 15, 2014, and to the NSIR between the NSIR start date in November 2008 and May 15, 2014. The goal was to identify all reported errors (including reports of near misses) involving mix-ups that occurred with a neuromuscular blocking agent in which labelling and packaging were reported as contributing factors. Incidents were included in the analysis if they occurred after the collaborative meeting on February 27, 2006. It is recognized that it is not possible to infer or project the probability of incidents on the basis of voluntary reporting systems.

Medication Incidents and Overview of Findings

A total of 4 reports, all from the ISMP Canada database, met the inclusion criteria. The following information and learning are shared.

One of the incidents was a near miss in which the neuromuscular blocking agent succinylcholine was selected instead of heparin. As the nurse was walking to the patient's bedside, she noticed white lettering on the red cap that read "WARNING: PARALYZING AGENT". This prompted her to realize that she had selected the wrong vial. The reporter noted that the enhanced labelling and packaging for the succinylcholine had made a difference and prevented the selection error from reaching the patient.[6]

Two of the incidents involved confusion between pancuronium, another neuromuscular blocking agent, and lorazepam, a benzodiazepine. In one case, the error was identified before the medication was administered; in the other case, the pancuronium was administered, the patient became apneic, and intervention was required. The findings indicated that in some patient care areas, unlike how these drugs are stored on anesthesia carts, neuromuscular blocking agents may be provided and stored within their outer package (i.e., outer box). Reporters for both of the incidents involving pancuronium identified look-alike labelling of the outer box, as well as look-alike labelling of the immediate containers, as potentially contributing to

* Before the collaborative meeting in 2006, recommendations for the colour on the closure system for vials of neuromuscular blocking agents included "anesthesia red", Pantone 805 and Pantone 811 (the latter being perceptually a bright orange colour); it was also recommended that the cap and overseal state in white print "Warning: Paralyzing Agent" or "Paralyzing Agent", depending on the size of container.[1,2] Use of a clear, concise warning or signal word along with a specific colour were intended to align with information in published warning literature (e.g., importance of signal-word prominence and use of the colour red to communicate "danger" or orange to communicate an alert or a warning).[7] The colour was also intended to align with other labelling standards and other information available at the time of the meeting.[8,9] Importantly, the use of high-contrast colours and the warning on the closure were intended to differentiate neuromuscular blocking agents from all other medications and to provide critical information at a key point of end-user interaction with the product. During the 2006 meeting, it was recognized that pharmaceutical manufacturers had limitations in terms of their ability to meet specific requirements and also in terms of making changes to ferrules and caps. The hue of red was therefore not specified.[5]

† The National System for Incident Reporting (NSIR), administered by the Canadian Institute for Health Information, is a component of the Canadian Medication Incident Reporting and Prevention System (CMIRPS) program. More information about the NSIR is available from: http://www.cmirps-scdpim.ca/?p=12

the errors; furthermore, in both cases, the pancuronium and lorazepam were stored in close proximity in the refrigerator. After these incidents were reported, ISMP Canada contacted the manufacturer of pancuronium. The manufacturer quickly revised the labelling of the neuromuscular blocking agent by adding a prominent bold warning on the outer package and immediate container labels and by changing the colour scheme to enhance differentiation. No further reports involving pancuronium have been received since this change was made several years ago.

The most recent report involved a near-miss substitution error between 2 neuromuscular blocking agents, one a nondepolarizing agent and the other a depolarizing agent. Before the near miss, the nondepolarizing and depolarizing agents available on anesthesia carts at the reporter's institution had slightly different closures: one product had a clear cap with the warning (white lettering on a red ferrule) visible underneath, while the other had a red cap (and ferrule) with the warning in white lettering. A drug shortage for one of the products led to a switch to a different manufacturer; after the switch, both of the neuromuscular blocking agents had a red cap with the warning in white print. The product change reduced the differentiation cues between the closure systems to which end users had become accustomed, potentially contributing to the near miss. Fortunately, the practitioner noticed that the drug name on the label did not match the intended drug, and the error did not reach the patient.

Review of International Recommendations

In 2008, the United States Pharmacopeia (USP) began to require a warning on the vial closures of neuromuscular blocking agents. The USP specified that the warning should be in black or white print (whichever would provide the greatest colour contrast with the ferrule or cap colour) but did not specify the cap or ferrule colour.[10] The USP requirement allows the cap to be transparent, allowing visualization of a warning printed on the ferrule.[10] Another USP standard that came into effect in 2013 restricts cautionary statements on the cap or ferrule of a drug vial to those intended to prevent imminent life-threatening situations.[11] If the medication does not need a cautionary statement, this area of the vial must remain blank, so that doctors, nurses, pharmacists, and other healthcare practitioners are more likely to see and act on any labelling statements that do appear. Manufacturers using USP standards must provide a rationale if they wish to place a cautionary statement on the closure of a medication container.

Updated Recommendations

Since the collaborative meeting in 2006, there has been a move toward use of a warning statement on the ferrule and/or cap of neuromuscular blocking agents, to allow them to be differentiated from other medications.

Recognizing the opportunity for continuous improvement and the need to sustain improvements already achieved, ISMP Canada is updating its recommendations for the ideal features to help differentiate neuromuscular blocking agents from all other drugs:

- At a minimum, adhere to the USP standard.[10, 11]
- Consider‡ using a red ferrule with white lettering: "Paralyzing Agent" or "Warning: Paralyzing Agent".
- Consider‡ using a red cap with white lettering: "Paralyzing Agent" or "Warning: Paralyzing Agent". Alternatively, use a clear cap to allow visualization of the ferrule and its warning.
- Include a prominent warning (e.g., white lettering on a red background) on the main panel of the inner and outer package label: "Paralyzing Agent" or "Warning: Paralyzing Agent".
- Limit the use of warnings on caps and ferrules to those intended to prevent imminent life-threatening situations (in accordance with USP standards).[11]
- Limit the use of a warning in white lettering on a red cap and/or ferrule to neuromuscular blocking agents.

‡ Some neuromuscular blocking agents do not have a red cap and a red ferrule. These agents may be well established and familiar to end users, and therefore any change to the colour needs to be carefully considered.

- Consider providing a peel-off label, using the colour scheme and content recognized by the Canadian Standards Association and the International Organization for Standardization,[12] which align with guidelines from the CAS[13] and the ASA.[14]
- Include automated identification (e.g., a bar code) on the label.
- Develop a universal symbol for neuromuscular blocking agents intended for global use (placement of this symbol [e.g., on the label] remains to be determined).
- Integrate these recommendations into operating manuals, so that future changes to products do not inadvertently reverse a key step forward. Organizational memory will be important until regulatory guidance is implemented.

Conclusion

Canadian manufacturers are to be commended for voluntarily implementing safety recommendations for labelling and packaging of neuromuscular blocking agents. Healthcare facilities are to be commended for using multiple strategies to support the safe use of neuromuscular blocking agents, such as restricting their availability to specialty care areas (e.g., operating room, critical care unit) and creating safer storage systems. Facility-based strategies, in combination with manufacturer labelling and packaging, continue to be crucial elements in preventing the accidental administration of a neuromuscular blocking agent.

ISMP Canada is now working with Health Canada to develop a labelling and packaging guide. It is anticipated that this guide will include recommendations for neuromuscular blocking agents to help sustain progress to date.

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Development of a National Medication Safety Action Plan for Canada

The Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI) hosted an invitational summit in Toronto on June 18, 2014, to support the development of a National Medication Safety Action Plan. Participants included representatives from patient and family-led organizations, along with leaders and decision-makers from provincial and national health ministries, patient safety and quality organizations, and national healthcare professional associations.

The summit was convened to develop a roadmap for a national medication safety strategy that would support and accelerate the adoption of safe medication practices across the Canadian healthcare system. Specific goals of the meeting were to identify emerging issues in medication safety, to determine the key themes and actions required for a national action plan, and to secure commitments from participants to support and advance the plan.

This segment of the bulletin describes a recent SafeMedicationUse.ca publication from ISMP Canada's Consumer Program.

June 2014 - Newsletter:

Ten-Fold Dose Errors

SafeMedicationUse.ca received a report about a consumer who was mistakenly dispensed 10 times the amount of drug that the doctor had prescribed. The consumer was prescribed the anti-rejection drug tacrolimus 0.5 mg by the physician, but received tacrolimus 5 mg capsules instead. The consumer experienced substantial weight loss and felt progressively worse after taking the incorrect dose of tacrolimus for 4 weeks.

The SafeMedicationUse.ca newsletter asks consumers to take an active role in their health by taking careful note of the appearance of each of their medicines. If any medication looks different from what is expected, consumers are encouraged to speak with a member of the pharmacy team. To further support this process, practitioners are advised to open the medicine container and review the appearance of each medicine with the consumer during counselling.

For additional recommendations for both consumers and practitioners, read the complete newsletter at:

www.safemedicationuse.ca/newsletter/newsletter_10FoldDoseErrors.html

CMIRPS SCDPIM

Canadian Medication Incident Reporting and Prevention System

Système canadien de déclaration et de prévention des incidents médicamenteux

The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.

HIROC

The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.

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The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada's mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

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