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CMIRPS Canadian Medication Incident Reporting and Prevention System
SCDPIM Système canadien de déclaration et de prévention des incidents médicamenteux

ISMP Canada Safety Bulletin

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Antidotes and Related Agents:
Recognition of Need, Availability, and Effective Use

- *Develop combination order sets that indicate the appropriate antidote (or reversal, neutralizing, decontamination or rescue agent), criteria for use, as well as how to obtain it, when a medication or hazardous material determined to have a high risk for toxic effects is administered.*
- *Work with antidote registries, regional hospital networks and/or poison centres to clearly identify how to promptly access needed agents.*
- *Establish regularly scheduled, facility-wide cycle counts to monitor expiry dates, availability, frequency of use, and adequate inventory levels of all agents stocked locally.*
- *Ensure that key information resources are up-to-date and readily available to support timely and effective use of these agents.*

Antidotes and reversal, neutralizing, decontamination, and rescue agents (referred to collectively as "antidotes" in this bulletin) are medications used to counteract the effects of toxicity caused by a drug overdose or by inadvertent exposure to a medication or hazardous substance, or resulting from a physiological imbalance (e.g., electrolyte abnormality). These medications can be life-saving. However, the ability of an agent to mitigate patient harm depends not only on its pharmacological mechanism of action, but also on its correct and timely administration.[1] ISMP Canada recently received several reports of incidents and near misses involving the use of an antidote. This bulletin highlights 3 key vulnerabilities that compromise the safety and efficacy of antidotes and suggests strategies for healthcare organizations to overcome these challenges.

Identifying the Need for Antidotes

To prevent harm to the patient, practitioners must first be able to recognize the risk, signs, and symptoms of toxic effects within the timeframe during which an antidote will be effective. The clinical manifestations of a drug's toxicity may be subtle and nonspecific, and symptoms may resemble the disease state for which the patient is being treated. In some of the reported incidents, the practitioner did not recognize the risk for or overlooked the signs of toxicity. All of these factors can impede prompt diagnosis and can delay treatment.

Incident Example

A patient ingested one dose of hydromorphone instead of hydrocodone following a dispensing error in the community care setting. Although the error was recognized by the pharmacist, the risk for toxic effects from the accidental ingestion was not (hydromorphone is approximately

4 times as potent as the prescribed hydrocodone).[2] The patient went home and was not advised to go to the hospital or to monitor for symptoms requiring intervention with naloxone. Over the next several hours, the patient experienced several adverse effects, including difficulty breathing.

When persons are exposed to a medication or hazardous materials with known toxic effects, proactive assessment for specific (and sometimes subtle) signs and symptoms of the toxicity can assist practitioners in anticipating the need for an antidote and help expedite the necessary subsequent course of action.

Recommendations

- For community practitioners, in cases of medications with a high risk for toxic effects, inform patients about the symptoms indicating toxicity and how to manage these situations (e.g., call the poison control centre, administer naloxone) if they arise. When feasible, consider proactively supplying patients with an antidote (e.g., naloxone kit) if there is a concern for toxicity.
- For healthcare facilities/organizations, develop combination order sets that indicate the appropriate antidote, criteria for use, and where to obtain it when a medication determined to have a high risk for toxic effects is administered.[3] A combination order set (consisting of an order for the high-risk medication and an order for its antidote, if needed) should outline patient monitoring parameters, including clinical signs that would signify the need for antidote administration. Details regarding the need for further assessment should also be included.

Ensuring Availability of Antidotes

The second vulnerability identified from the incident reports was inaccessibility of the required antidote. These agents should be stocked in sufficient quantities, should be stored in close proximity to clinical areas where they might be needed, and should be in-date. Factors that limit the supply of antidotes include cost, infrequent use, poor awareness of availability, and manufacturer shortages.[4]

Incident Example

A patient underwent a procedure that involved the topical application of phenol. Afterward, the patient's skin was cleansed with a clear fluid that was thought to be normal saline. The patient soon complained of a burning sensation in the cleansed area, which led the nurse to realize that the liquid used was actually phenol. A poison centre was contacted, and the area was immediately cleansed with water as directed. The patient suffered a burn for which additional care at a tertiary care centre was required. Following this incident, the facility developed a decontamination procedure, which includes consideration of polyethylene glycol (PEG) 300 or 400 as a decontamination agent as suggested by safety data sheets.[5,6]

Recommendations

- Emergency departments should stock minimum quantities of antidotes based on expert recommendations (e.g., provincial poison centre) and following a local vulnerability assessment.
- For other patient care areas, assess the types of medications or hazardous materials commonly used, as well as their relative potential to cause toxic effects, to inform a site-specific antidote inventory based on existing local, regional or provincial recommendations and repositories.
- Store antidotes close to care areas where they are expected to be used, and stock sufficient quantities. If agents will be accessed through an antidote network or other sharing arrangements, ensure that mechanisms are in place to obtain them promptly.
- Establish regularly scheduled, facility-wide cycle counts for these agents to monitor expiry dates, availability, frequency of use, and adequacy of stock levels. Work with established antidote, poison centre networks across the country and/or neighbouring hospitals to ensure adequate stocking and/or sourcing of antidotes. Most poison centres have online antidote stocking recommendations,[7-10] while some provinces have higher health authority antidote stocking recommendations or policies.[11]

The Canadian Antidote Registry is under development.[11] Currently, the registry is being piloted in Quebec. Once fully operational, healthcare

organizations from other provinces and territories will be invited to join and utilize the tools available. It is anticipated that users of the registry will be able to receive support from an antidote coordinator and the provincial poison centre to improve prompt access to needed agents in their jurisdiction.

Knowing How to Use Antidotes

The third and final error-prone step in the process of reversing the toxic effects of medications or hazardous substances is the timely and correct administration of the antidote. Correct administration of an antidote also requires an understanding of the physical, chemical, and physiological characteristics of the toxic substance (e.g., solubility, formulation, half-life), to ensure appropriate and adequate patient monitoring. For example, it may be necessary to administer multiple naloxone doses to reverse the toxic effects of a long-acting opioid. Knowledge deficits, together with infrequent need for and limited practitioner experience with most antidotes, contribute to gaps in appropriate patient care, as well as an increased likelihood of medication incidents.

> ***Incident Example***
>
> A calcium infusion was ordered for a patient with suspected mixed overdose of beta-blocker/calcium channel blocker. Healthcare staff consulted a poison centre to determine the appropriate dose and preparation instructions for the calcium infusion. However, the units of measure provided by the resource (mL/kg/h) differed from those on the product label (10% or 100 mg/mL), and instructions on how to prepare the dose were not provided. The differing units and absence of instructions caused confusion, which in turn led to incorrect calculations. As a result, the patient received only 1/100th of the dose of calcium needed to treat the overdose.

Healthcare providers should seek assistance from provincial poison centres when in need of information to administer an antidote. As well, written resources that clearly guide practitioners with key information, including indications, dosing, monitoring parameters, and preparation instructions, should be readily available onsite. The Canadian Antidote Guide in Acute Care Toxicology, a new resource, is now available online at https://www.ciusss-capitalenationale.gouv.qc.ca/antidotes?lang=en and will become available shortly through mobile apps.[12] This complimentary bilingual resource will be continually updated as the scientific evidence evolves. The guide can be used in conjunction with the advice given by the provincial poison centre, although there may be provincial variations in some recommendations.

Recommendations

- Incorporate patient monitoring guidelines as part of the order set for each antidote.
- Ensure that contact information for the provincial poison centre is readily accessible to practitioners.
- To support timely and effective use of antidotes, make key resources regarding their indications, dosing, monitoring parameters and preparation instructions readily available (e.g., online, via mobile app).[3]

Conclusion

Analysis of recent medication incident reports associated with the use of antidotes illustrates some current practice vulnerabilities that may hinder the optimal use of these agents. Early recognition of toxic symptoms, suitable inventory of antidotes, and availability of information resources to guide timely use and essential monitoring are prerequisites to the effective treatment of patients requiring antidotes. Practitioners in all healthcare settings are encouraged to review the recommendations offered in this bulletin to ensure that access to all types of antidotes is readily available and that these agents are administered and monitored appropriately.

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

March 2018 - Newsletter:

Do NOT Delay Starting Certain Medications

SafeMedicationUse.ca

SafeMedicationUse.ca received a report about a consumer who left the hospital with a prescription for an anticoagulant. However, his pharmacy was unable to fill the prescription for a few days, so he could not start the medication right away. While waiting for the medication to become available, the consumer's leg became swollen—possibly because of the delay in therapy. Fortunately, the consumer did not suffer any long-term harm.

This newsletter alerted consumers that some medications, such as anticoagulants, should be started right away, because a delayed start could lead to harm.

Tips for Practitioners

- All healthcare providers should alert consumers about any medications that should not be delayed and the consequences of a late start.
- If a pharmacy cannot dispense an urgent medication within an appropriate timeframe (e.g., because of limited access or technical issues), the pharmacy should attempt to arrange for the medication to be made available to the consumer some other way (e.g., by obtaining the medication from another pharmacy or by referring the patient to another pharmacy).

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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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