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ISMP Canada Safety Bulletin

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Epinephrine Use for Anaphylaxis – A Multi-Incident Analysis

Hospitals:

- Consider the use of epinephrine auto-injectors or prepared anaphylaxis kits with appropriate labelling to support correct epinephrine dose and route of administration.
- Provide regular training using mock scenarios so that healthcare providers maintain a high degree of competency in the accurate preparation of an appropriate dose using the correct concentration and safe administration of epinephrine via the appropriate site.

Prescribers and pharmacists:

• For pediatric prescriptions, weigh the child in kilograms at each encounter to ensure that the correct strength of epinephrine auto-injector (adult versus pediatric) is being prescribed.

Community pharmacy staff and managers:

 Review dispensary processes related to return of products to stock and methods of verifying expiry dates.

Anaphylaxis is an acute, life-threatening, systemic allergic reaction associated with various triggers, clinical presentations, and levels of severity.¹ Epinephrine is the only life-saving drug used to treat a person experiencing anaphylaxis. Recent epidemiological studies indicate that the prevalence of anaphylaxis is increasing.^{2,3} The Canadian Institute for Health Information (CIHI) reported that from 2006 to 2015, there was a 64% increase in the number of individuals for whom an epinephrine auto-injector was dispensed, and children were the top consumers.³ Because of the increased use of epinephrine, there is a need to better understand the potential risks and problems associated with use of this high-alert medication.

A multi-incident analysis was conducted to identify factors contributing to errors when epinephrine was used for the treatment of anaphylaxis and to suggest strategies to prevent or minimize potential harm when epinephrine is used for this indication.

Methodology

Reports of medication incidents related to epinephrine were extracted from voluntary reports* submitted to three ISMP Canada incident reporting databases (Individual Practitioner Reporting, Community Pharmacy Incident Reporting, and Consumer Reporting), and the National System for Incident Reporting† (NSIR) between April 2010 and October 2016.

The following medication names were used as search terms: "epinephrine", "adrenalin", "Epipen", "Epi-pen", "Twinject", "Allerject", "Anakit", and "Ana-kit". Almost 200 incidents were identified in

* It is recognized that it is not possible to infer or project the probability of incidents on the basis of voluntary reporting systems.
† The NSIR, provided 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

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the ISMP Canada databases, and 44 were found in the NSIR database. Incidents not related to epinephrine use in anaphylaxis were excluded, which left 146 incidents in the final analysis. The analysis was conducted according to the methodology for multi-incident analysis outlined in the Canadian Incident Analysis Framework.⁴

Quantitative Findings

The majority of the incidents were reported to the ISMP Canada databases. Of these reports, wrong dose errors (e.g., Epipen Jr. given to a child weighing 30 kg or greater) comprised the most commonly reported incident type, followed by products being prepared for the wrong patient and wrong quantity dispensed. Over 80% of incidents were caught before the error reached the patient.

Of the incidents reported to ISMP Canada databases, 3.5% of cases resulted in harm to the patient. The most common type of harm incident resulted from the intravenous administration of epinephrine – either due to selection of the incorrect route when ordering epinephrine treatment, or wrong-route administration (i.e., IM route ordered, but administered IV). All of the wrong-route incidents resulted in harm to the patients.

Qualitative Findings

Analysis revealed 3 main themes, each with multiple associated subthemes (see Figure 1). This bulletin describes each of the main themes and selected subthemes, along with illustrative examples.

THEME: Knowledge Gaps

Subtheme: Wrong route

For anaphylaxis, epinephrine should be administered intramuscularly (IM); the intravenous (IV) route of administration should be reserved for patients who have not responded to IM doses and those experiencing severe physiologic compromise.⁵ Wrong-route administration of epinephrine has been previously reported in an ISMP Canada Safety Bulletin⁶ and elsewhere in the literature.^{7,8} In a review of more than 600 cases reported to the Pennsylvania Patient Safety Reporting System, wrong-route errors involving IV administration were responsible for 25.4% of all epinephrine adverse events and 63.3% of the harmful events.⁸ Several studies have attributed this error to a lack of adequate education of healthcare professionals.⁹

Incident Example

A consumer reported receiving epinephrine by the IV route, rather than the recommended IM route, as treatment for a mild allergic reaction while in the emergency room. She experienced convulsions, angina, tachycardia, a severe headache, and difficulty breathing. As a result, intervention and additional monitoring were required.

Clinical areas and teams that need to treat anaphylaxis should receive regular training, including holding mock scenarios. Although not identified as an issue in this analysis, consider extending this recommendation to medical office staff.⁵

Figure 1. Main themes from the qualitative analysis



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Subtheme: Wrong dose

Incorrect dose incidents with epinephrine have occurred in both acute care and community settings. One potential contributing factor has been use of the historical ratio expressions (1:1000, 1:10,000) for strength. In 2016, because of an ongoing stream of serious errors related to confusion in understanding ratio expressions, the United States Pharmacopoeia eliminated ratio expressions on single-entity drug products such as epinephrine.¹⁰ Therefore, 1:1000 epinephrine products are now labelled as 1 mg/mL, while epinephrine 1:10,000 for IV injection is labelled as 0.1 mg/mL. A second potential factor contributing to incorrect dosing is the need for a dose calculation in the pediatric age group. The epinephrine dose for anaphylaxis in pediatrics must be calculated according to the patient's weight (0.01 mg/kg, up to a maximum of 0.5 mg);¹¹ this calculation step represents a risk for error.

Incident Example

An infant weighing 6.5 kg was treated with epinephrine in the emergency room for a possible anaphylactic reaction. The calculated dose, based on 0.01 mg/kg, should have been 0.065 mg IM; however, the infant received 0.65 mg IM, 10 times the intended dose. The baby became lethargic, pale, and cyanotic, and experienced cardiac ischemia. The child required an urgent transfer to a specialized pediatric centre and prolonged monitoring. Fortunately, there were no long-term cardiac effects.

Wrong-dose and/or wrong-route errors have occurred when adults with anaphylaxis have been treated with the cardiac resuscitation dose (1 mg IV) rather than the recommended anaphylaxis dose (0.2 to 0.5 mg IM⁵).⁶ These errors likely result from the comprehensive life-saving training required by emergency practitioners, who subsequently become more familiar with the cardiac resuscitation than the anaphylaxis treatment dose of epinephrine in adults.

In the current multi-incident analysis, dose-related incidents in the community resulted when prescriptions were renewed for the pediatric auto-injector when, in fact, the child's current weight would require that the "adult" device be dispensed. Because each device is designed to supply only a single, measured dose when activated, choosing the correct one is essential.

Practice Tip:

Pediatric patients are at particular risk from confusion and errors related to dose calculation. Verification of the child's weight before prescribing, dispensing, and administering epinephrine is an important measure to avoid a dosing error.

Pediatric devices contain an epinephrine dose appropriate for a child weighing between 15 to 30 kg (i.e., 0.15 mg); the 'adult' device delivers 0.3 mg and is recommended for children (and adults) weighing 30 kg or more.¹² In several of the incidents analyzed, verification of the child's weight at the pharmacy allowed interception and correction of dosing errors before they reached the patient. Current guidelines for pediatric use of epinephrine suggest that "giving a dose that is slightly above the ideal dose appears to be a better option than giving a dose that is below the recommended dose," given that underdosing may not be effective to treat anaphylaxis.5 So for children who weigh close to 30 kg, practitioners may choose to prescribe the 'adult' device, taking into account previous reactions and individual risk factors.

Previous recommendations and actions taken by facilities to support the correct dose and route of epinephrine administration in anaphylaxis are outlined in Box 1.

Subtheme: Insufficient quantity

The subtheme of knowledge gaps regarding the quantity to be prescribed was apparent in reports in which too few devices were prescribed for emergency treatment of anaphylaxis in the community. Current guidelines recommend that each patient be given 2 devices at a time, because up to 30% of anaphylaxis reactions require the administration of more than 1 dose of epinephrine.⁵ In particular, for children at risk of anaphylaxis, 1 device should be kept at school and 1 device always with the child, either on their person or with a caregiver.

Box 1. Measures taken to support correct dose and route for epinephrine injection⁶

- provision of epinephrine auto-injectors or prepackaged epinephrine for IM use, together with instructions for IM use, at the point of care
- written reminders (e.g., a dosing chart) in all locations where epinephrine is stocked
- separated storage of epinephrine products used for the treatment of anaphylaxis from those epinephrine products intended for resuscitation carts
- use of preprinted order sets for the management of anaphylaxis
- minimize use of verbal orders; if verbal orders are needed in emergency situations, use a "repeat back" or "closed loop communication" strategy to confirm drug name, dose, and route of administration

Subtheme: Erroneous deployment

Accidental or erroneous deployment of the auto-injector represents the last knowledge gap subtheme. Epinephrine auto-injectors are commonly carried by patients for self-administration should they experience symptoms of anaphylaxis; however, these devices can be difficult to use if patients or caregivers are unfamiliar with them. For example, accidental injection of epinephrine into the thumb of the person administering epinephrine has occurred, likely as a result of a knowledge gap about device deployment. This type of incident reinforces the need for practitioners to regularly confirm patients' and caregivers' understanding of the proper and safe use of these devices, both for therapeutic effect and to avoid injuries. Practitioners are encouraged to use a "teach back" method to confirm patient understanding.

THEME: Process Problems

Several reports described patients receiving an auto-injector device labelled with another person's

name. This situation can result when a prescription prepared for a specific patient is returned to stock in the pharmacy, because the patient either does not pick up the prescription or declines to purchase it because of cost. These types of incidents highlight problems in 2 community pharmacy processes—the process to return a product to stock, and the dispensing process for labelling and verification of both the outer packaging and the device inside the box.

Incident Example

An Epi-Pen was dispensed for a child. The caregiver at school noticed that the device was labelled with someone else's name, even though the outer box was labelled correctly. The school notified the parents, who contacted the pharmacy. The pharmacy determined that the device provided for the child had previously been returned to stock without removal of the old label.

Practice Tip:

Pharmacy staff is encouraged to review their processes for:

- returning devices to stock;
- verifying labelling of the outer packaging and device; and
- checking expiry dates at the time of dispensing.

Other pharmacy processes deemed problematic were dispensing expired epinephrine auto-injectors and failure to enter refills on prescription order entry.

THEME: Product Flaws

Three brands of epinephrine auto-injector—EpiPen, Twinject, and Allerject—were available in Canada during the period from which the data set was extracted. The latter 2 brands are no longer marketed. Common look-alike / sound-alike (LASA) incidents were reported when prescribers confused Twinject with Twinrix (hepatitis A and B vaccine). Fortunately, these errors were caught by community pharmacists during patient counselling.

Incident Example

A physician wrote a prescription for "Twinrix" with 6 refills. The pharmacist clarified with both the patient and the physician that the desired medication was Twinject.

LASA issues were also reported from the hospital setting, where ePHEDrine was mistaken for epinephrine when medication vials were being re-stocked.

Practice Tip:

Recommendations to prevent mix-ups between epinephrine and ePHEDrine include use of TALLman lettering throughout the medication-use system and avoidance of side-by-side storage of the 2 products.¹³

The following manufacturing deficits (which have since been addressed by the manufacturers), among others, were reported in the analysis:

- placement of the wrong bar code on an epinephrine product
- use of the same Drug Identification Number (DIN; used for verification in pharmacy processes) for both English and French Allerject products, which led to provision of a voice-enabled device (intended to walk the user through the administration process) in an incorrect language
- confusion in interpreting ratio expressions for epinephrine concentration appearing on labels

Conclusion

Epinephrine is a critical, life-saving treatment for anaphylaxis that can be administered by both healthcare professionals and the general public. Because anaphylaxis can occur anywhere, workers in all healthcare sectors are encouraged to review the information identified in this analysis and implement the recommendations in this bulletin to optimize the safe and correct use of epinephrine.

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References

- 1. Wood RA, Camargo CA Jr, Lieberman P, Sampson HA, Schwartz LB, Zitt M, et al. Anaphylaxis in America: the prevalence and characteristics of anaphylaxis in the United States. J Allergy Clin Immunol. 2014;133(2):461-467.
- 2. Tejedor-Alonso MA, Moro Moro M, Múgica-García M. Epidemiology of anaphylaxis: contributions from the last 10 years. J Investig Allergol Clin Immunol. 2015;25(3):163-175.
- 3. Anaphylaxis and allergy in the emergency department.Ottawa (ON): Canadian Institute for Health Information; 2015 Sep 10 [cited 2017 Mar 20]. Available from: https://secure.cihi.ca/free_products/Anaphylaxis_Infosheet_en.pdf
- 4. Incident Analysis Collaborating Parties. Canadian incident analysis framework. Edmonton (AB): Canadian Patient Safety Institute; 2012 [cited 2016 Nov 14]. Incident Analysis Collaborating Parties are Canadian Patient Safety Institute (CPSI), Institute for Safe Medication Practices Canada, Saskatchewan Health, Patients for Patient Safety Canada (a patient-led program of CPSI), Paula Beard, Carolyn E. Hoffman, and Micheline Ste-Marie. Available from: http://www.patientsafetyinstitute.ca/en/toolsResources/Incident Analysis/Documents/Canadian%20Incident%20Analysis%20Framework.PDF
- 5. Lieberman P, Nicklas RA, Randolph C, Oppenheimer J, Bernstein D, Ellis A et al. Anaphylaxis—a practice parameter update 2015. Ann Allergy Asthma Immunol. 2015;115(5):341-384.
- 6. Alert: wrong route incidents with epinephrine. ISMP Canada Saf Bull 2014 [cited 2017 Feb 2];14(4):1-3. Available from: https://www.ismp-canada.org/download/safetyBulletins/2014/ISMPCSB2014-4_Epinephrine.pdf
- Campbell RL, Bellolio MF, Knutson BD, Bellamkonda VR, Fedko MG, Nestler DM, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. J Allergy Clin Immunol Pract. 2015;3(1):76-80.
- 8. An update on the "Epi" demic: events involving EPINEPHrine. Pa Patient Saf Advis. 2009;6(3):102-103.
- 9. Cohen MB, Saunders SS, Wise SK, Nassif S, Platt MP. Pitfalls in the use of epinephrine for anaphylaxis: patient and provider opportunities for improvement. Int Forum Allergy Rhinol. 2017;7(3):276-286.
- 10. Changes in expression of strength: elimination of ratios on single-entity injectable products. ISMP Can Saf Bull 2016 [cited 2017 Feb 12]; 16(2):1-3. Available from:

https://www.ismp-canada.org/download/safetyBulletins/2016/ISMPCSB2016-02_ChangesInExpressionStrength.pdf

- 11. Cheng A, Canadian Pediatric Society (Acute Care Committee). Emergency treatment of anaphylaxis in infants and children [position statement]. Paediatr Child Health 2011 [reaffirmed 2016 Feb 1];16(1):35-40.
- 12. EpiPen/EpiPen Jr monograph. In: e-CPS. Ottawa (ON): Canadian Pharmacists Association; [cited 2017 May 14]. Available from: https://www.e-therapeutics.ca/search [Subscription required to access content].
- 13. Risk of mix-ups between ephedrine and epinephrine. ISMP Canada Saf Bull 2007 [cited 2017 Feb 2];7(2):1-3. Available from: https://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2007-02Ephedrine.pdf

Health Canada Seeking Feedback on Mandatory Reporting of Serious Adverse Drug Reactions and Medical Device Incidents

In late June 2017, Health Canada released the consultation paper "Mandatory Reporting of Serious Adverse Drug Reactions and Medical Device Incidents by Health Care Institutions" (https://www.canada.ca/en/health-canada/programs/consultation-reporting-serious-adverse-drug-reactions-medical-device-incidents.html) in support of the Protecting Canadians from Unsafe Drugs Act (Vanessa's Law). The paper presents proposals for comment, provides alternative options and poses a series of questions.

Health Canada is seeking feedback on the consultation paper. The feedback will provide a foundation for the development of proposed regulations. The deadline for submitting feedback is August 11, 2017.

Health Canada will be hosting a webinar on Tuesday, July 18, 2017, at 12:30 pm EDT to share information on the proposals within the consultation paper. Questions may be sent in advance to be answered by Health Canada during the webinar. Those interested in participating in the webinar should register by Wednesday, July 12, 2017, by sending their name and email address to: MHPD-stakeholders_intervenants-DPSC@hc-sc.gc.ca

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

June 2017 Newsletter:

Losing Medications Can Spoil Your Vacation

SafeMedicationUse.ca received a report from a consumer who lost his medications while on vacation. The newsletter provided recommendations for consumers on how to prevent the loss of medications while travelling, including the best ways to store medications during transit. Advice on dealing with lost or forgotten medications while away from home was also shared.

Tips for Practitioners:

- Give each of your patients a medication list, and help them to update it regularly. Updating this list is especially important before vacations and any other extended travel.
- Explain to your patients the purpose of each medication and how it should be taken. This information will be helpful if new prescriptions are needed in another country.

For more information, read the full newsletter: https://safemedicationuse.ca/newsletter/newsletter_LosingMeds.html

Consumers Can Help Prevent Harmful Medication Incidents

SafeMedicationUse.ca

Updated Labelling and Packaging Guide Will Make It Easier for Canadians to Use Health Products Safely

A newly revised guide released by Health Canada is expected to improve the safe use of nonprescription and natural health products by making labels easier for consumers to read and understand. In particular, the guide aims to ensure the prominence of critical information on product labels.

The updated guide incorporates requirements from Canada's Plain Language Labelling Regulations, such as the Drug Facts table for nonprescription drugs. Regulated parties must be in compliance as of June 30, 2021.

For more information, the revised Good Label and Package Practices Guide for Non-prescription Drugs and Natural Health Products is available at: https://www.canada.ca/en/health-canada/services/ drugs-health-products/reports-publications/medeffect-canada/good-label-package-practices-guide-non-prescription-drugs-natural-health-products.html

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Canadian Medication Incident Reporting and Prevention System 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.



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.



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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