

ISMP Canada Safety Bulletin

Medication Incidents Involving Digoxin Leading to Harm, Including Death

ISMP Canada has received a total of 414 reports involving digoxin since 2001. In total, 18 of these incidents have been reported to be associated with harm (n = 11) or death (n = 7). This safety bulletin is intended to remind Canadian healthcare professionals about the dangers of errors with digoxin, one of the oldest known cardiac drugs.

Example Incident

A patient received a prescription for digoxin 0.25 mg to be taken once daily. At the pharmacy, both the technician and the pharmacist misread the numeral “2” as “7” and therefore misinterpreted the prescription as “digoxin 0.75 mg po daily”. When a drug information reference was consulted to verify appropriateness of the dose, the dosage used in “rapid digitalization” was misinterpreted as an appropriate daily dose for digoxin. Several days later, after taking daily doses of 0.75 mg, the patient experienced nausea and dizziness, and admission to hospital was required.

Overview of Digoxin Incidents Reported to ISMP Canada

When the reports of harm and death were analyzed further, 4 types of errors were identified: incorrect dose (n = 8), omission of a dose (n = 4), incorrect drug (n = 2), and other (n = 4) (see Table 1). Notably, the category with the highest

overall number of incidents causing harm or death—incorrect dose—was also the category with the highest number of deaths: 6 of the 7 reported deaths were related to an incorrect dose.

Five of the deaths involved incidents with oral digoxin, and the other 2 involved incidents with intravenous digoxin. Two of the deaths were associated with incidents in the community, and the other 5 with incidents in the hospital setting.

Background Information about Digoxin

Digoxin is a digitalis glycoside used to treat congestive heart failure and to control the heart rate in atrial fibrillation.¹⁻⁷ It is available in an injectable formulation, as well as in liquid and tablet formulations for oral administration. Digoxin tablets are available in 0.0625 mg, 0.125 mg, and 0.25 mg strengths.¹

Digoxin has a narrow therapeutic window (the difference between an effective dose and a toxic dose).^{1,8} It is excreted primarily through the kidneys, and elderly patients in particular may be at higher risk of experiencing toxic effects of digoxin secondary to age-related renal impairment.^{1,8} A number of medications, herbal products, and other agents can affect serum levels of digoxin.^{1,8}

Table 1: Types of Medication Incidents Involving Digoxin Reported as Causing Harm to Patients*

Type of Error	Total No. of Incident Reports	Category of Harm [†] ; No. of Incident Reports with Harm		
		Mild to Moderate (NCC MERP Category E or F)	Severe (NCC MERP Category G or H)	Death (NCC MERP Category I)
Incorrect dose	96	2	0	6
Omission of dose	177	3	0	1
Incorrect drug	32	2	0	0
Other	24	3	1	0
Total	329[‡]	10	1	7

*These data come from voluntarily shared reports, and it is therefore impossible to infer or project the probability of specific types of incidents.

[†]Based on NCC MERP (National Coordinating Council for Medication Error Reporting and Prevention) Index for Categorizing Medication Errors (2001). Available from <http://www.nccmerp.org/pdf/indexColor2001-06-12.pdf>

[‡]This total includes reports of all incidents involving 1 of the 4 types of errors identified in the 18 reports of harm. Incident reports involving other types of errors are not included in this table.

The common signs and symptoms of digoxin toxicity include bradycardia (heart rate below 60 beats per minute), gastrointestinal problems (e.g., diarrhea, loss of appetite, nausea, and vomiting), headache, and visual disturbances (e.g., flashing lights, halo, and impairment of green–yellow perception). Serious adverse effects include cardiac dysrhythmia, which can lead to death.^{1,8}

Recommendations

The following recommendations are intended to minimize the potential for digoxin dosing errors that can lead to toxic effects:

- Computer order entry systems should have built-in alerts to warn practitioners of daily digoxin dosages that are outside normal limits. For patients with renal impairment, the dose should be reduced substantially.^{1,4,8,9}
- Order entry systems should also be tested to ensure that appropriate alerts are provided for drug interactions with digoxin.
- Monitoring is crucial in preventing digoxin toxicity. For example, hypokalemia may increase the risk of digoxin toxicity, so initiation of a drug that can cause hypokalemia (e.g., diuretic, corticosteroid, insulin) should

trigger closer monitoring of a patient and his or her digoxin dosage.⁸

- Engaging and educating patients (or families) about their digoxin treatment, including dosage, is paramount. Patients who are undergoing treatment in the community should know how to take their pulse rate, because a low heart rate can be an important indicator of problems before harm occurs. In fact, a pulse rate below 60 beats per minute is sometimes the only sign that a patient's digoxin level is abnormal.

Many hospitals already have safeguards in place for the parenteral and/or pediatric administration of digoxin (e.g., independent double checks) to prevent administration of an incorrect dose. A review of reported incidents with oral digoxin has revealed that incorrect dosing may lead to death after only a few incorrect doses. It is hoped that sharing information about reported incidents will remind practitioners about the dangers of errors with digoxin, and lead to additional system enhancements to ensure its safe use.

Please refer to page 3 for references.

Muscle Relaxant Cyclobenzaprine Ordered as “Cycloprine” and Interpreted as Immunosuppressive Agent Cyclosporine

An order for “cycloprine 10 mg po qhs”, which was intended to refer to the muscle relaxant cyclobenzaprine, was entered into a pharmacy system as “cyclosporine 10 mg po qhs”. Fortunately, the error was caught, and cyclosporine was not dispensed.

Cycloprine is not a generic drug name. The name of the generic drug cyclobenzaprine has been truncated to “cycloprine” in certain brand names (e.g., Riva-Cycloprine).

This term “cycloprine” resembles the drug name cyclosporine. Furthermore, cyclobenzaprine and cyclosporine are both available in a 10 mg dose form.

As noted above, cyclobenzaprine is a muscle relaxant, whereas cyclosporine is an immunosuppressive agent. As such, a mix-up between these 2 drugs could lead to patient harm. Although the incorrect medication did not reach the patient in the case summarized here, the incident became an important impetus for change. ISMP Canada contacted the manufacturers of generic cyclobenzaprine to seek their commitment to change any drug names containing the word “cycloprine”. One manufacturer, Laboratoire Riva Inc., was very receptive to the suggestion and is changing the name of its product. Teva Canada has changed the name of its product in the course of product rebranding (i.e., Novo-Cycloprine has been changed to Teva-Cyclobenzaprine). These newly renamed products will be available once existing stocks are depleted.

ISMP Canada reminds practitioners that removing the prefix (e.g., an abbreviated manufacturer's name) from a brand name to identify the official generic medication name may not always work. During the course of this review, other brand names with truncated versions of the generic drug name were noted. ISMP Canada encourages all manufacturers to avoid using truncated versions of generic drug names within product brand names. As the incident described above illustrates, this practice can lead to confusion and unanticipated look-alike, sound-alike drug names.

Mix-ups Continue between Conventional Amphotericin B and Lipid-Based Amphotericin B

Amphotericin B, a systemic antifungal medication, is not commonly used, and health care practitioners may be unfamiliar with its various formulations and the potential consequences of mix-ups among them. The standard dosing for conventional amphotericin B (brand name Fungizone) is substantially lower than those for the lipid-based formulations (AmBisome, a liposomal formulation, and Abelcet, a lipid complex formulation). **The dosage of conventional amphotericin B (Fungizone) should never exceed 1.5 mg/kg daily.** Higher doses can result in potentially fatal cardiac or respiratory arrest.

An article recently published on this topic in *Dynamics*, the Journal of the Canadian Association of Critical Care Nurses (entitled “*ALERT: Mix-ups between conventional and lipid formulations of amphotericin B can be extremely dangerous*”) provides an overview of incidents involving amphotericin B that have been reported to ISMP Canada. The article includes a description of a recently reported mix-up between the lipid complex formulation amphotericin B (Abelcet) and the conventional amphotericin B formulation (Fungizone), along with suggested strategies to prevent recurrence. This article is available from <http://www.ismp-canada.org/publications.htm>

ISMP Canada thanks the Canadian Association of Critical Care Nurses (www.caccn.ca) for granting permission to share this and other medication safety information with the healthcare community through its *Dynamics* journal.

References

1. Lanoxin. In: Health Canada Drugs Product Database. Ottawa (ON): Health Canada; [cited 2011 Apr 7]. Available from: <http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp> (use search term “digoxin” as active ingredient, and select “Lanoxin”).
2. National Clinic Guideline Centre for Acute and Chronic Conditions. Chronic heart failure: national clinical guideline for diagnosis and management in primary and secondary care. National Institute for Clinical Excellence Guideline No 108. London (UK): Royal College of Physicians; 2010 Aug [cited 2011 Apr 8]. Available from: <http://www.nice.org.uk/nicemedia/live/13099/50514/50514.pdf>
3. Jessup M, Abraham WT, Casey DE, Feldman AM, Francis GS, Ganiats TG, et al.; on behalf of the 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult Writing Committee. 2009 focused update: ACCF/AHA guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2009 [cited 2011 Apr 8];119:1977–2016. Available from: <http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.109.192064>
4. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005 [cited 2011 Apr 7];112:e154-e235. Available from: <http://circ.ahajournals.org/cgi/reprint/112/12/e154>
5. National Collaborating Centre for Chronic Conditions. Atrial fibrillation: national clinical guideline for management in primary and secondary care. National Institute for Clinical Excellence Guideline No 36. London (UK): Royal College of Physicians; 2006 [cited 2011 Apr 8]. Available from: <http://www.nice.org.uk/nicemedia/pdf/cg036fullguideline.pdf>
6. Fuster V, Rydén LE, Cannom DS, Crijns HJ, Curtis AB, Ellenbogen KA, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *Circulation*. 2006 [cited 2011 Apr 7];114:e257-e354. Available from: <http://circ.ahajournals.org/cgi/reprint/114/7/e257>
7. Wann LS, Curtis AB, January CT, Ellenbogen KA, Lowe JE, Estes NAM 3rd, et al. ; on behalf of the 2006 ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation Writing Committee. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2011 [cited 2011 Apr 7];123:104–123. Available from: <http://circ.ahajournals.org/cgi/reprint/123/1/104>
8. Vivo RP, Krim SR, Perez J, Inklab M, Tenner T, Hodgson J. Digoxin: current use and approach to toxicity. *Am J Med Sc*. 2008;336(5):423-428.
9. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean R, Beers MH. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med*. 2003 [cited 2011 Apr 7];163:2716-2724. Available from: <http://geriatrics.uthscsa.edu/tools/Beers%20Criteria.pdf>

©2011 Institute for Safe Medication Practices Canada. Permission is granted to subscribers to use material from the ISMP Canada Safety Bulletin for in-house newsletters or other internal communications only. Reproduction by any other process is prohibited without permission from ISMP Canada in writing.

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.

A Key Partner in the Canadian Medication Incident Reporting and Prevention System