Deaths Associated with Medication Incidents: Learning from Collaborative Work with Provincial Offices of the Chief Coroner and Chief Medical Examiner

Background

Each Canadian province and territory has an Office of the Chief Coroner or Chief Medical Examiner responsible for investigating deaths from unexplained, unexpected, or unnatural causes. Within the scope of these investigations are deaths associated with medication incidents. In-depth analysis of information from these cases offers unique opportunities to identify underlying factors and generate recommendations to reduce the chances of similar incidents in the future. ISMP Canada has had a formal collaborative relationship with the Office of the Chief Coroner in one province since 2004, and has worked with other Offices on selected cases. A collaborative medication safety project undertaken with the Offices of the Chief Coroner or Chief Medical Examiner in 4 provinces provided an opportunity to test a coordinated process for analysis of medication incidents from several jurisdictions, and to share learning broadly. This bulletin describes selected findings from the project.

Methods and Findings

An analysis team from ISMP Canada, consisting of 3 pharmacists, a registered nurse, and a physician with experience as a coroner, reviewed 523 death cases (from the years 2007 to 2012) in which a medication incident was potentially associated with the death. Of these, 122 cases were determined to have involved a medication incident and were abstracted into the ISMP Canada database for further analysis. In 115 of the 122 cases analyzed, the medication incident met the criteria for a category I incident (defined as an incident that may have contributed to or resulted in the patient’s death).

Medications Involved

The medication classes most commonly involved in incidents associated with death were opioids, psychotherapeutic agents (e.g., benzodiazepines, antidepressants, neuroleptics), anticoagulants, cardiovascular agents, and insulin (Table 1).

Table 1: Medication classes most commonly involved in incidents associated with death

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>No. (%) of Incidents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of category I cases</td>
<td>115 (100%)</td>
</tr>
<tr>
<td>Opioids</td>
<td>54 (47%)</td>
</tr>
<tr>
<td>Psychotherapeutic agents</td>
<td>28 (24%)</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>24 (21%)</td>
</tr>
<tr>
<td>Cardiovascular agents</td>
<td>11 (10%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>8 (7%)</td>
</tr>
</tbody>
</table>

*Some incidents involved more than one medication class.
The individual medications most frequently involved in medication incidents associated with death included HYDROmorphine, morphine, and warfarin (Table 2).

### Table 2: Medications most frequently involved in incidents associated with death

<table>
<thead>
<tr>
<th>Medication</th>
<th>No. of Cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYDROmorphine</td>
<td>19</td>
</tr>
<tr>
<td>Morphine</td>
<td>13</td>
</tr>
<tr>
<td>Warfarin</td>
<td>11</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>8</td>
</tr>
<tr>
<td>Insulin</td>
<td>8</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>7</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td>4</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>3</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>3</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>3</td>
</tr>
<tr>
<td>Potassium</td>
<td>3</td>
</tr>
<tr>
<td>Tissue plasminogen activator (tPA)</td>
<td>3</td>
</tr>
</tbody>
</table>

*Some incidents involved more than one medication.

Of interest, the top 6 medications associated with harm in incidents voluntarily reported from across the country to ISMP Canada as of July 2013, were (in descending order of frequency) HYDROmorphine, insulin, morphine, heparin, warfarin, and fentanyl.

### Incident Types and Stages of Medication-Use Process

The most common types of incidents associated with death were related to monitoring problems (e.g., monitoring of blood glucose, sedation level, or respiratory rate), followed by incorrect doses and extra doses. Medication incidents associated with death most frequently involved the administration, prescribing and monitoring stages of the medication-use process (more than one stage may have been involved in each incident).

### Discussion

#### Opioids

Given the incidents that have been reported to ISMP Canada and previous collaborative work, it was not surprising to learn that opioids constituted the drug class most frequently associated with medication incidents causing death. Medications in this class can be highly effective for treating pain, but the risk of harm when involved in error makes them high-alert medications.

HYDROmorphine was the opioid medication most frequently involved in these incidents, with morphine, fentanyl, oxycodone, and methadone accounting for the remaining opioids most frequently involved in incidents causing death. Although in some of these cases the exact mechanism of death was not determined during the coroner’s or medical examiner’s investigation, in several others the cause of death was determined to be respiratory arrest or cardiorespiratory arrest directly attributable to opioid toxicity.

Documents from these investigations indicated that in some cases signs and symptoms of opioid overdose were noted by healthcare workers or family members, but tragically these intervention opportunities were not recognized. This finding underscores the importance of monitoring patients during opioid therapy, the value of rescue therapy, and the necessity of educating patients and families on the signs of opioid overdose.

Several deaths were associated with the use of fentanyl patches, including patients receiving the wrong type of patch (e.g., fentanyl instead of nitroglycerin), patients using fentanyl patches concurrently with other potent opioids, and opioid-naïve patients using high-dose fentanyl patches.
Methadone deserves special mention as a medication requiring further examination. Its use is increasing—for management of addiction, for palliative pain control, and for management of complex chronic pain. The unique legal and procedural complexities associated with methadone increase the potential for errors causing harm.

As part of this collaborative project with Canadian coroners’ and medical examiners’ offices, a multi-incident or aggregate analysis of opioid-related incidents was completed. This analysis identified 3 key causes of death associated with opioids: overdoses, overlapping toxicities with other medications, and administration to people who should not have been receiving them. These findings suggest the need to improve the integration of best practices into opioid prescribing. The analysis also revealed knowledge deficits related to the recognition of signs and symptoms of toxicity and appropriate management. Details of this multi-incident analysis will be published in an upcoming ISMP Canada Safety Bulletin.

Learning from review of cases involving opioids informed the development of a consumer-oriented safety video that was produced during the project. The video details the steps consumers can take to avoid being harmed by an opioid-related error and provides information on how to recognize the signs of opioid overdose.

**Psychotherapeutic Medications**

A surprising finding that emerged from this analysis was that psychotherapeutic medications (e.g., benzodiazepines, antidepressants, neuroleptics) constituted the second most common drug class involved in medication incidents associated with death. Furthermore, amitriptyline was one of the top single medications involved in incidents associated with death (accounting for 4 incidents; see Table 2). The frequency of harmful incidents with this class may be related to the increasing use of psychotherapeutic agents in the general population or to their wider use in the management of complex and multifactorial pain syndromes. Given their side effect and adverse effect profiles, these medications have known potential to cause harm, either alone or through interaction with another medication, and the frequency with which these medications were associated with incidents causing death warrants continued attention.

Causes of death associated with the psychotherapeutic class of medications included accidental overdose of antidepressants, interactions between antidepressants and other routinely prescribed medications, multiple-drug toxicity, cardiovascular toxicity, and neuroleptic malignant syndrome. In some cases, the deaths were related to use of multiple drugs with overlapping toxicities or the inappropriate use of these drugs in patients with comorbid conditions.

**Anticoagulants**

Anticoagulants (e.g., warfarin, heparin, low-molecular-weight heparin, thrombolytic drugs) are known high-alert medications. Most causes of death related to this class pertained to hemorrhage (e.g., intracranial, gastrointestinal), concordant with the therapeutic properties of this drug. A number of cases occurred after either a change in a patient’s medication therapy or a transition in care. These 2 scenarios are known to increase the risk of medication error, and the findings of this analysis emphasize the need for appropriate monitoring. In particular, ongoing monitoring of the international normalized ratio (INR) is needed for patients receiving warfarin therapy, especially if there is concurrent use of interacting medications. The lack of such monitoring is a well-known factor contributing to harm associated with this drug, as borne out by several cases in the current analysis.

**Cardiovascular Medications**

Various cardiovascular medications were involved in medication incidents associated with death. Examples of such incidents include an incorrect dose of digoxin prescribed and dispensed (e.g., 1.25 mg instead of 0.125 mg) and administration of cardiovascular medications (e.g., diltiazem, metoprolol) to the incorrect patient.
Causes of death related to cardiovascular medications included drug toxicity and myocardial infarction. A number of deaths were attributable to lethal arrhythmia secondary to drug interactions. These cases highlight the need for improved methods of reviewing potential drug–drug interactions.

Insulin

Eight of the deaths involved patients who were receiving insulin. As expected, the cause of death in insulin-related incidents was hypoglycemia. Identified issues included administration of insulin to the incorrect patient, administration of the incorrect form of insulin (e.g., Humalog instead of Humulin N), failure to adequately monitor blood sugar, unintentional self-administered overdose, and lack of understanding of the mode of action of insulin and associated risks among patients in the community and their caregivers.

Additional Findings of Interest

- Deaths occurring in the community: The majority of incidents associated with death occurred in a regulated healthcare facility (47 in hospitals and 15 in long-term care homes); however, a substantial number occurred in the individual’s home (39) or a supportive housing environment (7). A multi-incident analysis of incidents occurring outside a regulated healthcare environment identified 3 key areas of knowledge deficit: (i) general risks associated with medication use, (ii) signs and symptoms of toxicity, and (iii) awareness of specific risks associated with high-alert medications. Details of this analysis will be shared in an upcoming ISMP Canada Safety Bulletin.

- Therapeutic duplication: In several instances, the patients who died had been receiving more than one medication from the same drug class (for example, lorazepam and temazepam; fentanyl, HYDROMorphone, and codeine; and citalopram and paroxetine). It is well known that the risk of toxicity increases when similar medications are used concurrently, and this finding illustrates the need for new strategies to detect and minimize the inadvertent concurrent usage of similar drugs.

- Fluid management: Fluid management issues were associated with several of the deaths. Fluid and electrolyte management is a common clinical activity, yet it remains a source of healthcare error and poor outcomes. This project highlighted deficiencies in the approach to correcting fluid disturbances and shortcomings in patient monitoring that need to be addressed. Fluid-related deaths reviewed in the course of this work will inform a 2013/14 ISMP Canada project on management of hyponatremia.

Conclusion

As with incidents reported voluntarily to ISMP Canada, it is not possible to infer or predict the probability of specific incidents on the basis of the type of analysis conducted in this collaborative project. However, the findings summarized here support existing knowledge about the need for additional safeguards with high-alert medications. A key area for attention to reduce the potential for catastrophic harm associated with medication incidents is the further development of prescribing and monitoring protocols for high-alert medications in general and opioids in particular. In addition, the prominence of psychotherapeutic agents in this data set warrants further study.

Harmful medication incidents carry a high price tag in terms of real treatment costs, impact on the health of individuals, and erosion of confidence in the healthcare system. Medication incidents that result in or contribute to death clearly represent the gravest concern. Because the causes of most, if not all, harmful medication incidents are multifactorial and system-based, a fatal medication incident that occurs in one jurisdiction is likely to recur in another jurisdiction unless preventive measures are implemented. Healthcare workers are therefore encouraged to report deaths to the coroner or medical examiner in their jurisdiction if a medication error is suspected to have caused or contributed to the death. Reporting these incidents allows for investigations into the contributing factors, which then improves analysis of the events, and subsequently provides opportunities to enhance patient safety by sharing learning.
ISMP Canada has previously worked with coroners and medical examiners in death investigations associated with medication incidents. The opportunity to formally and systematically review 5 years' worth of investigative files and associated case documentation has yielded further insights into these tragic events. It is anticipated that ongoing review and analysis of these data will offer additional understanding of medication incidents and that this knowledge will continue to inform efforts in patient safety.

Acknowledgments

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References

Risk of Look-Alike Arterial Blood Gas Syringes and Parenteral Syringes

ISMP Canada has received a report describing a near-miss incident in which a syringe intended for withdrawal of a sample for arterial blood gas (ABG) testing was nearly used for preparation of a parenteral injection for an infant. A shipment of Smiths Medical 3 mL dry lithium heparinized ABG Luer lock syringes had recently been procured by the hospital where the incident occurred. The similarity in appearance between these ABG syringes and the standard BD 3 mL Luer-Lok and Slip-tip parenteral syringes (see examples in Figures 1 and 2), typically used to prepare injections, was a contributing factor leading to this near-miss incident.

![Figure 1](image1.jpg)  ![Figure 2](image2.jpg)

**Figure 1:** Comparison of syringes in packaging. The Smiths Medical ABG syringe is at the top and BD parenteral syringe at the bottom.

**Figure 2:** Comparison of syringes after removal from packaging. The Smiths Medical ABG syringe is at the top and the BD parenteral syringe at the bottom.

Mistaken use of a heparinized syringe for anything other than its intended purpose can lead to inadvertent exposure to heparin and possible adverse outcomes. Likewise, the incorrect use of a parenteral syringe for withdrawal of an ABG sample could result in failure to procure the appropriate sample. As a result of the near miss, Healthcare Human Factors, a human factors team at the University Health Network, conducted an evaluation of the syringes at their simulation labs in the Centre for Global eHealth Innovation in Toronto. The study was designed to evaluate the safety impact of the new ABG syringe in various high-risk areas of the hospital.

Fourteen representative users participated, performing high-priority tasks to assess the syringes’ safety in the context of use at the hospital where the incident took place. The evaluation assessed participants’ ability to distinguish the heparinized syringe from the non-heparinized parenteral syringe, both before and after removal from packaging, as well as ability to detect when heparinized syringes had been prepared for procedures for which non-heparinized syringes were required.

In most scenarios, users could not distinguish the 3 mL heparinized syringes from the 3 mL non-heparinized parenteral syringes. The packaging, plunger colour, and labelling on the ABG syringes did not clearly differentiate them from non-heparinized parenteral syringes. Errors were observed and perpetuated through various stages of patient care, including at the supply
stocking level and the preparation and administration stages. As a result of the types of errors observed in the simulation sessions, it was concluded that the design of the Smiths Medical 3 mL heparinized syringes posed a significant risk to patient safety if used in care areas where regular, non-heparinized 3 mL parenteral syringes are already in place and commonly used.

The manufacturers and Health Canada have been notified of the problem. This information is being shared to raise awareness about these look-alike syringes, and to encourage other organizations to evaluate the potential for risk at their facilities. Information about the study will be presented in a 1-hour webinar on Wednesday, October 2, 2013 12:00pm EDT. Registration information for this webinar will be available soon.