

Opioid-Related Deaths Associated with Medication Incidents

Findings of a Multi-Incident Analysis

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Prepared by:

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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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Background

Opioids continue to be among the top medication classes associated with harmful incidents voluntarily reported to ISMP Canada. Numerous agencies across Canada, including Health Canada, provincial Ministries of Health, Accreditation Canada, and provincial and territorial Offices of the Chief Coroner and Chief Medical Examiner have recognized the potential problems associated with opioids. As a priority focus of a collaborative project between ISMP Canada and 4 provincial Offices of the Chief Coroner or Chief Medical Examiner,¹ a multi-incident analysis was conducted on medication incidents involving deaths associated with opioids.

Methodology

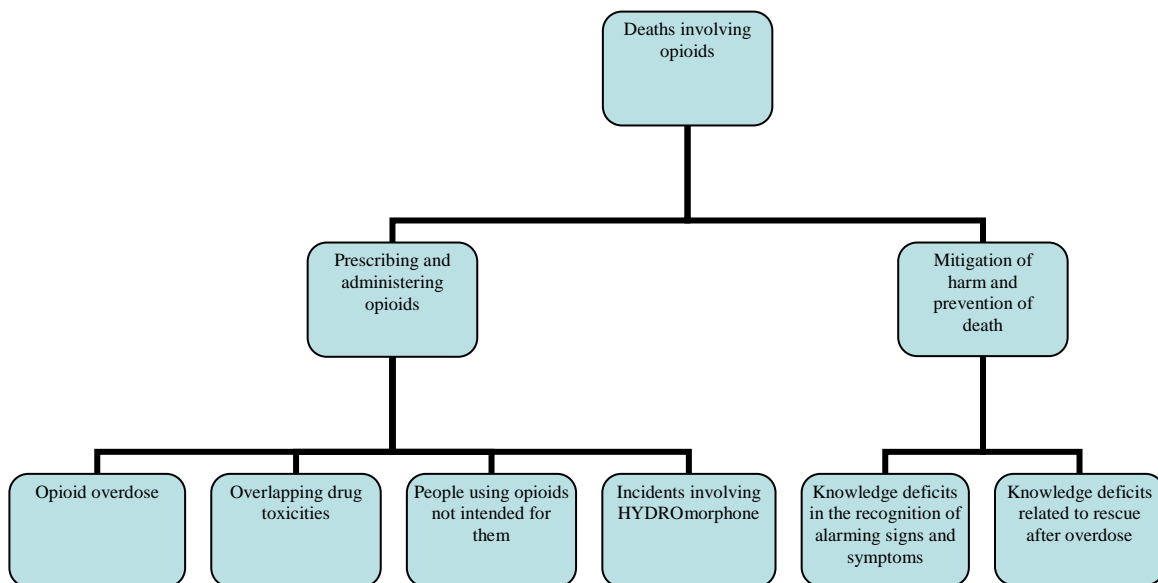
An interdisciplinary team at ISMP Canada reviewed 523 death cases spanning a 6-year period (January 1, 2007, to December 31, 2012) in which a medication incident was potentially associated with the death. Of these, 122 cases were determined to have involved a medication incident and were abstracted into 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 person's death).² Opioids were associated with 54 (47%) of the 115 Category I cases, making opioids the medication class most commonly involved in incidents associated with death.

A subanalysis of 32 of the 54 opioid-related incidents* was conducted using the multi-incident analysis technique outlined in the Canadian Incident Analysis Framework.³

Findings

The qualitative analysis of the 32 opioid-associated incidents generated 2 main themes and 6 subthemes, outlined in Figure 1.

Figure 1: Main themes and subthemes from a multi-incident analysis of deaths involving one or more opioids



* Due to project timing constraints, the subanalysis was conducted on cases from 2 of the 4 participating provinces.

Main theme: Prescribing and administering opioids

An increased understanding of how tragic incidents have occurred often suggests potential areas for system improvement. This multi-incident analysis revealed that most of the opioid-related deaths involved overdoses, overlapping drug toxicities, administration of opioids to people who should not have received them, and use of HYDROmorphone.

Subtheme: Opioid overdose

Analysis of the opioid overdose incidents revealed many situations in which opioids were prescribed, dispensed, or administered at doses that resulted in toxic effects. The following contributing factors were identified:

- opioid initiation at an inappropriately high dose
- failure to discontinue previous opioid orders
- incorrect pump programming
- inappropriate manipulation of available dosage forms (e.g., crushing long-acting formulations)
- routine administration of “as needed” doses

Incident example

A medication order for an elderly patient was changed from morphine to HYDROmorphone. However, the morphine was not discontinued, and both medications were given, which led to opioid toxicity and death.

Subtheme: Overlapping drug toxicities

In many instances, the decedents were taking multiple medications (both opioid and non-opioid) with similar toxicity profiles, which increased the risk of overlapping toxicities. In some instances, comorbid disease states (e.g., kidney or liver insufficiency) exacerbated the toxicities by reducing the clearance or metabolism of medications.

Incident example

An adult was found deceased at home. At the time of death, the person had been taking many medications, including the following central nervous system (CNS) agents: acetaminophen-codeine, bromazepam, chlorpheniramine, diazepam, nortriptyline, oxycodone, quetiapine, temazepam, and venlafaxine. Post-mortem toxicology investigations identified a potentially lethal concentration of oxycodone and the presence of several other drugs. The coroner concluded that although, individually, the levels of these other drugs were not potentially lethal, the combined effect of the medications would be associated with significant CNS depression.

In the incident example described, a comprehensive medication review by a pharmacist or other healthcare provider might have identified the potential harm of overlapping toxicities and allowed steps to be taken toward a safer and more effective medication regimen.

Subtheme: People using opioids not intended for them

Severe patient harm, including death, can result when opioids are given to people who should not be receiving them, including individuals who inadvertently receive opioids and those who take someone else's opioids purposefully.

Incident example

An individual with chronic pain, who was living at home, did not have a current prescription for opioids but was given a fentanyl patch by a friend. The individual was later found deceased.

Subtheme: Incidents involving HYDROmorphone

HYDROmorphone is well recognized as a high-alert medication. Despite numerous publications describing potential risks and safeguards for this medication,^{4,6} serious incidents continue to occur. More than one-third of the incidents reviewed in this analysis involved HYDROmorphone. The following key issues were identified:

- mix-ups between morphine and HYDROmorphone related to similarities in names and commonly used doses
- use of high-concentration and high-potency formats of HYDROmorphone for administration of small doses

Incident example

An elderly resident was prescribed HYDROmorphone 0.4 mg to be given subcutaneously. The resident was inadvertently given a 4 mg dose and died shortly thereafter. One of the contributing factors identified in an analysis of this death was the use of a 10 mg/mL vial of HYDROmorphone to prepare the dose.

Preparing a 0.4 mg dose from a highly concentrated product requires several steps (including a dilution), a process that increases the likelihood of a dosing error.

Main theme: Mitigation of harm and prevention of death

In many cases, opportunities exist to mitigate harm or prevent death after the occurrence of a medication-related incident. In several of the incidents included in this analysis, knowledge deficits hindered timely recognition of signs of toxicity and limited the opportunities for patient rescue.

Subtheme: Knowledge deficits in the recognition of alarming signs and symptoms

In the cases included in this analysis, caregivers did not always recognize the need for additional monitoring of patients who were receiving opioids. In some cases, the patient or the family expressed concerns about certain signs and symptoms, but healthcare practitioners did not recognize these signs and symptoms as indicative of opioid toxicity.

Incident example

An adult patient receiving palliative care was given subcutaneous morphine in the emergency department for presumed pain. After receiving the dose, the patient became agitated. The healthcare team thought that this agitation indicated continued suffering, and a higher dose of morphine was administered. The patient exhibited further agitation and aggression, and a fentanyl patch was applied. The patient then became confused, with continued agitation, and died shortly after another opioid dose was given.

Subtheme: Knowledge deficits related to rescue after overdose

Naloxone, the antidote for opioid overdose, should be considered for any patient with suspected opioid toxicity.⁷ This multi-incident analysis identified several cases in which naloxone might have been

beneficial but was not given; in other cases, naloxone was administered, but the dose of naloxone and/or the duration of subsequent monitoring were insufficient to prevent death.

Incident example

A hospital inpatient inadvertently ingested methadone intended for another patient. Despite the administration of several doses of naloxone over a 6 hour period, the patient died.

The elimination half-life of methadone is more than 24 hours, much longer than that of naloxone. As a result, prolonged monitoring and repeated doses of naloxone and/or a continuous naloxone infusion are required to counteract an overdose of methadone.

Conclusion

The findings of this multi-incident analysis support previously recommended opioid safety strategies such as use of order sets for prescribing; availability of dosage forms appropriate to the dose ordered; independent double checks for dose calculations, pump programming, and medication administration; predetermined parameters for monitoring with defined triggers for intervention; and clear guidelines for appropriate use of naloxone. Additionally, ongoing efforts are required to educate healthcare providers, patients, and families about the early signs of opioid toxicity.

Healthcare practitioners and organizational leaders in all care settings where opioids are used are encouraged to use this report and the highlighted case examples to assess and address vulnerabilities in their own settings.

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