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Change in Methadone Concentration Results in an Overdose in a Post-Partum Patient

Methadone is a potent synthetic opioid analgesic that has been used for decades, in conjunction with supportive psychological and social services, to manage and treat addiction to other opioids.[1] Numerous incidents involving methadone have been reported,[2] and methadone continues to be implicated in preventable deaths.[3] This bulletin describes an incident involving a 10-fold overdose of methadone associated with a changeover of a hospital's supply from methadone 1 mg/mL to a newly available 10 mg/mL product. The findings and recommendations from this case are shared in the hope that similar events in the setting of methadone maintenance treatment can be prevented.

Incident Example

A patient who was receiving a methadone maintenance dose of 85 mg daily by mouth was admitted to hospital after giving birth to her child at home. Just hours after the birth, the patient received her first hospital dose of methadone. Soon after, the patient's husband noted that she was becoming increasingly delirious and agitated. As the patient became progressively sedated, the hospital staff intervened with the administration of intravenous (IV) naloxone. Despite several doses of naloxone, the patient's respiratory rate continued to drop. This resulted in admission to the intensive care unit (ICU), initiation of an IV naloxone infusion, multiple other interventions, and an extended hospital stay.

As a result of the overdose, the patient missed valuable bonding time with her infant and was advised not to breastfeed. Her breast milk was pumped and discarded to prevent harm to the infant, given the potential presence of high concentrations of methadone in the milk. In addition, the baby's father stayed in the birthing unit with the infant to provide skin-to-skin care to the newborn while the mother was in the ICU.

The patient's methadone therapy was placed on hold. When she exhibited signs of opioid withdrawal, methadone was restarted much lower than her previous maintenance dose. Breastfeeding was introduced as the methadone dose was gradually titrated upward. The infant required an extended hospital stay to allow for close monitoring of both opioid withdrawal and potential toxicity with the introduction of breast milk.

An investigation of the incident revealed that the patient's first hospital dose was 850 mg (85 mL of a 10 mg/mL methadone solution), rather than 85 mg (85 mL of a 1 mg/mL formulation). The change in hospital supply to the concentrated product resulted in a 10-fold overdose.

Background

Despite its longstanding history of use for the treatment of opioid dependence, methadone's

pharmacologic properties (e.g., long and variable half-life, rapid loss of tolerance on cessation) and special considerations (e.g., carries*, split doses) are not universally understood.[2] This knowledge gap places patients who are taking methadone at risk of harm from medication incidents. To support practitioners in the management of patients receiving methadone in the hospital and in the community, several jurisdictions have developed clinical guidelines.[4,5]

Methadone maintenance therapy remains the most widely used form of treatment for opioid dependence. Relative to illicit opioid use, which has numerous risks and complications, methadone is safe and cost-effective, provided appropriate safeguards are in place.[6,7] Methadone is considered medically safe for opioid-dependent pregnant women, as well as for women who breastfeed.[8] Comprehensive prenatal care, including methadone maintenance therapy, can reduce the risk of obstetric, fetal, and neonatal complications resulting from opioid dependence.[1,8,9]

Although oral methadone solutions (Metadol-D) in concentrations of both 1 mg/mL and 10 mg/mL have been on the market for over 10 years,[10] community pharmacies have typically used the 1 mg/mL or compounded a 5 mg/mL strength to support outpatient methadone programs. Recently, however, regulatory authorities in several provinces have specified that a new 10 mg/mL product (Methadose) will be the only methadone product eligible for reimbursement.[11-13] As a result, community pharmacies must stock the higher-concentration product. However, inventory in hospital pharmacies will vary, as hospitals may choose to stock either or both concentrations.

Discussion

After the error was discovered, the facility conducted a full analysis and identified the following contributing factors.

- Lack of awareness of both the existence of a new high-concentration methadone product and the hospital's recent switch to this new product: introducing a new drug concentration may create additional complexity and opportunities for error in the processes of medication prescribing, preparing, administering, and monitoring. The error in this particular incident occurred despite the pharmacy having applied additional labelling to the methadone bottles (see Figure 1). The facility had also provided proactive education (through in-service sessions, emails, and posted notices) to alert practitioners to the change in concentration, efforts that were acknowledged by staff.

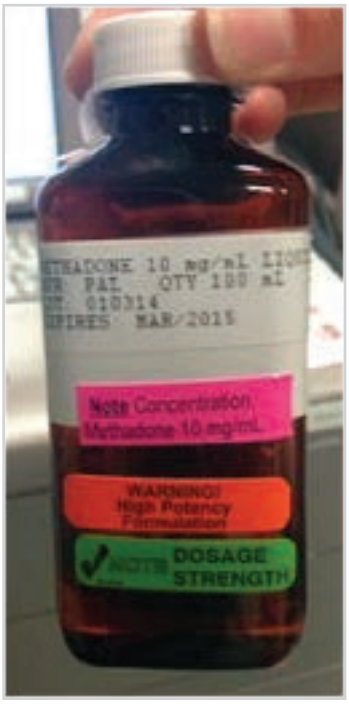

Figure 1. Methadone bottle with warning sticker about new concentration (in use when the incident occurred)

- Availability of a stock bottle of methadone in the automated dispensing cabinet: a 100 mL bottle of methadone 10 mg/mL was available to the nursing staff at the time of the error. The stock bottle was properly fitted with an oral syringe adaptor to prevent free pouring of inappropriate volumes. In response to identification of this contributing factor to the incident, the facility investigated the possibility of providing the concentrated

* Carries are methadone doses that are allowed to be taken home for self-administration so that the patient does not have visit the pharmacy daily to receive the dose; this privilege is given to patients meeting specific requirements.[4]

methadone solution in a smaller volume. However, the facility rejected this approach when it resulted in near miss situations because the smaller bottle was mistaken for a unit-of-use dose and almost administered.
- Single-practitioner verification of the dose administered (i.e., lack of an independent double check).

Recommendations

To increase their effectiveness, error-prevention plans should incorporate high-leverage strategies along with lower-leverage strategies such as education and reminders.[2] The following considerations are suggested to reduce the risk of similar occurrences, specifically in the setting of methadone maintenance treatment:

Hospitals and/or Pharmacies

- Provide methadone solution in unit-of-use, patient-specific doses, rather than as ward stock. This approach avoids relying on front-line practitioners to perform calculations and make adjustments during drug preparation.
  - An example checklist and pharmacy worksheet for preparation of unit-dose methadone, designed and tested with end users and shared with permission from Alberta Health Services, is available at: www.albertahealthservices.ca/10880.asp
- Limit hospital pharmacy inventory to only 1 concentration of oral methadone solution. Ensure that order-entry systems reflect the concentration of methadone available.
  - Multisite organizations should stock just one concentration of methadone at all sites.
  - If more than 1 concentration must be available, processes should be in place to prevent mix-ups (e.g., differentiation through packaging and labelling).
  - Consider conducting a prospective analysis with any planned changes in order to identify risks.
- Develop and implement policies and practices for independent double checks of methadone. In certain circumstances, the patient may be able to provide the double check before administration.
- Ensure that staff involved in the care of patients who are receiving methadone have ready access to resources to aid in the management of these patients (e.g., information about monitoring parameters and the signs, symptoms, and treatment of methadone overdose).
- Develop standardized order sets (for hospitals and other institutional facilities) that will be consistently used by all those who are authorized to prescribe methadone. Such a system (a preprinted prescription form) is currently in place in British Columbia where Methadose is prescribed for methadone maintenance therapy in community practice.[12]
- Perform and document an independent double check during preparation and administration of every methadone dose (in both the pharmacy and patient care areas).
- Throughout the medication use system, methadone doses must be communicated in milligrams (mg). This includes ensuring that patients know the dose of methadone they are to receive in milligrams (mg), not millilitres (mL).
- When transitioning from one methadone concentration to another:
  - Provide clear communication of the change both in advance and after the change has occurred.
  - Remove all stock of the original concentration from the facility at the same time, so that only the new concentration is available once the change has been made. The new concentration should be clearly differentiated from the previous product (e.g., through warning labels, packaging and labelling, copy of a communiqué provided with the product).
  - Add a prominent warning (e.g., auxiliary label) to methadone containers or packages to alert users to the change in concentration. If an auxiliary label is applied, consider using bold text to identify the concentration on the label, when this typographic option is available in the pharmacy computer system.

Prescribers

- Write methadone orders using words as well as numerals, and clearly express doses in milligrams (mg). When using preprinted orders or prescription forms, additional information such as the concentration of methadone and equivalent volume (if known) may be captured.

Conclusion

Any change to a well-established product or process carries the risk for inadvertent error. The period of transition to the new product or process is especially important for high-alert medications such as methadone, where the outcome of an error can be fatal. The case described in this bulletin demonstrates the risks and consequences of such changes.

Provinces that have decided to reimburse only the new product (Methadose) have warned healthcare practitioners in their respective jurisdictions of the risk for error during the changeover period.[11-13] However, a warning alone is insufficient to prevent incidents; system-based safeguards are also required. It is hoped that the contributing factors and recommendations identified in this bulletin will provide insights for hospitals and other institutional facilities, community pharmacies, and their associated healthcare practitioners in developing and implementing safeguards and quality improvement initiatives.

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References

1. Best practices methadone maintenance treatment. Ottawa (ON): Health Canada; 2002 [cited 2014 Oct 16]. Available from: http://www.hc-sc.gc.ca/hc-ps/alt_formats/hecs-sesc/pdf/pubs/adp-apd/methadone-bp-mp/methadone-bp-mp-eng.pdf
2. Methadone: not your typical narcotic! ISMP Can Saf Bull. 2003 [cited 2014 Oct 16];3(12):1-2. Available from: http://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2003-12Methadone.pdf
3. Deaths associated with medication incidents: learning from collaborative work with provincial offices of the chief coroner and chief medical examiner. ISMP Can Saf Bull. 2013 [cited 2014 Oct 17];13(8):1-7. Available from: http://www.ismp-canada.org/download/safetyBulletins/2013/ISMPCSB2013-08_DeathsAssociatedWithMedicationIncidents.pdf
4. Methadose and the Policy for Methadone Maintenance Treatment Reimbursement under the Ontario Drug Benefit Program. Toronto (ON): Ministry of Health and Long-Term Care, Ontario Public Drug Programs; 2014[cited 2014 Oct 16. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/notices/cmmt_faq_pharmacists_20140620.pdf
5. Methadone maintenance program: clinical practice guideline. Vancouver (BC): College of Physicians and Surgeons of British Columbia; 2014 Feb [revised 2014 Jul; cited 2015 Jan 13]. Available from: https://www.cpsbc.ca/files/pdf/MMP-Clinical-Practice-Guideline.pdf
6. Volkow ND, Frieden TR, Hyde PS, Cha SS. Medication-assisted therapies—tackling the opioid-overdose epidemic. N Engl J Med. 2014;370(22):2063-2066.
7. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev. 2009(3):CD002209.
8. Opioids. In: Centre for Addiction and Mental Health knowledge exchange [website]. Toronto (ON): Centre for Addiction and Mental Health; 2009 [cited 2014 Oct 23]. Available from: http://knowledgex.camh.net/primary_care/guidelines_materials/pregnancy_lactation/pages/per_opioids.aspx
9. National Consensus Development Panel on Effective Medical Treatment of Opiate Addiction. Effective medical treatment of opiate addiction. JAMA. 1998;280(22):1936-1943.
10. Metaldol-D [product monograph]. Saint-Laurent (QC): Paladin Labs, Inc.; revised 2014 Feb 17 [cited2014 Apr 22]. Available from: http://www.paladin-labs.com/our_products/Metadol-D_En.pdf
11. Notice from the Executive Officer: policy for methadone maintenance treatment reimbursement under the Ontario Drug Benefit Program. Toronto (ON): Ministry of Health and Long-Term Care, Ontario Public Drug Programs; 2014[cited 2014 Oct 16]. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/opdp_eo/notices/exec_office_20140620.pdf
12. Updates from the methadone maintenance program. College Connector [College of Physicians and Surgeons of British Columbia]. 2013 [cited 2014 Apr 22];1(3). Available from: https://www.cpsbc.ca/for-physicians/college-connector/2013-V01-03/07
13. Methadone reimbursement procedure. Winnipeg (MB): Manitoba Health, Healthy Living and Seniors; 2014 Oct 9 [cited 2014 Oct 22]. Available from: http://mpha.in1touch.org/uploaded/web/Legislation/MB%20Health%20QA%20to%20Pharmacists%20-%20Methadose.pdf

Methadone Medication Incidents in Community Pharmacy

Methadone is a long-acting synthetic opioid prescribed to manage chronic pain and to treat opioid dependence in methadone maintenance treatment programs.[1] Despite the benefits of methadone in these clinical settings, questions about its safety within the medication-use process continue to challenge healthcare practitioners. Given this drug's unique pharmacokinetic properties and complex dispensing requirements, it is one of the least understood narcotics used in the community setting and is therefore inherently more prone to the occurrence of medication incidents.

ISMP Canada's Community Pharmacy Incident Reporting (CPhIR) Program is a voluntary program used by community pharmacies across Canada to analyze underlying process and system vulnerabilities that contribute to medication incidents in this healthcare sector, with the goal of preventing future incidents. To identify specific issues leading to problems with methadone therapy in the community, data were collected from incidents involving methadone that had been reported to the CPhIR Program between April 2010 and August 2012.[2] A total of 72 incidents were included in a qualitative, multi-incident analysis conducted by 2 independent analysts.[2]

The analysis revealed 2 underlying themes that facilitated the occurrence of methadone incidents. The first theme focused on characteristics unique to methadone, with subthemes related to compounding and confirmation bias.[2] In compounding incidents, pharmacies either dispensed or prepared incorrect dosages, which led to under- or over-doses.[2] Incidents involving confirmation bias resulted from pharmacy staff making assumptions based on inaccurate information. Potential contributing factors to incidents within this theme included, but were not limited to, environmental distractions, lack of independent double-checks, and lack of communication among healthcare professionals within the circle of care.[2] ISMP Canada's recommendations to prevent these types of incidents from recurring include aligning prescription writing practices to those found in methadone prescribing guidelines, incorporating independent double checks, and re-evaluating all prescribed doses following any dosage adjustments.[2]

The second main theme arising from this analysis encompassed the medication-use process, namely, the prescribing, order entry, dispensing, and administration stages.[2] Potential contributing factors within this theme included inappropriate prescribing, inappropriate order entry protocols, unnecessary storage of prepoured methadone doses, and use of multiple stock solutions with different concentrations.[2] Recommendations to address these vulnerabilities include using standardized, preprinted order forms, preparing methadone in a dedicated area in the pharmacy, and implementing independent double checks.[2]

The full analysis report can be found at:
https://www.ismp-canada.org/download/PharmacyConnection/PC2013Summer_MethadoneMedicationIncidents.pdf

References

1. Methadone: not your typical narcotic! ISMP Can Saf Bull 2003 [cited 2014 Nov 10];3(12):1-2. Available from: http://ismp-canada.org/download/safetyBulletins/ISMPCSB2003-12Methadone.pdf
2. Kawano A, Kong JH, Ho C. Methadone medication incidents. Pharm Connect [Ontario Col-lege of Pharmacists] 2013 [cited 2014 Nov 10];20(3):38-41. Available from: https://www.ismp-canada.org/download/PharmacyConnection/PC2013Summer_MethadoneMedicationIncidents.pdf

Drug Labelling and the Application of TALLman Lettering for Select High Alert Drugs

Learning from reported medication incidents has helped identify the drugs most frequently associated with harmful medication incidents and factors contributing to such incidents. A notable theme in qualitative analyses has been medication mix-ups due to look-alike/sound-alike drug names.

TALLman lettering involves the application of UPPER CASE lettering to certain syllables or groups of letters within names to bring attention to the points of dissimilarity between them. For example: vinCRIstine / vinBLAstine.

We are seeking participation and input from Canadian healthcare professionals. Please complete a brief survey to assist us in the identification of confusable drug name pairs and to provide us with your suggestions or comments about the application of TALLman lettering.

Complete the survey (https://www.ismp-canada.org/TALLman/survey.php).

Deadline for submission is ***Friday, February 20, 2015***.

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