Importance of Medication Error Reporting: A Spotlight on Oral Methotrexate

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25 YEARS ADVANCING MEDICATION SAFETY

Overview

- The importance of medication error reporting
- A focus on methotrexate errors

A Brief History of Medication Error Reporting in the US

- 1975: Institute for Safe Medication Practice's (ISMP's) work officially begins with a continuing column on medication safety in *Hospital Pharmacy*
- 1990: United States Pharmacopeia (USP)-ISMP Medication Error Reporting Program is started
- 1993: U.S. Food and Drug Administration (FDA) MedWatch program was founded to collect data regarding adverse events in healthcare
- 1994: ISMP is officially incorporated as a nonprofit organization
- 1999: The Institute of Medicine publishes *To Err is Human*
- 2007: The Institute of Medicine publishes *Preventing Medication Errors*

To Err is Human: Building a Safer Health System

- The report confirmed:
  - Human beings, in all lines of work, make errors
  - As healthcare becomes more complex, the opportunities for errors increase
  - Medication errors place an immense burden on patient safety and healthcare

To Err is Human: Building a Safer Health System

- The report confirmed:
  - Errors can be prevented by designing systems that make it hard for people to do the wrong thing and easy for people to do the right thing
  - Building a safer system means designing processes of care to ensure that patients are safe from accidental injury

High-Alert Medications

- High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error

- In 2004, ISMP identified 106 cases of reported medication errors associated with methotrexate, including 25 deaths and 48 serious outcomes

ISMP List of High-Alert Medications
in Acute Care Settings

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistak
may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. We hope you v
use this list to determine which medications require special safeguards to reduce the risk of errors. This may include strategies such as standardizi
the ordering, storage, preparation, and administration of these products; improving access to information about these drugs; limiting access to hi
alert medications; using auxiliary labels; employing clinical decision support and automated alerts; and using redundancies such as automated
independent double checks when necessary. (Note: manual independent double checks are
not always the optimal error-reduction strategy and may not be practical for all of the
medications on the list.)

Classes/Categories of Medications

- adrenergic agonists, IV (e.g., **EPINEPH**rine, phenylephrine, norepinephrine)
- adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)
- anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)
- antiarrhythmics, IV (e.g., lidocaine, amiodarone)
- antithrombotic agents, including:
  - anticoagulants (e.g., warfarin, low molecular weight heparin, unfractionated heparin)
  - direct oral anticoagulants and factor Xa inhibitors (e.g., dabigatran, rivaroxaban, apixaban, edoxaban, betrixaban, fondaparinux)
  - direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran)
  - glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)
  - thrombolytics (e.g., alteplase, reteplase, tenecteplase)
- cardioplegic solutions
- chemotherapeutic agents, parenteral and oral
- dextrose, hypertonic, 20% or greater
- dialysis solutions, peritoneal and hemodialysis
- epidural and intrathecal medications
- inotropic medications, IV (e.g., digoxin, milrinone)
- insulin, subcutaneous and IV
- liposomal forms of drugs (e.g., liposomal amphotericin B) and conventional counterparts (e.g., amphotericin B desoxycholate)
- moderate sedation agents, IV (e.g., dexmedetomidine, midazolam, **LOR**azepam)
- moderate and minimal sedation agents, oral, for children (e.g., chloral hydrate, midazolam, ketamine [using the parenteral form])
- opioids, including:
  - IV
  - oral (including liquid concentrates, immediate- and sustained-release formulations)
  - transdermal
- neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)
- parenteral nutrition preparations
- sodium chloride for injection, hypertonic, greater than 0.9% concentration
- sterile water for injection, inhalation and irrigation (excluding pour bottles) in containers of 100 mL or more
- sulfonylurea hypoglycemics, oral (e.g., chlorpro**PAMIDE**, glimepiride, gly**BURIDE**, glipi**ZIDE**, **TOLBUT**amide)

Specific Medications

- **EPINEPH**rine, IM, subcutaneous
- epoprostenol (e.g., Flolan), IV
- insulin U-500 (special emphasis*)
- magnesium sulfate injection
- methotrexate, oral, nononcologic use
- nitroprusside sodium for injection
- opium tincture
- oxytocin, IV
- potassium chlo…
- pot… …jection
- …injection
- vasopressin, IV and intraosseous

**All forms of insulin, subcutaneous and IV, are considered a class of high-alert medications. Insulin U-500 has been singled out for special emphasis to bring attention to the need for distinct strategies to prevent the types of errors that occur with this concentrated form of insulin.*

Background

Based on error reports submitted to the ISMP National Medication Errors Reporting Program (ISMP MERP), reports of harmful errors in the literature, studies that identify the drugs most often involved in harmful errors, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential high-alert medications. During June and July 2018, practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert medications. Further, to assure relevance and completeness, the clinical staff at ISMP and members of the ISMP advisory board were asked to review the potential list. This list of medications and medication categories reflects the collective thinking of all who provided input.

Abbreviation definitions: IV—intravenous IM—intramuscular

chemotherapeutic agents, parenteral and oral

Oral Methotrexate

- Indications
  - Oncologic (e.g. leukemia)
  - Non-oncologic (e.g. dermatologic, rheumatologic)
- Oncologic dosing regimens
  - Can be dosed as frequent as once daily
- Non-oncologic dosing regimens
  - Should be dosed once weekly

Patient Case #1: How would you interpret this prescription label?

Methotrexate 2.5 mg

Take one tablet every 12 hours for three doses each week

12 tablets
No refills

Patient Case #1: The Patient

- The patient misunderstood the directions for use and took methotrexate 2.5 mg **every 12 hours for six consecutive days** and ran out of tablets.

- The error resulted in the patient's death.

Patient Case #2: How would you interpret this prescription label?

Methotrexate 10mg

Take one tablet every Monday

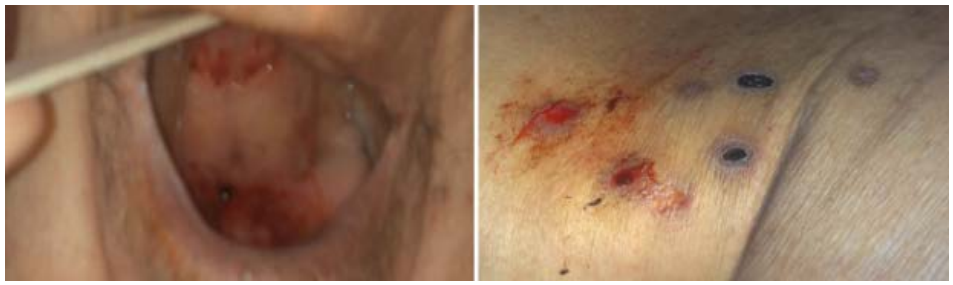
12 tablets
3 refills

Patient Case #2: The Patient

- The patient misread the directions on the prescription bottle and took 10 mg every **morning** instead of every **Monday.**
- The error resulted in the patient's death.

Key Points

- Serious medication errors involving methotrexate have been reported resulting in harm and patient death
  - Bone marrow suppression
  - Liver toxicity
  - Mucositis and mucocutaneous lesions



Key Points

- Errors typically involve some aspect of the dosing regimen
- In some instances one dose is prescribed but multiple tablets may be needed to complete the total dose (e.g. 10 mg dose = 4 tablets x 2.5 mg)
- Most medications utilize daily dosing versus weekly

IMSN Global Targeted Medication Safety Best Practice: Oral Methotrexate

- Goal: prevent errors involving inadvertent daily dosing instead of weekly dosing of oral methotrexate for non-oncologic conditions in the ambulatory and inpatient settings

IMSN Global Targeted Medication Safety Best Practice: Oral Methotrexate

- Recommendations
  - Prescribe, dispense, and administer oral methotrexate **once weekly**
  - Have medication systems default to weekly
  - Require an **indication** for all daily oral methotrexate orders
  - Remove oral methotrexate from nursing wards
  - Provide proper patient **education**
  - Educate clinical staff
  - Dispense in a **one-month supply**

European Medicines Agency recommendations regarding methotrexate

- EMA has recommended new measures to prevent serious and potentially fatal errors with the dosing of methotrexate for treating inflammatory diseases such as rheumatoid arthritis, psoriasis and Crohn's disease. The recommendations result from a review of reports that patients are using methotrexate incorrectly despite previous measures to prevent errors.

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Group Discussion:

Have oral methotrexate dosing errors or deaths been reported to your pharmacovigilance centers?