Methotrexate Mistakes

Methotrexate is an antimetabolite that interferes with DNA synthesis, repair, and cellular replication. Initially developed as a cancer treatment, methotrexate dosing is based on body surface area and is administered in cycles, rarely daily. The indications for methotrexate expanded to include treatment of rheumatoid arthritis and psoriasis which requires a low dose typically once or twice a week. Because only a few medications are dosed weekly, overdoses have been common, resulting in vomiting, mouth sores, stomatitis, skin lesions, liver failure, renal failure, myelosuppression, gastrointestinal bleeding, pulmonary symptoms, and death.

Methotrexate errors have occurred in the following scenarios:

- **Medication reconciliation and transitions-of-care:** missteps happen when patients are admitted to the hospital and upon discharge to home or other healthcare facilities.
    - Orders may be entered incorrectly into the electronic medical record (EMR).
    - Errors occur with medication transcription.
    - Failure to verify the correct indication (cancer versus non-oncologic).
    - Medications are not reconciled prior to discharge.
- **Confusing instructions misunderstood by the patient:** Methotrexate dosing is complex, often involving titration or escalating weekly doses. This can be very confusing for patients.
    - For example, an 8-week supply of 2.5 mg tablets (30 tablets) were dispensed with a prescription that read “Take 3 tablets by mouth 1 day for 2 weeks then increase to 4 tablets by mouth 1 day per week thereafter”. The patient erroneously took 3 tablets (7.5 mg) daily for 5 days which caused serious illness.
- **Look-alike and sound-alike drug names:** Methotrexate has been mistaken for metolazone, a diuretic prescribed daily to treat congestive heart failure or kidney disease.
    - Both have similar dosage strengths: 2.5, 5, and 10 mg.
    - Both start with “met” and one pharmacist selected methotrexate instead of metolazone from the drop down menu in the computer system which did not flag the order for an oncology indication; the patient took 2.5 mg daily and died one month later.
- **Mix up with folic acid tablets:** Methotrexate is a folic acid antagonist, thus folic acid may be prescribed to prevent folate deficiency and side effects such as mouth sores, abdominal pain, liver toxicity, hair loss, and anemia.
    - Folic acid tablets may resemble methotrexate tablets – both are small, yellow, and round.

The following strategies may help decrease the risk of methotrexate errors:

- Include “take as directed” on all orders and prescriptions for oral methotrexate and emphasize clear instructions for weekly dosing.
- Limit the patient’s prescription quantity to a 4-week (30-day) supply to decrease the risk of overdose.
- Verify the dose and frequency of methotrexate on all medication lists and discharge instructions.

References

1. Institute for Safe Medication Practices. (2018). *Nurse Advise-ERR.* Retrieved from Institute for Safe Medication Practices: http://www.ismp.org/newsletters/nursing/issues/NurseAdviseERR201908.pdf

  - Update and edit the patient's home medication list throughout the hospital stay so that it remains correct at discharge.
  - Review all discharge orders and prescriptions to ensure the dose and frequency are based on the right diagnosis.
- Educate patients and provide them with verbal and written instructions that specify a weekly dosing schedule and stress the lethal risks with daily dosing.
  - Request all patients and family repeat back the instructions for taking oral methotrexate to confirm their understanding.
  - Advise patients to select one day of the week that they will take their oral methotrexate and to ask their pharmacist to include that on the label instructions (avoid Monday as that has been misread as "morning").
  - Provide the patient with a visual calendar to emphasize the weekly dosing schedule.
  - If available, patients should ask the pharmacy to provide the oral methotrexate in a dose pack that helps remind them to take the right dose weekly.
- Program pharmacy and prescriber order entry systems to default to a weekly dosing schedule.
- Ensure that verification of an appropriate oncologic indication is required for daily orders in all order entry systems.
- If folic acid is prescribed with methotrexate, instruct the patient on:
  - Differences between the drugs
  - Individual administration schedules
  - How to avoid mix-ups between the tablets (keep methotrexate tablets in the original packaging instead of weekly pill organizers)
- Teach patients the symptoms of methotrexate toxicity and whom to contact to report symptoms.
- Advise the patient to seek immediate medical attention if a dosing error occurs.

prone abbreviations that should never be used and provide their staff with an accessible online database of medical abbreviations. If drug abbreviations are used in the clinical setting, the prescriber should be contacted for clarification.

References

1. Institute for Safe Medication Practices. (2018). *Nurse Advise-ERR.* Retrieved from Institute for Safe Medication Practices: http://www.ismp.org/newsletters/nursing/issues/NurseAdviseERR201908.pdf