



Poison HOTLINE

1-800-222-1222

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Did you know

Leucovorin (folinic acid) is the activated form of folic acid. Folic acid requires DHFR to be activated to folinic acid. MTX inhibits DHFR, so folic acid is not effective when treating MTX toxicity.

However, folic acid is used as supplemental therapy for methanol toxicity. Methanol is metabolized by alcohol dehydrogenase, then aldehyde dehydrogenase to its toxic metabolite, formic acid. Folic acid or leucovorin work by accelerating the inactivation of formic acid.

The administration of folic acid or leucovorin in methanol toxicity is performed in addition to fomepizole. Fomepizole prevents the metabolism of methanol to formic acid and folic acid or leucovorin help accelerate the inactivation of formic acid.

Call the IPCC to speak to our specially trained nurses, pharmacists, or toxicologists.

Methotrexate

Methotrexate (MTX) is a folate antagonist that is used therapeutically for its immunosuppressive ability. It is commonly used for conditions such as rheumatoid arthritis, psoriasis, and ectopic pregnancy. Mechanistically, MTX inhibits dihydrofolate reductase (DHFR) and thymidylate synthetase. These enzymes are responsible for DNA and RNA synthesis and repair, as well as cellular replication. By inhibiting these enzymes, the processes cease.

Unintentional acute ingestions are typically benign or produce only minor symptoms. Significant toxicity associated with MTX is more common in chronic supratherapeutic exposures, intentional acute ingestions, or with accidental high-dose IV or intrathecal MTX administration. Severe toxicity and death are associated with multisystem organ failure and sepsis. The most common symptoms from oral exposure include ulcerative stomatitis, nausea, vomiting, and diarrhea.

Initially it is important to determine if the exposure is acute or chronic. Chronic exposures are at a higher risk for infection and sepsis due to MTX's bone marrow suppression whereas acute exposures should have attempts at limiting absorption (with activated charcoal) and administration of antidotes. Initial lab monitoring includes serum MTX, CBC with differential, platelets, and CMP. Obtain a chest x-ray in patients with respiratory symptoms.

Specific antidotes for MTX include leucovorin and glucarpidase. Leucovorin works by augmenting the intracellular biological processes that are dependent on folates which are otherwise inhibited by MTX. Glucarpidase is an enzyme that quickly hydrolyzes MTX to an inactive metabolite and glutamic acid. Glucarpidase, however, does not work intracellularly so it must be co-administered with leucovorin although separated by 2 hours so as not to inactivate the leucovorin.

Although MTX may be administered intrathecally, leucovorin should **NEVER** be administered intrathecally. Leucovorin should still be administered IV.

Call the IPCC at **1-800-222-1222** regarding MTX toxicity in your patient.

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