

Toxicology Update: Methotrexate

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Accidental ingestion of human prescriptions of methotrexate (MTX) by dogs often results in signs of severe toxicosis. MTX is a chemotherapeutic drug infrequently used in veterinary medicine but commonly used in human medicine to treat cancers and act as an immunosuppressant.

How does it work?

MTX competitively inhibits an enzyme that produces the active form of folate. Cells rely on folate for DNA synthesis and cellular replication, so the drug's effects are most pronounced in rapidly dividing cells.¹ This primarily impairs growth in malignant tumors but also affects other rapidly dividing cell lines like those found in the gastrointestinal tract epithelium and bone marrow.

What is seen in canine toxicosis?

Overdosage compounds the effects on the bone marrow and gastrointestinal tract and can cause nephrotoxicity, hepatocellular injury, and CNS damage. Common symptoms include vomiting, diarrhea, gastrointestinal ulceration, anemia, leukopenia, thrombocytopenia, acute renal failure, hepatotoxicity, sepsis, and seizures. MTX-associated toxicosis has significant variability in individuals,² so a specific toxic dose has not been established in the literature. Doses in the therapeutic range (0.8 mg/kg) can result in gastrointestinal effects and myelosuppression.

How is toxicosis treated in dogs?

In an acute oral overdose, induction of emesis is indicated if the patient is neurologically appropriate. This can be followed by activated charcoal administration. Intravenous fluids with added sodium bicarbonate alkalinize the urine, which enhances excretion of MTX while reducing renal insult. Leucovorin, an injectable folic acid derivative, is the mainstay of treatment for MTX toxicosis. This medication is given every 6 hours for 8 doses. Consultation with a toxicologist is recommended for guidance since the dosage is adjusted based on actual or estimated serum levels of MTX. Leucovorin can usually be obtained from the pharmacy at a human hospital.

What new developments in treatment are there?

Extracorporeal therapy has been known to be an effective intervention for MTX overdose in human medicine for some time. A recent case report³ showed that a combination of charcoal hemoperfusion and hemodialysis rapidly reduced MTX serum concentration and prevented the development of toxicosis in a dog that ingested about 2 mg/kg of MTX.

References

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