

PEER-REVIEWED

Disulfoton: A deadly threat in pets

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Disulfoton (O, O-diethyl-S-2-ethylthioethylphosphorodithioate), also called *oxydisulfoton*, is an organophosphorus insecticide and acaricide that is highly toxic in mammals. Trade names include Di-Syston, Dimaz, Disultex, Ekanon, Frumin AL, Knave, Solvigran, and Solvirex. Disulfoton is considered a systemic insecticide because it is absorbed by plant roots and distributed systemically to the rest of the plant. It is especially effective against sucking insects, such as aphids.¹ Dogs are most commonly exposed to disulfoton by ingesting granular rose care products applied to the soil at the base of the plant by pet owners. Dogs are attracted to the disulfoton when it is formulated with or applied with fertilizers. Disulfoton may also be applied to potted roses before purchase, so pet owners may be unaware of any danger.

Mechanism of action

Organophosphorus insecticides such as disulfoton affect the nervous system by binding to the enzyme acetylcholinesterase, allowing the neurotransmitter acetylcholine to accumulate at autonomic and somatic nerve synapses. Excessive acetylcholine causes continued stimulation of parasympathetic muscarinic receptors, preganglionic sympathetic receptors, and somatic nicotinic receptors. Sites affected include the brain, heart, lungs, skeletal muscle, stomach, intestines, pancreas, urinary bladder, adrenal medulla, salivary and lacrimal glands, and iris.²

Toxicity

Disulfoton's oral LD₅₀ in rats is 2 mg/kg, placing it in the most toxic, Category I, group of pesticides (*i.e.*

those having an LD₅₀ ≤ 50 mg/kg).¹ Because of disulfoton's extremely toxic nature, dogs may ingest a sufficient amount to cause toxicosis while digging around treated plants. For example, a 55-lb (25-kg) dog would need to ingest only about a teaspoon of a pesticide containing 1% disulfoton to reach the LD₅₀.

Clinical signs

Dogs usually present with signs typical of organophosphorus insecticide toxicosis. Muscarinic stimulation may cause miosis, salivation, lacrimation, dyspnea, tachypnea, vomiting, diarrhea, and urination. Frank blood may be seen in the vomitus and stool if vomiting and diarrhea are severe. Muscle tremors or fasciculations, muscle weakness (including diaphragm weakness), mydriasis, tachycardia, and ataxia are signs of nicotinic stimulation. Central nervous system effects of organophosphorus insecticides include seizures and coma.

Physical examination findings

A patient's mucous membranes may be tacky and pale or cyanotic. Bradycardia may be present as a result of organophosphate-induced parasympathetic stimulation. Conversely, tachycardia is possible from overriding sympathetic tone.³ Evidence of bronchial secretions may be heard on thoracic auscultation. Hyperthermia may be seen with muscle tremors or fasciculations, while hypothermia may be encountered after these signs resolve. Signs of pain may be elicited on abdominal palpation. Intussusceptions have been reported in some dogs with disulfoton toxicosis (ASPCA Animal Poison Control Center [APCC] Database: Unpublished data, 2003).

Clinicopathologic findings

The packed cell volume may be elevated from dehydration secondary to severe vomiting and diarrhea. Electrolyte imbalances are possible because of severe fluid losses. Amylase and lipase activities may be markedly elevated from autonomic stimulation of the pancreas or secondary to pancreatitis. Increases in aspartate transaminase and creatine kinase activities can

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result from excessive muscle activity. Hyperglycemia and leukocytosis have also been reported.⁴

Making a definitive diagnosis

A 50% or more decrease of acetylcholinesterase in whole blood, serum, or plasma is suggestive of organophosphorus insecticide toxicosis.⁴ Analysis of whole blood is preferred. Because a variety of methods are used to determine acetylcholinesterase activity, the test results should be interpreted by a laboratory that has established normal values in dogs. Severe organophosphorus toxicosis may lower acetylcholinesterase activities to less than 25% of normal.⁴

The results of acetylcholinesterase testing are usually not available in time to make treatment decisions when an exposure history is uncertain. Observing the response to a low (preanesthetic) dose of atropine sulfate (0.02 mg/kg intravenously) may help you establish a tentative diagnosis. Since large doses of atropine are required to control the clinical signs of organophosphorus toxicosis, a lack of response to a low dose is suggestive of exposure to an acetylcholinesterase inhibitor. If, after administering a low dose of atropine, you observe an increased heart rate, dry mucous membranes, and mydriasis, search for a different diagnosis.⁴

Treatment

Because clinical signs often begin before treatment is sought, typical

decontamination measures usually cannot be used in disulfoton toxicosis. Do not induce vomiting in patients exhibiting vomiting, diarrhea, and abdominal pain. Emetics may exacerbate these signs and are unlikely to help the patient. Gastric lavage may be useful once the patient is stabilized if large amounts of disulfoton have been ingested. Administering activated charcoal is recommended in most cases, but only after vomiting has been controlled and the patient is stable. Cathartics may exacerbate diarrhea and are not indicated.

Tailor treatment for disulfoton toxicosis to the individual patient. Clinical signs and their severity may differ, depending on the quantity of disulfoton ingested and the length of time after exposure. Prompt and aggressive supportive care must be provided for any life-threatening signs. Establish an airway, and administer oxygen if a patient is in respiratory distress. Place an intravenous catheter for drug and fluid therapy administration. Atropine is usually recommended early in the course of organophosphorus insecticide toxicosis to counteract potential life-threatening pulmonary and cardiac effects. Atropine decreases the bronchial secretions, bronchoconstriction, and bradycardia that may compromise adequate oxygenation. Depending on the severity of signs, the recommended dose of atropine in organophosphorus toxicosis is 0.2 to 2 mg/kg. Give one-fourth to one-half intravenously

and the rest intramuscularly or subcutaneously.⁵ Overuse of atropine can cause central nervous system excitation, tachycardia, hyperthermia, and intestinal stasis. Since atropine should only be used to treat the life-threatening effects of acetylcholinesterase inhibition, discontinue its use when muscarinic signs are under control to avoid potential adverse effects. Repeated doses of atropine may be needed if muscarinic signs recur.

When treating disulfoton-induced seizures, start with diazepam because it is short-acting and has a minimal effect on the cardiovascular system. Barbiturates may be considered if diazepam is ineffective. Inhalant anesthetics may be needed if seizures are refractory to other medications.

Fluid therapy is indicated to improve blood pressure in patients experiencing shock and hypotension. Fluids are also often needed to replenish water and electrolytes lost through vomiting and diarrhea. Base the choice of fluids on a patient's needs, but a first choice would be lactated Ringer's solution when laboratory test results are not back yet.

Treat hyperthermia or hypothermia supportively. Hyperthermia is caused by excessive muscle activity, and body temperature may normalize or drop below normal once these signs are controlled, so treat accordingly.

Pralidoxime chloride (2-PAM chloride) is an acetylcholinesterase reactivator used in moderate to severe cases of organophosphorus toxicosis. Pralidoxime may help relieve the muscle weakness and tremors associated with disulfoton toxicosis. It should be administered in stable patients at 20 mg/kg given intramuscularly or subcutaneously every 12 hours until severe weakness and tremors have resolved.⁵ Pralidoxime may be administered as a slow intravenous bolus or intravenous infusion. Neuromuscular blockade may occur with rapid administration.² If the patient does not respond after three doses, discontinue the pralidoxime. Muscle weakness may be prolonged if pralidoxime is not administered.

Vomiting, diarrhea, and abdominal pain may be severe with disulfoton toxicosis (ASPCA APCC Database: Unpublished data, 2003). The severe pain may lead to shock, so administer opioids when severe abdominal pain is suspected. Elevated pancreatic enzyme activity and abdominal pain may indicate pancreatitis. Supportive care may include administering sucralfate, H₂ blockers, antibiotics, and bland diets as needed for gastrointestinal signs and pancreatitis. Varying degrees of gastrointestinal upset often last for two or three days and possibly longer in severe cases. Monitor dogs for intussusception, and treat them appropriately.

A lack of response to a low dose of atropine suggests exposure to an acetylcholinesterase inhibitor.

Prognosis

A patient's prognosis depends largely on the amount of disulfoton ingested and the treatment provided. A delay in treatment may considerably worsen the prognosis. Animals with serious underlying health conditions may have a poorer prognosis than those in good health. A good to fair prognosis can be expected if the amount of disulfoton ingested is small and prompt medical care is provided. In cases of exposure to large amounts of disulfoton, such as access to the container, a guarded to poor prognosis is more likely.

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