

ANTIDEPRESSANT DRUG OVERDOSES

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Accidental antidepressant
ingestion is a common
cause of toxicosis in pets.



In 2005, the ASPCA Animal Poison Control Center received over 2,200 calls concerning accidental ingestion of antidepressant medications by pets. Most cases involved dogs, but cats, birds, and potbellied pigs were also exposed.

Antidepressants are divided into groups depending on their effects on the central nervous system (CNS) neurotransmitters dopamine, epinephrine, norepinephrine, and serotonin. Abnormal levels of these neurotransmitters are associated with depression, migraine, bipolar disorder, and anxiety. An antidepressant's effectiveness and potential side effects are determined by its specificity for each neurotransmitter. The major antidepressant groups encountered in cases of accidental ingestion are tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), and novel (or atypical) antidepressants.

TRICYCLIC ANTIDEPRESSANTS Mechanism of Action

TCAs have been used to treat depression since the 1950s. TCAs include a large number of different medications. These drugs block the reuptake of norepinephrine and serotonin, causing increased levels of these

neurotransmitters.¹ They also inhibit impulses through the parasympathetic nerves,¹ which help regulate intestinal peristalsis and cardiac conduction. TCAs are absorbed rapidly from the digestive tract (within 30 to 60 minutes) and take effect quickly. The anticholinergic effects of TCAs delay gastric emptying and decrease intestinal peristalsis. Because of these effects, drug absorption is increased in animals that ingest TCAs.²

Clinical Signs

Signs can appear quickly after ingestion. The first clinical signs of

lethargy and ataxia can quickly progress to tachycardia, vomiting, hypotension, cardiac arrhythmias, vocalizing, dyspnea, seizures, coma, and death.² Death can occur within 1 to 2 hours if signs are left untreated.³ Idiosyncratic hyperactivity is occasionally seen. The most serious effects of TCA overdoses are the effects on the heart. With high enough doses, TCAs can actually stop the electrical impulses from traveling through the heart.² Toxicity varies by medication. The oral lethal dose for amitriptyline is as low as 15 mg/kg, while clomipramine is much safer with an oral lethal dose of 100 mg/kg.⁴

Treatment

The recommended treatment for TCA overdoses includes emesis only in cases of recent ingestion (<15

Glossary

Alkalosis — Condition of having excess base in the body (blood pH >7.4)

Cathartic — A medication that stimulates evacuation of the bowels

Enterohepatic recirculation — Substance is absorbed from the intestine and carried to the liver, where it is secreted in the bile back into the intestine

Mydriasis — Dilated pupils

Serotonergic — Activated by or capable of releasing serotonin

minutes). If clinical signs are present, inducing vomiting is not recommended because of the increased risk of aspiration. In these cases, activated charcoal with a cathartic should be given. Repeated doses may interrupt enterohepatic recirculation. Sodium bicarbonate is needed if the patient is acidotic (blood pH: <7.4) or hypotensive or if cardiac arrhythmias are present. Inducing alkalosis (blood pH: 7.45 to 7.55) with sodium bicarbonate prevented death after TCA overdose in experimentally poisoned dogs.³

MONOAMINE OXIDASE INHIBITORS Mechanism of Action

Monoamine oxidase is an enzyme that helps break down epinephrine, norepinephrine, dopamine, and serotonin.¹ When monoamine oxidase is inhibited, concentrations of these neurotransmitters rise. MAOIs are still used to treat depression in humans but have lost favor to safer medications. MAOIs can interact with many other medications and with certain foods. MAOIs are used to treat other disease processes in humans (e.g., narcolepsy, obsessive compulsive disorder) and animals (e.g., selegiline for canine cognitive disorder).

Clinical Signs

Overdoses of MAOIs can cause hypo- or hypertension, depression, ataxia, and restlessness. This can progress to tachycardia, arrhythmias, coma, seizure, respiratory depression,

fever, and shock.⁵ Most patients develop signs within 1 to 2 hours, but a few patients have delayed signs 12 to 24 hours after ingestion.

Treatment

MAOI overdoses should be treated with emesis (if asymptomatic) or gastric lavage and followed by activated charcoal with a cathartic and IV fluids. Body temperature, respiration, and blood pressure should be monitored closely. A baseline liver panel should be obtained at admission and again 4 to 6 weeks after exposure because liver enzymes may become elevated after ingestion.¹

SELECTIVE SEROTONIN REUPTAKE INHIBITORS Mechanism of Action

SSRIs, as their name indicates, inhibit the reuptake of serotonin. They have minor or no effects on other neurotransmitters. SSRIs have fewer side effects than TCAs or MAOIs.¹ Fluoxetine, paroxetine, and sertraline are the most commonly used SSRIs.

Clinical Signs

Clinical signs of an SSRI overdose are caused by increased serotonin in the CNS and include lethargy or agitation, vomiting, ataxia, tremors, seizures, hypertension, and tachycardia. Fortunately, SSRI overdoses, if treated promptly, have fewer cardiac effects and are much less likely to be fatal than overdoses of TCAs or MAOIs.

Treatment

These medications are well absorbed orally, and signs can be seen in 30 minutes to 1 hour.¹ Emesis or gastric lavage should be performed in asymptomatic animals. Activated charcoal with a cathartic should be given every 6 hours while signs continue. A plain water enema is recommended if sustained-release products are consumed. Fluids do not enhance excretion, but fluid therapy should be given to help support blood pressure, aid in thermoregulation, and maintain renal function. Seizures often respond to diazepam or barbiturates. Heart rate, blood pressure, and blood gases should be monitored. Treatment is otherwise symptomatic and supportive. Signs generally resolve over 12 to 36 hours.

NOVEL ANTIDEPRESSANTS

Venlafaxine is a bicyclic antidepressant. It causes large increases in CNS levels of serotonin and norepinephrine and a small increase in dopamine levels.² Although it is rare for cats to willingly ingest medications, cats seem to readily eat venlafaxine capsules. Venlafaxine is well absorbed orally. Mild depression is seen at oral doses of 1 mg/kg PO. With increasing doses, other signs such as mydriasis, vomiting, tachypnea, tachycardia, ataxia, tremors, and agitation are commonly seen.

Bupropion is another novel antidepressant used in human medicine. It is also used to help people stop smoking. Bupropion causes increased levels of dopamine and, to a lesser

Classes of Antidepressants

TCAs	MAOIs	SSRIs	Novel Antidepressants
Amitriptyline	Isocarboxazid (Marplan)	Citalopram (Celexa)	Bupropion (Wellbutrin, Zyban)
Amoxapine	Phenelzine (Nardil)	Escitalopram (Lexapro)	Duloxetine (Cymbalta)
Clomipramine	Tranylcypromine (Parnate)	Fluoxetine (Prozac)	Maprotiline (Ludiomil)
Desipramine (Norpramin)		Fluvoxamine (Luvox)	Venlafaxine (Effexor)
Doxepin		Nefazodone (Serzone)	
Imipramine		Paroxetine (Paxil)	
Nortriptyline		Sertraline (Zoloft)	
Protriptyline (Vivactil)		Trazodone (Desyrel)	
Trimipramine (Surmontil)			

extent, norepinephrine in the CNS.² Absorption is very quick in dogs, and peak plasma levels are reached in 26 to 32 minutes.⁶ Severe signs, such as tremors and seizures, can be seen within 1 to 4 hours. Extended-release products can have a delayed onset. Overdoses of bupropion can cause vomiting, dyspnea, salivation, ataxia, seizures, arrhythmias, tremors, and hypotension.

Treatment for novel antidepressant overdoses is similar to that for SSRI overdoses.

INGESTION OF MULTIPLE DRUGS

Ingesting more than one class of antidepressant medication increases the likelihood of serotonin syndrome developing. These different medications have an additive effect in increasing CNS levels of serotonin. Other drugs, such as tryptophan, dextromethorphan, and lithium, act synergistically with antidepressants and can also lead to serotonin syndrome. Serotonin syndrome can cause changes in mental status (e.g., disorientation, vocalization) and behavior (e.g., agitation, depression), altered muscle tone or neuromuscular activity (e.g., stiffness, hyperreflexia, tremors, ataxia, seizures), hyperthermia, and diarrhea.⁵ Because of the severity of serotonin syndrome, it is much more difficult to treat than a simple antidepressant overdose.

In addition to symptomatic and supportive care, specific medications can be given to decrease serotonin levels in the CNS. Phenothiazines (e.g., acepromazine, chlorpromazine) are serotonergic antagonists that also have antimuscarinic and antihistaminic effects. They are the drugs of choice for treating serotonin syndrome in humans. Phenothiazines can be used to treat agitation; however, these drugs should be avoided if hypotension is present. Propranolol, a β -blocker, is also a serotonin receptor antagonist and may be used to counter tachycardia and hypertension.² Cyproheptadine is a nonspecific serotonin antagonist in addition to being an

antihistamine and appetite stimulant. Cyproheptadine has been used to treat agitation and vocalization in pets caused by serotonin syndrome (dogs: 1.1 mg/kg PO; cats: 2 to 4 mg PO).² Although there are no controlled studies, if the animal is vomiting, cyproheptadine may be crushed in saline and given rectally at the same dose.⁷

ROLE OF THE VETERINARY TECHNICIAN

Veterinary technicians have an important role in potential toxicity situations. It starts from the first contact with the owners and ends several days after the animal goes home. The first task is to get an accurate history from a potentially distressed client. Finding out what type of medication the pet was exposed to, how many pills are missing, and how long ago the ingestion occurred are all critical to help the veterinarian make the appropriate treatment decisions.

Once the animal has been admitted to the hospital, the technician's role changes to one of patient care. The technician must closely monitor heart rate, blood pressure, and body temperature as well as monitor for CNS signs. The status of animals affected by antidepressant overdoses can change quickly; therefore, the veterinarian should be notified as soon as any changes occur. Attentive monitoring by the technician can make the difference between a good and bad outcome.

CONCLUSION

Prognosis of antidepressant toxicoses depends on dose, treatment, and exposure to other medications. The outcome also depends on the overall health of the animal. Preexisting liver and/or renal disease can interfere with good outcomes because of inhibited metabolism and decreased excretion.

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