PEER-REVIEWED

The dangers of nicotine ingestion in dogs

Nicole C. Hackendahl, DVM, and Colin W. Sereda, DVM

A 10-year-old, 70.4-lb (32-kg) spayed female Labrador retriever mix was presented to the emergency service at the Virginia-Maryland Regional College of Veterinary Medicine for evaluation of hypersalivation, tremors, and disorientation. The dog had gotten outside at some point during that day and was exhibiting these clinical signs when the owner returned home from work.

At presentation, the dog was responsive but disoriented. Spinal reflexes in all four limbs were normal, but the dog exhibited incoordination and hypermetria. Generalized whole-body tremors were also noted. The dog's body temperature and heart rate were normal, and strong femoral pulses were present. The dog's respirations were rapid and shallow, and its mucous membrane color and capillary refill time were normal. The patient was salivating profusely.

Shortly after arriving at the hospital, the dog vomited. The vomitus consisted of aluminum foil, dog food, plant material, multiple cigarette butts, the remnants of a cigarette package, potato peels, and several other pieces of garbage. The vomitus had the distinct odor of cigarettes.

Blood was drawn for a complete blood count, serum chemistry profile, and serum nicotine assay based on the suspicion of nicotine toxicosis. The complete blood count results were normal. Serum chemistry profile abnormalities included mild increases in blood urea nitrogen (33 mg/dl; normal = 8 to 27 mg/dl), total protein (7.6 g/dl; normal = 5.4 to 7.2 g/dl), and albumin (3.9 g/dl; normal = 2.7 to 3.8 g/dl) concentrations. Marked lipemia and hemolysis of the sample were also noted.

"Toxicology Brief" was contributed by Nicole C. Hackendahl, DVM, and Colin W. Sereda, DVM, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610-01426. The department editor is Petra A. Volmer, DVM, MS, DABVT, DBVT, College of Veterinary Medicine, University of Illinois, Urbana, IL 61802.

About 15 minutes after the first vomiting episode, the dog vomited a second time, expelling a substantial volume of similar contents. Apomorphine hydrochloride was administered (0.25 mg dissolved in water and applied to the conjunctiva). An hour and a half after the first vomiting episode, the dog vomited a third time, and the contents appeared dilute compared with those of the previous two episodes. Visible clinical improvement was noted after the second vomition and again after the third. The tremors began to subside after the third vomiting episode, and the dog appeared to be less disoriented. The patient was still mildly ataxic and continued to salivate excessively. Activated charcoal (4 g/kg once) was administered orally, intravenous lactated Ringer's solution was given at a dosage of 3.8 ml/kg/hr, and the dog was hospitalized for close observation.

The fluid rate was decreased to 2.5 ml/kg/hr after six hours of treatment, and the dog rested quietly overnight. The next morning, the dog showed marked improvement. It was alert and responsive, although still ataxic. Five hours after the last reduction in the fluid rate, the rate was decreased to 1.3 mg/kg/hr, and five hours later, the fluids were discontinued. The dog was sent home that evening. The owner was instructed to closely observe the dog and gradually reintroduce food over two or three days. Four days after the initial incident, the owner reported that the dog appeared normal. The result of the serum nicotine assay, which was received five days after presentation, was 0.2 ppm.

Sources and toxicity of nicotine

Nicotiana tabacum is the principal source of tobacco today.[1] Products containing nicotine include cigarettes, cigars, chewing tobacco, snuff, insecticides, and nicotine gum, patches, inhalers, and nasal spray. In addition, nicotine has been used as an immobilizing agent in wild animals, but its narrow margin of safety has made this use extremely uncommon.[2] ➤

Continued

TABLE 1 Nicotine Content in Tobacco Products

Product	Nicotine Content	References
Cigarette	9–30 mg/cigarette*	2, 6
	3–8 mg/low-yield cigarette	1
Cigar	15–40 mg/cigar	1
Chewing tobacco	6–8 mg/g	1
Snuff	12–16 mg/g	1, 2
Nicotine gum	2–4 mg/piece	1, 2
Nicotine patch	8.3–114 mg/patch	1, 2
Nicotine nasal spray	100 mg/10 ml spray bottle; 0.5 mg/spray	1
Nicotine inhaler	10 mg/cartridge; 4 mg/puff	**

*The average cigarette contains 15 to 20 mg nicotine, so a box of 20 cigarettes would contain 300 to 400 mg nicotine.
**Source: Nicotrol: Nicotrol inhaler. http://www.nicotrol.com/inhaler/index.asp; February 2004.

Table 1 shows the amount of nicotine in various tobacco products. As stated above, some insecticides also contain tobacco. The registration of nicotine insecticides was discontinued in 1992, but these products can still be found.[1] Nicotine insecticides (nicotine sulfate) were available in dusts and sprays ranging from 0.05% to 4%.[2] Black Leaf 40 (Chemical Foundations), a specific brand of a concentrated nicotine insecticide, contained a 40% solution.[2] These solutions can be quickly absorbed through the skin or oral mucosa.[3]

In a human cigarette smoker, serum concentrations of nicotine range from 5 to 30 ng/ml after a single cigarette.[1] A typical smoker will strive to maintain a serum concentration of 30 ng/ml.[1] Nicotine gum chewers (of the 2-mg gum pieces) average plasma concentrations of 12 ng/ml.[4] Pipe smokers average plasma concentrations of 4 ng/ml.[4]

An approximate toxic dose of nicotine in nonhabituated human adults is 4 to 8 mg and in children is 1 to 2 mg.[1] Although one cigarette has a nicotine content of 9 to 30 mg, the nicotine delivered (through the intended route) is 0.5 to 2 mg.[1] In people, toxic blood concentrations are about 50 ng/ml.[1,4] A minimum lethal dose in dogs and cats is reported to be 20 to 100 mg, which may consist of one to five regular cigarettes, or one-fifth of to a whole regular cigar.[2,3,5-7]

Ingestion and toxicosis appear to be more common in young animals, namely puppies, perhaps as a result of their indiscriminant eating behavior.[5] Chewing tobacco contains additives such as honey, sugars, syrups, molasses, licorice, and other flavoring agents to increase palatability, which may increase the likelihood of an animal

Continued

ingesting these products.[2,5] However, toxicosis in small animals appears to be rare. Several factors may be responsible for this rarity. First, most tobacco products are relatively unpalatable. In addition, ingestion results in slow absorption of nicotine because of the stomach's acidic pH.[1,5] Finally, spontaneous vomition often occurs soon after ingestion because of nicotine's stimulation of the chemoreceptor trigger zone.[5]

Metabolism

Nicotine is a water-soluble alkaloid readily absorbed through the gastrointestinal tract, respiratory tract, skin, and mucous membranes.[1,2,8] As mentioned previously, ingested nicotine is poorly absorbed across the gastric mucosa because the low gastric pH keeps the nicotine ionized.[1] Absorption increases once the product reaches the intestines, because nicotine is more readily absorbed in an alkaline environment.[1,8] Smokeless tobacco and nicotine gums are buffered to increase the pH and enhance buccal absorption.[1]

The liver readily extracts nicotine, and removal is dependent on blood flow and subject to first-pass extraction.[8] The resulting half-life of nicotine in people is about two hours.[2,5] The half-life of nicotine in dogs is unknown. Nicotine has two principal oxidative metabolites, cotinine and nicotine-1'-N-oxide. Both of these metabolites are inactive and extracted by the kidneys.[1,4,8] Urinary excretion is pH-dependent, with excretion enhanced by a low urinary pH.[2,5,8] Renal excretion of unchanged nicotine varies from 2% to 35% of the total dose, depending on the urine flow and urine pH.[1] About 16 hours after ingestion, nicotine will be completely excreted through the kidneys.[2,5-7]

Mechanisms of action

Nicotine receptors are present in the autonomic ganglia, adrenal medulla, central nervous system (higher density in the limbic system, midbrain, and brainstem), spinal cord, neuromuscular junctions, and chemoreceptors of the carotid and aortic bodies.[1] Nicotine first stimulates and then depresses all levels of the nervous system.[7] It causes a rapid response via ligand-gated ion channels, increasing sodium and potassium permeability in the process of depolarization and excitation.[8] Nicotine is a rapidly acting sympathetic and parasympathetic ganglion depolarizer. At low doses, the ganglia are stimulated, and at high doses, a ganglionic blockade occurs. High doses of nicotine result in the initial stimulatory effects and then cause persistent depolarization and blockade of the nicotinic receptors.[2,3] Similar effects occur on the neuromuscular junction endplates.[8]

Clinical signs

Clinical signs of nicotine toxicosis are dose-dependent and can occur within one hour of nicotine exposure.[2,3] Low doses and the early phase of high-dose intoxication stimulate the central nervous system, leading to excitement, tremors, auditory and visual disturbances, incoordination, weakness, twitching, and possible convulsions.[2,5] High doses result in progression of the above signs to depression and descending paralysis associated with the depolarization and blockade of the neuromuscular junctions.[2] This blockade can lead to respiratory arrest and death.

Cardiovascular signs can include hypertension and tachycardia resulting from stimulation of the sympathetic ganglia and the adrenal medulla, in addition to sympathomimetic activation of chemoreceptors of the carotid and aortic bodies. Paroxysmal atrial fibrillation and cardiac standstill can occur because of vagal stimulation and vasomotor collapse.[5] Small doses can stimulate all autonomic ganglia, resulting in bradycardia due to vagus nerve stimulation and peripheral vasoconstriction due to sympathetic stimulation. High doses may block autonomic ganglia and result in skeletal muscle paralysis, vascular dilation, and hypotension.[2,6]

Respiratory signs often include tachypnea resulting from direct stimulation of the medulla oblongata and a reflex excitation of the carotid and aortic bodies.[5] Gastrointestinal signs include salivation, emesis, and diarrhea from parasympathetic stimulation.[1,2,5] Vomiting may occur soon after ingestion because of chemoreceptor trigger zone stimulation.[2] ➤

Continued

Diagnosis

Differential diagnoses include intoxication with strychnine, methylxanthines, tremorgenic mycotoxins, organophosphates, carbamates, and depressants.[2,3] Nicotine toxicosis can be diagnosed by direct observation of the ingestion; antemortem toxicologic analysis of blood, vomitus, gastric contents, and urine; or postmortem analysis of the liver, the kidneys, and other tissues.[2,5] Serum concentrations can be measured by spectrophotometry, thin-layer chromatography, high-performance liquid chromatography, fluorescence polarization immunoassay, and gas chromatography.[4] Postmortem findings in animals with nicotine toxicosis are usually nonspecific and include anoxia and internal organ congestion.[2,5]

Treatment and prognosis

Initial treatment consists of inducing emesis or performing gastric lavage, followed by activated charcoal administration. In addition, intravenous fluids may hasten renal elimination.[2,5] Urine acidification might increase excretion, as long as the patient is not acidotic. Gastric antacids are not recommended because they can increase gastric nicotine absorption. Monitor the patient's heart rate and blood pressure, and treat any abnormalities. Oxygen or ventilatory support may be necessary. Seizures can be treated with diazepam or barbiturates.[2,3] In cases of recent exposure, sedation with diazepam may be required. In patients with longer periods of exposure, stimulants such as phenylephrine (0.15 mg/kg slowly intravenously) or amphetamine sulfate (4.4 mg/kg subcutaneously) may be required.[3] Mecamylamine hydrochloride (Inversine Tablets—Targacept) is a direct nicotine antagonist used in people to treat hypertension, but it is only available in tablet form,[9] and its use has not been reported in dogs.

In dogs, the prognosis is grave to poor when large amounts of nicotine have been ingested.[2,5] The prognosis is good if an animal survives the first four hours.[2,5,7]

Conclusion

The patient described in this report had a nicotine serum concentration of 0.2 ppm, or 200 ng/ml. This concentration was sufficient to cause clinical signs of nicotine toxicosis and is well over the toxic serum concentration reported in people. But it was not lethal in this patient, and complete recovery was achieved with aggressive supportive therapy. Nicotine is available in many products, but nicotine toxicosis in small animals is uncommon, and reports in the veterinary literature are rare. Clinical signs are dose-dependent and are due to nicotine receptor stimulation at low doses and receptor blockade at high doses. Nicotine toxicosis is best diagnosed by directly observing the ingestion of nicotine products. The prognosis in dogs is grave when large amounts are ingested. However, the prognosis improves if the animal survives the first four hours after ingestion because of nicotine's short half-life. Treatment is aimed at removing sources of nicotine, decreasing absorption, and promoting continued clearance. Supportive care is given to address clinical signs.

REFERENCES

1. Salomon, M.E.: Nicotine and tobacco preparations. *Goldfrank's Toxicologic Emergencies*, 6th Ed. (L.R. Goldfrank *et al.*, eds.). Appleton and Lange, Stanford, Conn., 1998; pp 1145-1157.
2. Plumlee, K.H.: Nicotine. *Small Animal Toxicology*, 1st Ed. (M.E. Peterson; P.A. Talcott, eds.). W.B. Saunders, Philadelphia, Pa., 2001; pp 600-602.
3. Osweiler, G.D.; Carson, T.L.: Household drugs. *Handbook of Small Animal Practice*, 3rd Ed. (R.V. Morgan, ed.). W.B. Saunders, Philadelphia, Pa., 1997; pp 1279-1283.
4. Leikin, J.B.; Paloucek, F.P.: Diagnostic tests/procedures. *Poisoning and Toxicology Compendium with Symptoms Index*. Lexi-Comp Inc., Hudson, Conn., 1998; pp 879-1011.
5. Vig, M.M.: Nicotine poisoning in a dog. *Vet. Hum. Toxicol. 32* (6):573-575; 1990.
6. Kaplan, B.: Acute nicotine poisoning in a dog. *VM/SAC 63* (11):1033-1034; 1968.
7. Atkins, C.E.; Johnson, R.K.: Clinical toxicities of cats. *Vet. Clin. North Am. (Small Anim. Pract.) 5* (4):623-652; 1975.
8. Burrows, G.E.; Tyrl, R.J.: Solanaceae Juss. *Toxic Plants of North America*, 1st Ed. Iowa State University Press, Ames, 2001; pp 1104-1148.
9. Hsu, W.H.: Toxicity and drug interactions of levamisole. *JAVMA 176* (10):1166-1169; 1980. ■