

Topical Minoxidil Exposures and Toxicoses in Dogs and Cats: 211 Cases (2001–2019)

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ABSTRACT

Topical minoxidil is a medication for hair loss, initially available in the United States by prescription only and available since 1996 as an over-the-counter product. To determine the epidemiology of minoxidil exposures and toxicoses in dogs and cats, 211 dog and cat cases with topical minoxidil exposure were identified from the American Society for the Prevention of Cruelty to Animals Animal Poison Control Center database. In 87 cases with clinical signs of toxicosis (62 cats, 25 dogs), case narratives were reviewed and coded for exposure-related circumstances. Unintentional delivery, especially while pet owners applied minoxidil for his/her own hair loss (e.g., pet licked owner's skin or pillowcase, pet was splashed during a medication spill), was the most common cat exposure circumstance. Exploratory behavior (e.g., searching through trash) was the most common dog exposure circumstance. Clinical signs occurred in dogs and cats even with low exposure amounts, such as drops or licks. In patients that developed clinical signs, most developed moderate or major illness (56.0% dogs, 59.7% cats). Death occurred in 8/62 (12.9%) cats that developed clinical signs after the pet owner's minoxidil use. Pet owners should be educated on the risk of dog and cat toxicosis from accidental minoxidil exposure. (*J Am Anim Hosp Assoc* 2021; 57:■■■-■■■. DOI 10.5326/JAAHA-MS-7154)

Introduction

Topical minoxidil is available internationally as an over-the-counter treatment for androgenetic alopecia (pattern hair loss) in humans. It has also been used off-label as a treatment for various alopecic conditions in dogs, cats, and horses.^{1–4} However, minoxidil is a potent vasodilator. Oral minoxidil is a treatment for systemic hypertension through its vasodilatory effects via actions on the adenosine triphosphate-sodium channels in vascular smooth muscle cells.^{5,6} Topical minoxidil can be absorbed systemically, and adverse effects in humans include hypotension, tachycardia, myocardial infarction, elevated liver enzymes, and fetal malformations.^{7–10}

Children especially appear to be sensitive to the effects of topical minoxidil, possibly because of their small body size and/or thinner skin.^{11–13} Similar to children, veterinary patients can be exposed to topical dermatologic products used by other household members.^{14,15} Secondary exposure may occur especially with a product such as topical

minoxidil, which is applied daily and must be used long term for continued effect.

Because minoxidil toxicosis can also occur in dogs and cats,^{16–18} the purposes of this study were to provide information on the epidemiology of topical minoxidil exposures and toxicoses in dogs and cats. In particular, we sought to characterize the exposure circumstances that lead to dog and cat minoxidil toxicosis cases, as this can inform poisoning prevention strategies. Additionally, we sought to increase awareness that severe toxicosis can occur in dogs and cats exposed to even small amounts of topical minoxidil.

Materials and Methods

Epidemiologic and clinical information was obtained from the computerized record database of the American Society for the Prevention of Cruelty to Animals Animal Poison Control Center (APCC). The APCC is a 24 hr consultation service that receives calls from

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throughout the United States and Canada concerning incidents of animal poisoning from animal owners and practicing veterinarians. APCC staff collect the following information on each animal: species, breed, sex, age, body weight; number of animals exposed and at risk; number of affected animals; source of exposure; amount of product ingested; and assurance of exposure (whether observed [i.e., witnessed] or evidenced [e.g., empty and chewed medication packaging]). Information was obtained on time of onset, types and duration of clinical signs, serum biochemical alterations, pathologic findings, and response to treatment. Follow-up calls are made as deemed necessary to update records as to progression of clinical signs, response to treatment, and final outcome. The APCC veterinarian categorizes each incident on the basis of exposure history and clinical information available, expected clinical signs of toxicosis as described in the literature, amount ingested, and previous experience dealing with the agent (i.e., active ingredient). Incidents are categorized as toxicosis if all temporal, clinical, and historical data are consistent with the expected syndrome; as suspected toxicosis if clinical signs are characteristic of the expected syndrome, but some data are not available; as possible toxicosis if only a few signs are consistent with the expected syndrome; as doubtful if clinical signs and exposure history are not consistent with the expected syndrome; and as exposure only if no signs were present at the time of the call and none were reported on follow-up. The APCC database was searched for records of minoxidil cases involving dogs and cats from January 2001 through December 2019.

For all toxicosis cases, full APCC case records were reviewed to confirm route of exposure and illness level. Circumstances of exposure were coded into four categories using a modification of a previously published exposure circumstance categorization scheme for pediatric poisonings¹⁴: (1) mistaken identification (e.g., inadvertent use of minoxidil when intending to use another product), (2) exploratory behavior (e.g., from searching through the trash and licking or chewing on application materials or medication bottle), (3) unintentional delivery (e.g., accidental exposure of pet to topical minoxidil while attempting to apply the product to self), and (4) intentional delivery (e.g., direct application of minoxidil by pet owner to the pet for alopecia). Clinical outcomes were categorized as mild illness if signs were non-life-threatening and transient, requiring no or minimal veterinary intervention (e.g., administration of antiemetics) to resolve; moderate illness if signs were more intense or of longer duration, requiring some veterinary intervention (e.g., administration of IV fluid therapy) to resolve; major illness if signs were potentially life-threatening, generally requiring intensive veterinary intervention and/or resulting in long-term or permanent sequelae (e.g., renal insufficiency); and death if the animal was found dead, died, and/or was euthanized as a result of the toxicosis.

Results

Minoxidil exposure occurred in 294 cases (138 dogs, 156 cats). After excluding cases that involved exposure to other pharmaceutical agents in addition to minoxidil (49), cases involving oral minoxidil tablets instead of topical minoxidil (22), and cases in which the only clinical signs reported were considered to have a low likelihood of being from the agent (12), a total of 211 minoxidil exposures were included (78 dogs, 133 cats). For dogs, 53 (68%) incidents were classified as exposure with no signs of toxicosis, 10 (12.8%) incidents were classified as suspected toxicosis, and 15 incidents (19.2%) were classified as toxicosis. For cats, 71 incidents (53.4%) were classified as exposure with no signs of toxicosis, 17 (12.8%) incidents were classified as suspected toxicosis, and 45 incidents (33.8%) were classified as toxicosis.

Clinical signs of toxicosis developed in 25 of 78 dogs (32.1%) and 62 of 133 cats (46.6%). Onset of clinical signs ranged from within 1 to 67 hr after exposure. In both dogs and cats, vomiting and/or drooling was observed immediately to within a few hours after exposure, hypotension was recorded as early as 3 hr in a cat and 3.5 hr in a dog, and lethargy was observed beginning within 3–36 hr after exposure. In both dogs and cats, the most common route of exposure was oral only followed by combined dermal and oral exposure (**Table 1**). However, exposure circumstance differed by species. Exploratory behavior was the cause of exposure in 88.0% of clinical dogs, whereas 88.7% of cats were exposed through unintentional delivery (e.g., licking off owner skin or product splashed or spilled on cat; **Table 1**). The amount involved in a product splash or spill that led to clinical signs was sometimes small. In one cat that developed hypotension requiring hospitalization and IV therapy, the exposure amount was one drop that had splashed on the cat and then was licked off. In five dogs, the exposure involved eating discarded tissues or cotton swabs that had dried product on them.

In two cats, the product was intentionally applied for the treatment of alopecia by the pet owner without the guidance of a veterinarian, and these cases have previously been published.¹⁸ A liquid form of minoxidil, rather than foam, was involved in 67.8% (59 of 87) of clinical cases (41 cats, 18 dogs). The product form of topical minoxidil involved was unknown in four cases.

The amount of drug (dose) could not be estimated in 16 of 25 dogs (64.0%) and 55 of 62 (88.7%) cats. However, in many cases this was because the amount was so low that exposure could not be quantified through traditional units of measurement, such as milliliters. In 38 cases with clinical signs ranging from mild illness to death, exposure amount could only be reported in licks (**Table 2**). The product was licked from the following surfaces: site of application (owner scalp and/or hair, 28); pillowcase (3); owner hands (4); and the product applicator or bottle (3). A dose per body weight was able to be calculated in 10 cases. In these 10 cases, the lowest dose at which signs developed was a dog that received 0.79 mg/kg.

TABLE 1**Characteristics of Dog and Cat Cases Involving Topical Minoxidil and Resulting in Clinical Signs**

Characteristics	Dogs (n = 25)	Cats (n = 62)
Age*		
Adult	15 (60.0)	51 (82.3)
Elderly	4 (16.0)	6 (9.7)
Juvenile	5 (20.0)	5 (8.1)
Pediatric	0 (0)	0 (0)
Unknown	1 (4.0)	0 (0)
Exposure route		
Oral only	23 (92.0)	39 (62.9)
Dermal only	0 (0)	6 (9.7)
Oral and dermal	2 (8.0)	17 (27.4)
Unknown	0 (0)	0 (0)
Exposure circumstance†		
Exploratory behavior	22 (88.0)	3 (4.8)
Unintentional delivery	2 (8.0)	55 (88.7)
Mistaken identification	1 (4.0)	2 (3.2)
Intentional delivery	0 (0)	2 (3.2)
Illness level		
Mild	11 (44.0)	17 (27.4)
Moderate	9 (36.0)	20 (32.3)
Major	5 (20.0)	17 (27.4)
Death	0 (0)	8 (12.9)

Data are presented as n (%).

*American Society for the Prevention of Cruelty to Animals Animal Poison Control age categories defined as follows based on breed: pediatric = birth to weaning, juvenile = weaned to sexual maturity, adult = sexually mature, elderly > 80% of life expectancy.

†Exposure circumstance defined as follows: exploratory behavior = unintentionally obtained medication, for example, from searching through the trash and licking or chewing on application materials or medication bottle; unintentional delivery = accidental exposure to topical minoxidil while attempting to apply the product to self; mistaken identification = inadvertent use of minoxidil when intending to use another product; intentional delivery = direct application of minoxidil by pet owner to the pet for alopecia.

In 18 of 87 (20.7%) cases with clinical signs, the pet was exposed through a product spill. In 2 cat cases, the pet owner reported that toxicosis occurred even though the topical minoxidil application site had dried to the touch. In 4 cat cases, pet owners had tried decontamination measures, such as bathing of the paws or hair coat, in an effort to avoid clinical signs of toxicosis.

Hospitalization for treatment occurred in 82 of 87 (94.3%) clinical dog and cat cases. However, severe clinical signs also occurred in patients that were not hospitalized, with 1 case involving a dog that later collapsed at home. Eight of 62 (12.9%) cats with clinical signs died (Table 1). In both species, the following types of clinical signs were common: cardiovascular (hypotension, tachycardia); respiratory

TABLE 2**Clinical Dog and Cat Cases in Which Exposure Amount Was Reported in Licks**

Characteristics	Dogs (n = 2)	Cats (n = 36)
Surface licked		
Owner scalp or hair	2 (100.0)	26 (72.2)
Owner hands	0 (0)	4 (11.1)
Pillowcase only	0 (0)	3 (8.3)
Product applicator or bottle	0 (0)	3 (8.3)
Illness level		
Mild	1 (50.0)	12 (33.3)
Moderate	1 (50.0)	12 (33.3)
Major	0 (0)	11 (30.6)
Death	0 (0)	1 (2.8)
Veterinary medical care		
Hospitalization	2 (100.0)	35 (97.2)
IV therapy	1 (50.0)	35 (97.2)
Supplemental oxygen	0 (0)	6 (16.7)
Diagnostic imaging	0 (0)	13 (36.1)

Data are presented as n (%).

(tachypnea); and gastrointestinal (anorexia, vomiting; **Figures 1, 2**). Other reported signs included lethargy, neurologic changes, and biochemical changes such as azotemia or electrolyte abnormalities (**Figures 1, 2**). Hypertrophic cardiomyopathy was diagnosed in 4 cats via imaging during the course of hospitalization for minoxidil toxicosis.

Discussion

We report 87 cases of dogs and cats that experienced clinical signs of toxicosis after exposure to topical minoxidil. Previous publications on dog and cat minoxidil toxicosis have been limited to case reports and experimental studies in laboratory animals.^{16,18,19} Ours is the first study to document that severe clinical signs can occur in dogs and cats exposed to extremely low doses of topical minoxidil, such as one drop or 1–2 licks (Table 2). Using a modified pediatric toxicosis exposure categorization system,¹⁴ our study is also the first to characterize the household circumstances that lead to dog and cat topical minoxidil exposures. Particularly in cats, exposure was often secondary to a household member's use of topical minoxidil. Before our study, no cat cases of topical minoxidil toxicosis secondary to human use had been published. Additionally, both dogs and cats were accidentally exposed to topical minoxidil through exploratory behavior, similar to the situation of pediatric oral exposures to topical minoxidil.^{11,19,16} Clinical signs of toxicosis occurred in cases after the product had dried to the touch after application and after at-home decontamination steps by owners, such as bathing. Toxicosis also occurred in pets that did not

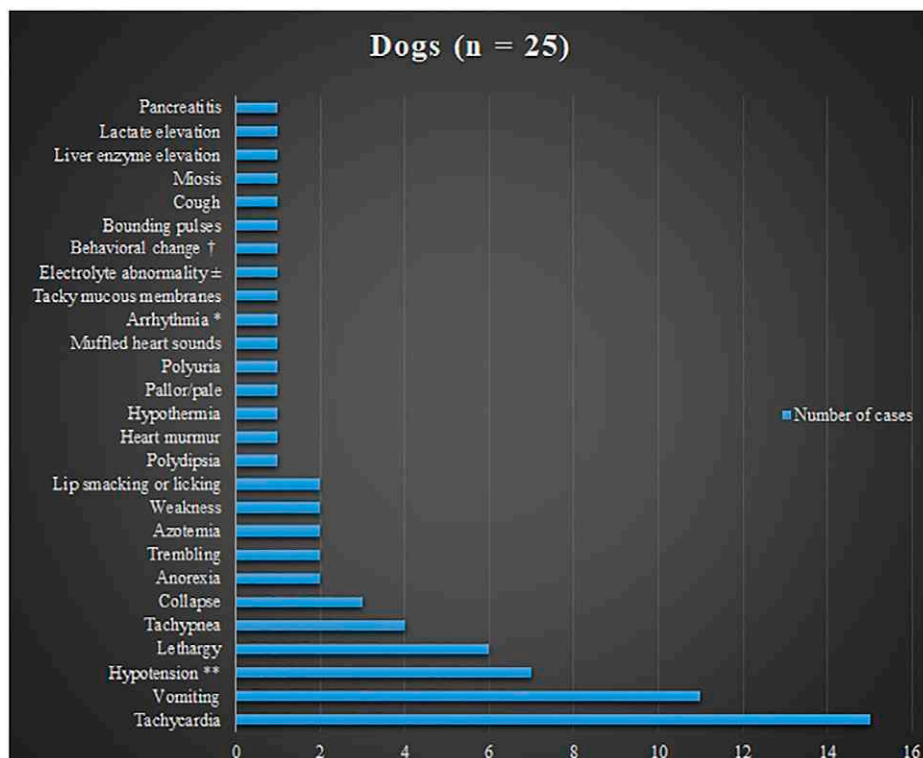


FIGURE 1

Clinical findings in dogs with topical minoxidil toxicity. *One dog each with ventricular tachycardia, premature ventricular contractions, and unspecified arrhythmia. ±One dog with hyponatremia, hypokalemia, and hypochloremia. †Subdued behavior in one dog. **Hypotension as defined and reported by the attending veterinarian.

have direct contact to a person's treated skin but rather were exposed via contact with other surfaces such as pillowcases that had contact with minoxidil-treated scalps.

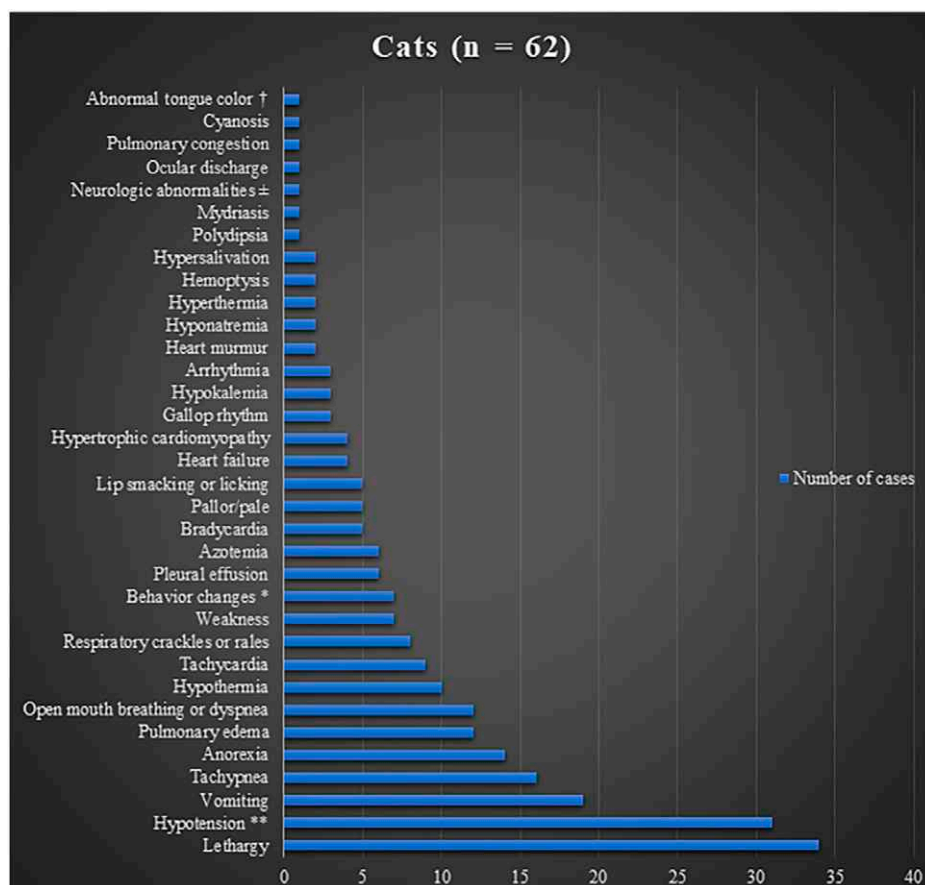
Following topical minoxidil exposure, 53.4% of cats and 68% of dogs developed no clinical effects. These percentages are consistent with data from animal poison control centers, which report that 57–63% of animal exposures to toxicants do not result in development of clinical signs, generally due to insufficient level of exposure to induce toxicosis, self-decontamination (e.g., spontaneous vomiting), or human intervention (e.g., induced vomiting, other decontamination measures).^{20,21} However, in the dogs and cats that did develop clinical effects from minoxidil exposures, the severity scores of clinical signs are skewed toward being more severe when compared with overall poison control center data (Figure 3).^{20,21} Additionally, more topical minoxidil cases occurred in cats than in dogs, and this is in contrast to other toxicants, with dogs making up 86% of U.S. poison control cases (Figure 4).²² This may be because most topical minoxidil cases were exposed through unintentional delivery instead of exploratory behavior, as expected for most other toxicants in dogs and cats.

Juveniles make up more than a third of dog (34%) and cat (36%) cases reported to poison control centers, but in this study juveniles were

involved in only 20% of canine cases and 8.1% of feline cases (Table 1), whereas adults represented a majority of dog (60%) and cat (82.3%) cases. The cause for this age difference between topical minoxidil and other toxicants is unknown. However, a prior study of dog and cat toxicosis cases involving a human-labeled dermatological topical product also found that adults represented a majority of cases (59.4%).¹⁵

A variety of clinical signs were observed in the dogs and cats exposed to topical minoxidil. Most of these signs were attributed to the active ingredient in the product because minoxidil can result in hypotension, pulmonary edema, arrhythmias, tachycardia, pleural effusion, myocardial damage, and heart failure. Other findings were also considered related to the vasodilation and hypotension: hypothermia, azotemia from decreased renal perfusion, and seizure from cerebral hypoxia. Additionally, topical minoxidil products contain a high amount of alcohol and propylene glycol. Both of these ingredients can cause central nervous system depression, ataxia, and nauseous behaviors (anorexia, licking lips, vomiting),²³ and these clinical signs were observed in some dogs and cats exposed to topical minoxidil products (Figures 1, 2).

Hypertrophic cardiomyopathy was diagnosed via imaging in a small number of cats while hospitalized for topical minoxidil exposure.

**FIGURE 2**

Clinical findings in cats with topical minoxidil toxicity. * Behavior changes such as increased vocalization, hiding, and inappropriate urination.

± Ataxia, trembling, and seizure in one cat. † Reddened tongue margin in one cat after licking topical minoxidil from the owner's scalp and hand.

** Hypotension as defined and reported by the attending veterinarian.

Although these cats had a history of being clinically asymptomatic before the minoxidil exposure, the prevalence of asymptomatic hypertrophic cardiomyopathy in cats may be as high as 25%.²⁴ Thus, it is possible that topical minoxidil acted as a precipitating factor for the development of clinical cardiac and respiratory signs in some cats with previously undetected hypertrophic cardiomyopathy.

Aside from dose, species and body size may be a factor in the severity of topical minoxidil toxicosis. Topical minoxidil appeared to be more toxic in cats than dogs. Cats may be more prone to developing prolonged and severe signs because minoxidil requires glucuronidation for metabolism, a pathway that is deficient in cats.²⁵ Additionally, we believe that species differences in pet-to-human interactions may play a role in topical minoxidil toxicoses. Cats especially may be able to reach a person's treated scalp for licking behavior when the person is seated by perching on the back cushions of sofas and armchairs. Smaller-size animals such as cats may sleep at the head of the bed and thus may have more exposure to a person's treated scalp.

Our study analyzed cases voluntarily reported to the APCC. Similar to other studies using poison control center data, other exposures to topical minoxidil may not have been reported and some cases may not have sought any medical advice or treatment. Thus, this study may underestimate both the number and severity of dog and cat exposures and toxicosis from topical minoxidil. Information provided by the pet owner may be subject to recall or reporting bias, and this may have led to miscategorization of exposure circumstances for some cases. Another limitation of this retrospective study is that the exact dose of topical minoxidil could not be determined in all cases. The minimum toxic or lethal dose for this drug is not well established in the literature. However, even if the product dose was known in each case, it may not have been possible to determine the systemic level of minoxidil in the animal. For dermatologic topicals, percutaneous absorption varies depending on the carrier used, area in which the product was applied, and the health of the treated skin. Additionally, in dogs and cats, both

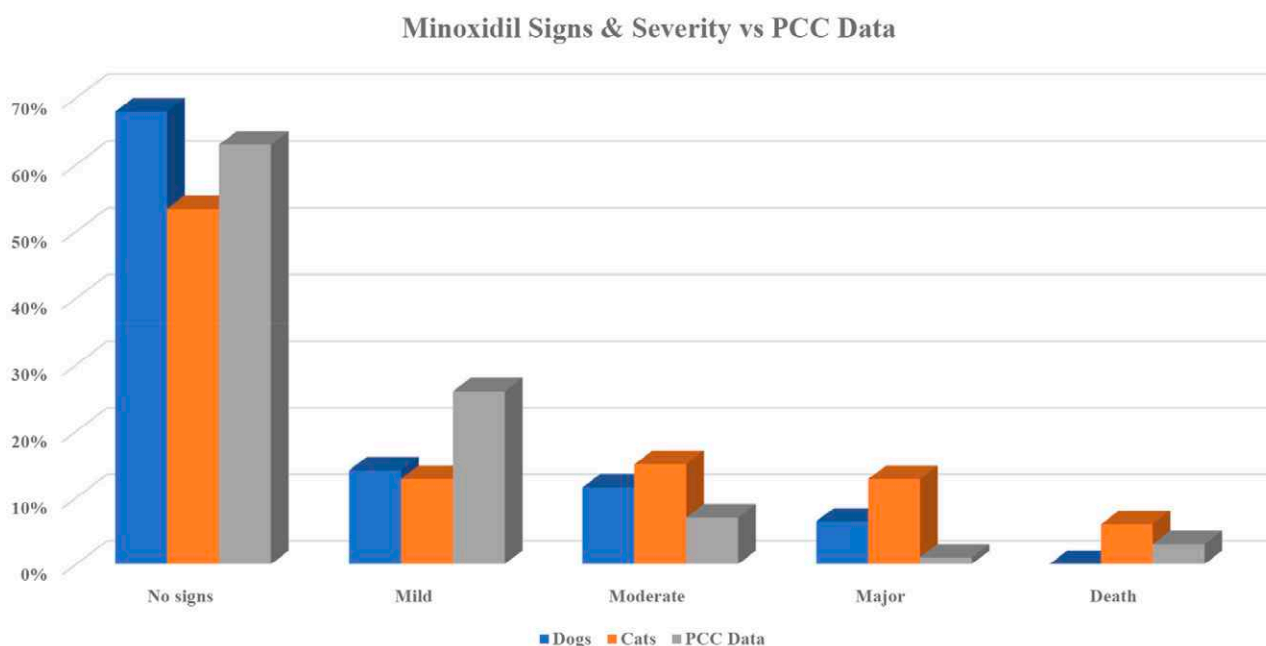


FIGURE 3

Signs and severity of dog and cat cases involving topical minoxidil in comparison to overall PCC data.²¹ PCC, poison control center.

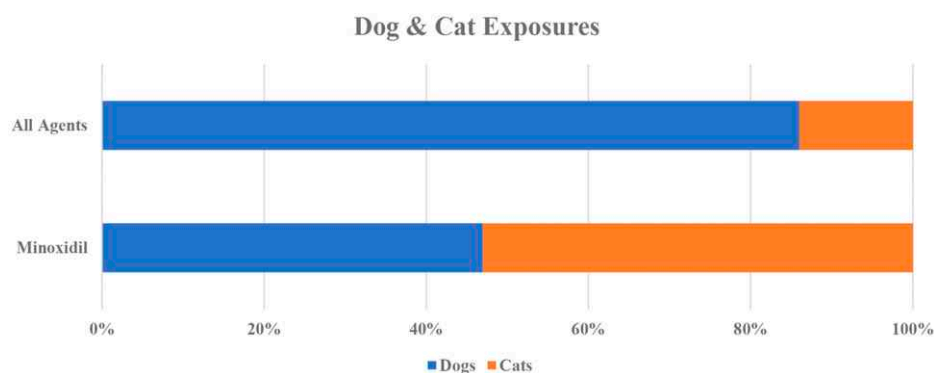


FIGURE 4

Dog versus cat exposures for topical minoxidil in comparison to exposures to all agents reported to animal poison control centers.²²

an oral and dermal route of exposure to dermatologic topicals may occur because of grooming behavior.^{2,15}

Multiple medication storage tips have been published to prevent accidental poisonings from medications.²⁶ Although our study was not designed to evaluate the efficacy of specific interventions to prevent minoxidil poisoning, we believe various common-sense measures could reduce the likelihood of accidental poisonings in dogs and cats. Do not allow pets to have access to the room in which the product is applied, sites of application, or surfaces that may have product transfer. Because topical minoxidil is applied daily for the treatment of human alopecia, this may mean that pet owners who use topical minoxidil will need to significantly change their behaviors. For

example, pet owners using topical minoxidil may need to refrain from allowing their pets to sleep with them because the product can transfer to pillowcases and/or be licked off while the pet owner sleeps. In households with dogs, safely store topical minoxidil to avoid exposure through exploratory behavior. Any trash that may have product residue such as paper towels or empty bottles should be securely stored away from pets. Packaging changes by the manufacturers of topical minoxidil product to reduce spills could also decrease the risk of accidental exposures and poisonings to pets.

We recommend that veterinarians educate pet owners about the risks of topical minoxidil and ask specifically about household minoxidil use when obtaining a patient history. We believe it is likely that

some minoxidil toxicosis cases are not being identified because some pet owners perceive dermatologic topical medications as being more benign than oral medications and do not report them as medications or potential toxicants to pets unless specifically asked.²⁷ Additionally, the over-the-counter status of minoxidil in the United States may mistakenly lead pet owners to believe the medication is benign to dogs and cats. No information currently exists on minoxidil product labels warning pet owners about the risks of even low exposures to dogs and cats. In multiple cats, nonspecific behavioral changes such as lethargy or hiding preceded the development of severe cardiorespiratory signs. Thus, early recognition through increased veterinarian and pet owner awareness could reduce harm and deaths by enabling prompt and aggressive treatment.

Conclusion

Pets in households with topical minoxidil use may be at risk for toxicosis even with low exposure amounts. Clinical signs occurred in dogs and cats even with exposures measured only in drops or licks. In households with human topical minoxidil use, inform pet owners of the risk of dog and cat toxicosis from accidental minoxidil exposure. Minoxidil is not recommended as a treatment for alopecic dogs and cats owing to the risk of severe toxicosis. ■

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