PROPER USE OF IVERMECTIN IN CATS

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Large animal formulations of ivermectin should never be left in areas where cats have access

vermectin belongs to a family of compounds produced by the microorganism Streptomyces avermitilis, which was first isolated from soil in Japan.¹ The structure of ivermectin is similar to macrolide antibiotics, but it appears to lack any antibacterial or antifungal activities. Dosages at microgram levels are used to treat numerous external and internal parasites in a variety of species, including cats, dogs, horses, cattle, sheep, swine, and even humans.

Ivermectin was sold commercially on the international market in 1981 and was licensed for sale in the United States in 1983.² The drug was approved as a feline heartworm preventative in 1996.³ Ivermectin has proven to be a very valuable drug to veterinarians in that when given at the appropriate preparation and the recommended dosage, it has a wide margin of safety in all sizes and breeds of cats.

RECOMMENDED AND EXTRA-LABEL USE

Ivermectin is approved by the FDA for use as a heartworm preventative in cats. The recommended minimum dose in cats is 24 μ g/kg of body weight.

Although manufacturers do not recommend use outside of approved label instructions, the FDA allows extralabel use under the specific conditions of the Animal Medicinal Drug Use Clarification Act.^a Ivermectin prepara-

^aFor more information about this act, visit www.fda.gov/cvm/index/amducca/ amducatoc.htm.

tions formulated for sheep and cattle are the most common forms of the drug used extralabel in cats and dogs (for heartworm prevention).¹ Although extralabel use of ivermectin is not recommended by product manufacturers, uninformed but well meaning owners sometimes use large animal formulations as treatment for parasites in an attempt to save money. However, it is extremely difficult to titrate the dose from a product meant to treat a 1,200lb horse to safely treat a 10- or 12-lb cat; in addition, dosing errors are not uncommon. Many owners are unaware that the dose for cats must be in micrograms (µg), not milligrams (mg) per kilogram.

In cats, ivermectin is also used at extralabel doses to treat ectoparasites. A single dose of 200 µg/kg SQ has been used to treat *Otodectes cynotis* (ear mites).¹ However, a topical product (Acarexx Otic Suspension, IDEXX Laboratories, Westbrook, ME) has been approved to treat adult ear mites in cats and kittens 4 weeks of age and older. Ivermectin is also considered effective against *Notoedres cati* (mange) at 400 µg/kg SQ and has been used to treat *Cheyletiella* spp infestation in cats, especially in large catteries.¹

Ivermectin Formulations^a

Cats: Oral tablets Cattle: Pour-on, paste, and injectable Dogs: Oral tablets Horses: Paste and injectable Sheep: Oral drench Swine: Injectable

^{*a*}POISINDEX Editorial Staff: Ivermectin and related agents. POISINDEX System, vol. 121. Englewood, CO, Micromedex.

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MECHANISM OF ACTION

In nematodes and arthropods, ivermectin binds to glutamate-gated chloride channels in peripheral neurons. These channels do not exist in mammals.4 The generally accepted mode of action is that ivermectin produces its toxic effects in mammals by increasing the release and binding of y-aminobutyric acid (GABA) at certain nerve synapses in the central nervous system. The wide margin of safety in mammal species may be explained by the fact that, in mammals, GABA-mediated neurotransmission is restricted to the central nervous system, and ivermectin does not normally penetrate the mammalian central nervous system.²

Mammals are generally unaffected by appropriate doses of ivermectin because of the blood-brain barrier exclusion of ivermectin. Only a few canine breeds, such as collies, have a genetic mutation that results in the blood-brain barrier being defective at excluding ivermectin.1 Additionally, the exclusion of ivermectin by the blood-brain barrier can be overcome in any species with a sufficiently high dose of ivermectin. In simple-stomached animals, oral ivermectin is 95% absorbed.5 Absorption after oral dosing is more rapid than subcutaneous administration, although there is greater bioavailability after subcutaneous administration.5 Ivermectin bioavailability has been reported to be lower in cats; therefore, a higher dose is required for the prevention of heartworm disease.5 Ivermectin concentrates in the liver and body fat.6 It is excreted in the feces and has a low degree of liver metabolism. The persistence of the parent compound in the body may partly explain the long half-life, which is reported to be 2 to 3 days.

CLINICAL SIGNS

Clinical signs of toxicosis may include depression, mydriasis, blindness (especially in cats), weakness, recumbency, ataxia, and coma. Less frequently reported signs include abnormal behavior, tremors, and seizures. Bradycardia, sinus arrhythmia, and hyperthermia are also possible. No lesions have been found on necropsy. Signs usually diminish over several days, and most animals completely recover within 2 to 4 weeks. There was an unpublished report of a cat in a coma for 18 days.⁷

TOXICITY

Cats as well as dogs may be overdosed with ivermectin because of inappropriate, extralabel use of cattle, sheep, or horse products. In addition, careless owners may also leave large animal formulations in areas that cats may have access to. For example, an unused portion of a syringe of horse dewormer paste may be left lying out in the barn or on a counter and may be discovered by a cat that then licks residue or drippings from the syringe.

Doses large enough to achieve serious toxicosis are not likely to be reached through accidental ingestion of heartworm preventive tablets. For example, serious toxicosis is unlikely to occur with the ingestion of multiple heartworm preventive tablets. However, if exposure to multiple heartworm preventive tablets occurs, the dose should still be calculated to verify a low level of risk.

Although uncommon, signs of toxicosis have been reported in cats at the extralabel dose of 200 μ g/kg.⁷ The toxicity of ivermectin products may have a cumulative effect, which can vary with species, breed, and age of the animal.² In general, signs may occasionally be delayed for 2 to 3 days in any species; however, acute toxic signs in cats may appear within 10 hours of ingestion.⁶

DIAGNOSIS AND TREATMENT

Diagnosis of ivermectin toxicosis in cats may be made by evaluating clinical signs and obtaining a complete history. Although it would be useful to know the heartworm status of a cat prior to initiating therapy, unlike in dogs, adverse effects are not expected with prophylaxis in heartworm-positive cats. If ivermectin toxicosis is suspected, serum blood levels can be

determined; however, this may take several days, which may not aid in diagnosing acutely ill animals. If a cat is presented within 2 hours of ingestion, emesis can be induced with hydrogen peroxide or xylazine. Multiple doses of activated charcoal with a cathartic should be given every 8 to 12 hours.7 The cathartic should only be given every third dose to prevent diarrhea. The cathartic of choice is 70% sorbitol.7 Repeated doses of activated charcoal may be beneficial in lessening the half-life in animals because of the possible enterohepatic recycling of ivermectin.6 Care should be taken when administering activated charcoal to small or dehydrated animals or with multiple dosing to avoid serious electrolyte derangements. If ivermectin was recently administered by subcutaneous injection and lifethreatening toxicosis is anticipated, it may be possible to lessen the fraction absorbed by surgical excision of the injection site.6

Symptomatic and supportive care is a must. Good nursing care is most important because affected animals may be hospitalized for days to weeks. When treating a cat with ivermectin toxicosis, patience is required from both the owner and clinician.⁷ The long periods of recumbency require appropriate bedding, frequent turning of the cat, managing of body temperature, and other standard treatment and supportive care. If bradycardia is present, atropine may be used; however, overadministration of atropine should be avoided to reduce the risk of ileus.⁶

The GABA–antagonist picrotoxin is sometimes recommended in human literature but is not currently available to veterinarians. Although physostigmine is also recommended in human literature, it is not recommended for cats as it may induce seizures and is very short acting.⁷

PROGNOSIS

If clinical signs are of a rapid onset (within 2 to 3 hours), this may indicate a high level of exposure and, therefore, a more guarded prognosis. A

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slower onset (6 hours), may indicate a lower level exposure and a more favorable outcome.⁶

CONCLUSION

Ivermectin is a valuable drug that is used to prevent heartworm disease in cats and prevent internal and external parasites in numerous other species. Inappropriate use, however, can cause toxicosis, which can result in blindness and prolonged coma in cats. Proper fluid therapy and maintenance of electrolyte balance, nutritional support, and prevention of secondary complications as well as the previously discussed nursing care can result in a successful outcome.

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