PERMETHRIN SPOT-ON TOXICOSES IN CATS

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SUMMARY

Spot-on insecticides are becoming popular type of flea control for pets. Spot-on products available include those containing fipronil, imidicloprid, methoprene, and permethrin. Currently, over 15 brands of permethrin spot-on products are labeled for "use in dogs only." These products contain high concentrations (45-65%) of permethrin insecticide and are becoming a very popular choice for flea and tick control for dogs. Cats are highly sensitive to permethrin and inappropriate or accidental application of these products could be fatal. Though they have a wide margin of safety when used appropriately on dogs, even small amounts of permethrin spot-on products can cause severe clinical signs in cats. Indications of this species sensitivity have been documented by the APCC. In most cases, the owner applied the concentrated permethrin-containing product to cats accidentally or intentionally. In some situations, the exposure seems to have resulted when the product was used on the dog and cats were playing with the dog. (ASPCA, APCC, Unpublished data, 1995-1997.) (Vet. Emerg. Crit. Care, 10:103-106, 2000)

PERMETHRIN

Pyrethrins are derived from a combination of six insecticidal esters (pyrethrins, cinerins, and jasmolins) that are extracted from dried chrysanthemum flowers. [3,4,5] Permethrin (3-phenoxyphenyl)-methyl(+)cis-trans-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate) is a synthetic pyrethroid insecticide. Permethrin is used in agricultural and household insecticides and also in flea control preparations. [2,3,4] Permethrin has been shown to be effective against insects and are considered to have low toxicity in most mammalian species. [4] They are fat soluble compounds that undergo rapid metabolism and excretion after oral or dermal absorption. [2] Rapid hydrolysis of ester linkage in digestive tract results in low oral toxicity. [4]

Permethrin is a neurotoxicant. [2] The mechanism of action of permethrin is similar to those produced by organochlorines, such as DDT, and involves interference with the axonal sodium gate. [2,3,5] Permethrin is classified as producing a Type I syndrome. Type I pyrethroid esters affect the sodium channels in nerve endings. [2,3,4]

During normal membrane depolarization, sodium channels open and permit an influx of sodium ions into the nerve axon. [2] Type I pyrethroids act on sodium ion channels by decreasing peak sodium conductance, prolonging the sodium conductance, and suppressing potassium conduction. [4] Decreased conductance of sodium causes inactivation of the action potential. [2] Due to this action, sodium influx is prolonged and the closing of the sodium activation window is delayed. This can result in increased and prolonged sodium current. A blockage of impulse conduction occurs because depolarization does not occur. The result is repetitive nerve firing. [2,3,4] Glucuronidation is another pathway of permethrin metabolism and this may be a possible explanation for their sensitivity since cats are deficient in glucuronidase transferase.[6] Permethrin has also been shown to inhibit Ca2+, Mg2+-ATPase, which would result in increased intracellular calcium levels causing increased neurotransmitter release and postsynaptic depolarization. [3] Pyrethroids also inhibit various adenosine triphosphatases including the calcium ATPase and the calcium magnesium-ATPase in nervous tissue.[4]

The effects at the pre-synaptic nerve ending are most likely responsible for the clinical signs of toxicosis. In the insect, Type I syndrome is shown to cause restlessness, incoordination, and paralysis. [3] However, in the rat, Type I syndrome causes hyperexcitation, aggressiveness, hyperaesthesia , and whole body tremors. [3,4] The oral LD50 has been reported to be 2000mg/kg in the rat. [4] The minimum lethal dose of permethrin has not yet been established in cats. The specific reason for the sensitivity of the cat is also unknown. Pyrethroids are metabolized by ester

hydrolysis and through oxidation by liver microsomal enzymes. [4] Species susceptibility to permethrin is likely dependent on the nature of the tissue esterase, the level of activity detected, the substrate specificity, and the rate of hydrolysis encountered. [3] Since hydrolytic enzymes degrade pyrethroid esters, it is suspected that the species susceptibility of permethrin could be due to the rate of hydrolysis being slower in cats than other species. [3]

CLINICAL SIGNS

According to APCC public database information, the clinical signs most commonly seen with permethrin toxicosis in cats are generally related to the central nervous system. Hyperesthesia, generalized tremors, muscle fasiculations, hyperthermia, and seizures are the most common signs seen. [1,7,8] Clinical signs can develop within hours or may be delayed up to 72 hours. Clinical signs generally last 2-3 days.

DIAGNOSIS

The diagnosis of permethrin toxicosis is primarily based upon exposure history and the development of associated signs. [2,4] Permethrin analysis could be performed on skin or hair samples to confirm exposure. In vivo tests to confirm permethrin are not yet available because of a lack of reference values. [2,4]

Other toxicological rule outs would include exposure to strychnine, human medications such as pseudoephedrine or amphetamines, bromethalin rodenticides, tremorgenic mycotoxins, nicotine, and lead. In addition, encephalitis, epilepsy, hypoglycemia, hypocalcemia, hepatic encephalopathy, and traumatic damage should be ruled out.

TREATMENT

The treatment of permethrin toxicosis in the cat can be challenging. Fortunately, when cats are treated early and aggressively, most will recover without sequelae. With permethrin toxicosis, seizure control and stabilization is a priority. Prolonged uncontrolled seizures could cause cerebral edema, irreversible brain damage, traumatic damage, and break down of muscle tissue leading to a myoglobinuria-induced nephropathy. Seizures and tremors can be best managed with intravenous methocarbamol, which is a centrally acting muscle relaxant structurally related to guaifenesin. [7,8] For mild tremors, a dose of 44mg/kg could be used and for controlling moderate to severe tremors or seizures 55-220mg/kg is recommended. [7,8,9] Half the dose should be given rapidly (do not exceed 2ml per minute when injecting IV), then the rest to effect. Depending on the reoccurrence of signs, methocarbamol may be repeated; however, a dose of 330 mg/kg/day should not be exceeded. [7,8,9] Other options for seizure control include propofol, barbiturates, diazepam, or inhalant anesthetics. Gas anesthesia would be indicated when seizures are refractory to all other types of therapy. [10]

Once the seizures are controlled, the animal should be examined thoroughly. Fluids may be needed to correct the hydration level. Hyperthermia can occur as result of muscle fasciculation or seizures. [2,10] Typically, hyperthermia is corrected once tremors are controlled. Aggressive cooling, by means of ice baths or cold water enemas, may result in hypothermia and should be avoided. All cooling measures are stopped when rectal temperature reaches 102° F, to prevent rebound hypothermia. [10] Following stabilization, the cat should be bathed thoroughly to remove the product from its fur. Bathing is most effective when a mild detergent is used. [7,8,11] Despite bathing, clinical signs often continue for several days. Supportive care should be given as needed until the cat completely recovers.

CASE STUDY

A 2-year-old 4.5-kg cat was presented to an emergency clinic showing severe tremors. The owner had purchased a flea control product from a grocery store and had applied one vial to the cat the evening before. The product was identified as containing 45% permethrin. The cat appeared to be completely normal until the next afternoon, when the owner noticed the cat's ears and whiskers were twitching. A few hours later, the cat had two brief seizures and then started tremoring. The veterinary staff contacted the APCC for treatment recommendations. The APCC veterinarian recommended controlling the tremors with 100mg/kg IV of methocarbamol repeated as needed, not to exceed a total dosage of 330mg/kg per day. Once the tremors were controlled the attending veterinarian examined the cat and determined all other physical parameters were normal. The APCC veterinarian then advised bathing the cat with mild dishwashing detergent and monitoring for reoccurrence of tremors over the next several days. The case was followed up three days later. At that time, the attending DVM said that the cat had been successfully treated

according to APCC recommendations. The tremors did reoccur over the next 48 hours, but were controlled adequately. The cat was released to the owner fully recovered.

CONCLUSION

Although most cats will recover with veterinary care, the best way to avoid serious problems is by educating pet owners to use products strictly by their label directions. Advise clients using flea care products to read and follow label instructions completely before using them on or around their pets. Products that are labeled for "dogs only" should never be used on cats.

REFERENCES

1. ASPCA Animal Poison Control Center. Unpublished data. Urbana, Illinois. 1995-1997.
2. Hansen, SR: Pyrethrins and Pyrethroids in Dogs and Cats, Compendium on Continuing Education, Vol.16, No 6, June 1994; pp 707-712.
3. Ecobichon, Donald J.: Toxic Effects of Pesticides, Casarett & Doull's Toxicology, 5th edition, McGraw-Hill, New York. 1996; pp 643-689.
4. Beasley, Val R., et al: A Systems Affected Approach to Veterinary Toxicology, Urbana, University of Illinois college of Veterinary Medicine, 1997:178-180.
5. Saunders, Stephen D. Pesticides, Principles and Methods of Toxicology, 3rd Edition. Raven Press, New York, 1994: 389-415.
6. Meyer, Kathryn E. *Toxicois in cats erroneously treated with 45-65% permethrin products.* JAVMA, Vol 215, No 2, July 1999; 198-202.
7. Volmer PA, Kahn SA, Knight MW, et al. *Warning against use of some permethrin products in cats.* Letter to the editor. J am Vet Med Assos. Vol 213, No. 6. September; pp 800-801.
8. Volmer PA, Kahn SA, Knight MW, et al. *Warning against use of some permethrin products in cats.* Letter to the editor. Veterinary Medicine. Volume 93, Number 12. December 1998; pp???
9. Plumb DC: Veterinary Drug Handbook 3rd Edition, St. Paul, MN, PharmVet Publishing, 1999; pp 412-413.
10. Podell, Michael, Seizures and Sleep Disorders, Handbook of Small Animal Practice, 3rd Edition.W.B. Saunders Company, Philadelphia, 1997:220-229
11. Poisindex® editorial staff: Pyrethrins (Toxicologic Managements). Poisindex® System Vol. 100 (B.H. Rumack et al.,eds) Micromedex, Englewood, Colorado. Expires June 2000.