



Risk Factors and Determinants of Poisoning by Ivermectin and Deltamethrin in Routine of Small Animal Medical Clinics

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Abstract

Antiparasitic drugs stand out as important causative agents of poisoning in veterinary medicine. Cases of poisoning by ivermectin and deltamethrin are common in domestic animals, due to indiscriminate use, which requires some care with administration. This article aimed to investigate and describe, based on the literature, risk factors and determinants of poisoning by ivermectin and deltamethrin used in the medical clinic of dogs and cats. The results showed that some species of parasites from companion animals have relevance in public and environmental health due to their zoonotic potential, and need to be combated pharmacologically. However, treatments with ivermectin and deltamethrin require careful administration, since iatrogenic intoxications are highly prevalent and are associated with the fact that these antiparasitic drugs are low-cost medications that are easy to acquire by the population, without requiring a veterinary prescription. Another risk factor is that the age of the animals is lower than that indicated for the use of these antiparasitic drugs. Due to the recklessness of tutors and employees of agricultural establishments, preventive actions are necessary to reduce the incidence of drug poisoning in pets, and it is necessary to raise awareness among the population regarding the use of antiparasitics, which can be toxic to animals when administered in contraindicated situations.

Keywords: Antiparasitics; Dogs; Iatrogenic Science; Public Health

Introduction

Parasitic infections are of great importance in domestic animals, both in the field of veterinary clinic and in public health. Although companion animals, particularly dogs and cats, play an important role in people's development and social, physical and psychological well-being, they can also pose risks of disease transmission due to their proximity to humans [4].

Dogs, for example, are unwittingly involved in the transmission of more than sixty zoonoses, among which parasitic ones stand out [8]. Therefore, epidemiological studies of parasitic diseases in pets are important in public and veterinary health, as the benefits pro-

vided by animals to humans can be lost if the health of animals is not taken into account [6].

Some species of parasites, which affect dogs and cats, have relevance in public and environmental health due to their zoonotic potential. Studies show that dogs can be a source of environmental contamination through endoparasites, which requires greater attention to the health of these animals, with a view to reducing risk factors for the incidence of zoonoses in the population [22].

Among the parasites that can be transmitted from pets to humans, those belonging to the genera *Ancylostoma*, *Toxocara* and

Dipylidium stand out. The adult forms of *Ancylostoma* attach themselves to the mucosa of the small intestine of the host and after copulation, the females lay thousands of eggs, which are eliminated along with the host's feces and can contaminate humans through the penetration of the larvae into the skin, conjunctiva, mucous membranes causing damage to health. Toxocariasis, caused by *Toxocara*, is a tropical disease transmitted through the ingestion of eggs present in the feces of infected dogs or cats [7]. In addition, *Dipylidium caninum* is a prevalent parasite in dogs and cats, whose intermediate host is fleas. Thus, the importance of controlling ectoparasites is highlighted, since they have a direct impact on human and animal health [3].

Due to the zoonotic potential of some parasites, the prophylactic use of antiparasitics in companion animals is of great importance for public and animal health. The control of these parasites is carried out almost generally, with the use of anthelmintics. The use of antiparasitics in dogs and cats promotes health protection against diseases caused by worms and external parasites, which ensures the quality of life of animals and promotes the health of the population [2].

Drug poisoning represents a considerable number of cases in small animal medicine and results from the interaction of a certain toxic agent with a biological system, causing an imbalance in homeostasis [12]. According to Gwaltney-Brant [5], cases of poisoning are related to the greater availability and use of drugs in human and veterinary medicine in the last thirty years. These authors also point out that the real incidence of cases may be underestimated, since toxicity events are not all reported to official services. According to Pinto [15], approximately 81% of poisonings are due to self-medication, while 19% of them occur accidentally, which represents serious harm to animal health.

Self-medication with ivermectin and deltamethrin is one of the major causes of drug poisoning in pets, with ivermectin accounting for 20% of cases of poisoning due to self-medication [11]. Siroka and Svobodova [19] contraindicate the use of ivermectin in pets, since poisoning has been described in many breeds of dogs and cats. Clinically, animals poisoned by ivermectin may present with loss of motor control, lethargy, weakness, loss of visual reflexes, respiratory depression, bradycardia, mydriasis, tremors, hypersalivation, coma, and eventually death [10]. Reports of deltamethrin poisoning are ignored, however, the animal may present with drooling, emesis, tremors, hyperexcitability, dyspnea, bronchospasm, weakness, hypothermia or hyperthermia, prostration, convulsion, and death [13].

In view of the above, the general objective of this study was to investigate and describe, based on the literature, risk factors and determinants of poisoning by ivermectin and deltamethrin used in the medical clinic of dogs and cats. The specific objectives were to point out the causes and toxic effects of the drugs, as well as to survey the frequency of poisonings, the diagnostic resources and the appropriate treatment measures.

Methodology

The present study was carried out based on an exploratory bibliographic research in the scientific databases SciELO, PubMed, CAPES, LILACS, MEDLINE and Google Scholar. For the search, the time frame of publication between the years 2008 and 2019 was carried out, using the following keywords: intoxication, antiparasitics, ivermectin, deltamethrin, dogs, cats, accidental, iatrogenic, veterinary medicine and prevalence.

Articles that addressed the topic of poisoning by ivermectin and deltamethrin in the medical clinic of dogs and cats and that established a relationship with risk factors and determinants for the occurrence of these conditions were included in the study, totaling 15 selected articles.

From the collected material, a qualitative analysis of the chosen articles was carried out, seeking to highlight the risk factors, causes and toxic effects caused by ivermectin and deltamethrin, as well as the incidence of poisoning by these antiparasitic drugs in companion animals.

Results and Discussion

Ivermectin is a drug belonging to the group of avermectins, which is prescribed in veterinary medicine for the treatment and prophylaxis of fleas, ticks, scabies and nematodes [12] point out that ease of access and low cost are factors commonly related to the incidence of poisoning in dogs and cats by ivermectin. In addition, these authors warn that the age of the animals is an important risk factor and potentiator of the toxic effect of ivermectin, since the use in animals younger than the indicated for the use of the drug is determinant for the incidence of cases.

The main commercial presentation of ivermectin is the tablet, and it can also be found in injectable and pour *on* liquid form. However, poisonings associated with the avermectin group have been described due to extrapolation of the therapeutic dose, since many commercially available formulation presentations are intended for large animals. The use of ivermectin for small animals from

presentations of other species requires large dilutions, as well as the choice of an appropriate diluent [9].

In general, cases of antiparasitic poisoning are described due to individual sensitivity. The risks of ivermectin poisoning are related to doses greater than the therapeutic dose and administration in animals less than 6 weeks of age. In addition, cases of intoxication have also been described as being associated with racial predisposition. Collie, Old English, Sheepdog, Shetland Shepherd, German Shepherd, Afgan Hounds and their crossbreeds are particularly sensitive because the blood-brain barrier of dogs of these breeds is more permeable to ivermectin, causing depression of the central nervous system [16].

According to Papich [14], ivermectin at doses of 400 µg/kg causes poisoning in Siamese kittens and at lower doses, such as 300 µg/kg, it is lethal to kittens. In addition, the patient's prognosis depends on the dosage administered and the sensitivity of the animal, while recovery depends on the early treatment.

In parasites, ivermectin is neurotoxic as it acts on the nervous system causing paralysis and death. On the other hand, under normal dosing conditions, animals do not undergo the same action observed in parasites, as they are protected by the blood-brain barrier, which prevents the accumulation of the drug in the central nervous system [16]. In cases of animal poisoning, Nogueira [12] points out that ivermectin crosses the blood-brain barrier and triggers neurological signs. Furthermore, according to Reichert [16], toxicity in mammals results in a reduction in cell membrane resistance to ivermectin, manifesting neurological symptoms.

Because ivermectin is metabolized in the liver, it causes liver damage and systemic debility. In addition, signs of intoxication are intense salivation, vocalization, shortness of breath, convulsions, depression, vomiting, muscle tremors, loss of pupillary reflexes, tachycardia, coma, and death. In cases of poisoning, the recognition of the clinical manifestations is extremely important for treatment. It is important to highlight that there is no specific antidote for ivermectin poisoning and, therefore, Nogueira [12] recommends that symptomatic and supportive treatment be performed; However, they warn that the prognosis is reserved to poor.

The diagnosis of ivermectin poisoning is based on anamnesis and clinical signs; and the treatment consists of maintaining physiological parameters and helping to eliminate the drug from the body. In the case of topical exposure to ivermectin, the animal should be bathed with mild soap and water before symptomatic and supportive treatments [17].

Deltamethrin is an ectoparasiticide belonging to the group of pyrethroids, whose presentations are feasible for topical use, such as shampoos, collars and spray solutions. It is a drug widely used in the fight against fleas, ticks, mites, lice and mosquitoes. Situations of poisoning result from the improper use, mainly, of the solution for spraying in high concentrations [21].

The mechanisms of action of pyrethroids are numerous and, for this reason, poisoning in animals determines a complex and nonspecific clinical picture. Deltamethrin acts on the nervous system, where it binds to sodium channels, induces opening and prevents them from closing for a prolonged period, leading the animal to a state of excitement. In addition, it can inhibit GABA-A chlorine channels and trigger seizures. On the other hand, deltamethrin acts on sodium channels of the axon membrane, decreasing and delaying sodium conductance into the cell and suppressing potassium efflux, in addition to inhibiting the ATPase enzyme with a decrease in action potential. Another site of action of type II pyrethroids is the interference in the binding of GABA-A receptors and glutamic acid, especially in GABAergic neurotransmission that competitively blocks nicotinic receptors [1].

Thus, due to the numerous mechanisms of action of pyrethroids, the pharmacological actions are quite variable. Animals poisoned by deltamethrin may present with convulsions, drooling, vomiting, tremors, hyperexcitability, dyspnea, bronchospasm, weakness, hypothermia or hyperthermia, prostration, disorientation, motor incoordination, and death from respiratory failure. In cats, you can also observe rapid ear movements, paw tremors and contractions of the superficial cutaneous muscles [21].

The diagnosis of deltamethrin poisoning is based on the symptoms presented by the animal and the clinical history. The treatment aims to detoxify the animal, support recovery and accelerate the excretion of the drug, through gastric lavage, use of antiemetics and activated charcoal. Supportive treatment is based on the use of atropine to control ptialism, fluid therapy, and diuretics to accelerate excretion, anticonvulsants, myorelaxants to control spasms, and sodium bicarbonate to reduce the absorption of the active ingredient [18].

Most cases of deltamethrin poisoning occur accidentally, and usually in the home environment itself, due to carelessness or even inappropriate use. Oliveira, *et al.* [13] reported a case of poisoning due to accidental ingestion of deltamethrin, in which a 5-month-old male dog presented hyporexia, tremors, dehydration, excessive synchronous blinking, non-reactive lymph nodes, intense dis-

comfort on abdominal palpation, adynamia and paresis. During the clinical examination, the patient presented vomiting and fragments similar to the antiparasitic collar whose active ingredient was deltamethrin were observed in the contents. After the epidemiological investigation, it was concluded that the accident occurred after the ingestion of an antiparasitic collar forgotten after bathing.

Deltamethrin is a safe and effective medication, as long as it is used carefully and under the guidance of a veterinary medical professional, with the proper dosages and correct application. The responsibility of the owner should be considered to avoid accidental poisoning, since collars with deltamethrin should not be ingested by animals, due to risks of poisoning.

Final Considerations

Due to the incompetence of owners, there is a high incidence of cases of poisoning by ivermectin and deltamethrin in dogs and cats. The search for solutions to combat parasitic agents and medicate animals without a veterinary prescription is a risky practice, as it can cause disorders, sequelae and even deaths, as a result of the contraindicated use of active ingredients and dosages of these antiparasitic drugs in animals.

Despite progress in the formulation of anthelmintics for the prevention and control of parasitosis in dogs and cats, these diseases are still problems for pets, in some cases due to lack of information on the part of owners. Thus, the veterinarian is the main mediator for guidance to dog and cat owners, since he has information regarding the prescription of antiparasitic drugs to be used, as well as sanitary guidelines to avoid environmental contamination and zoonoses.

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