Indian J. Vet. Med. Vol. 43, No. 1, 2023 pp. 101-102

Ivermectin toxicity in a dog: A case report

Manu Jaiswal, Sveta Singh, Padma Nibash Panigrahi, Arvind Kumar Tripathi, Ram Sagar*
Department of Veterinary Medicine, CVSc&AH, U.P. Pt. Deen Dayal Upadhyay Pashu Chikitsa Vigyan Vishwavidyalay evam Go Anusandhan Sansthan (DUVASU), Mathura- 281001 (UP)

Abstract

A 10 year old bitch was presented at TVCC, DUVASU, Mathura with the history of acute illness and apparent blindness after being exposed with high dose of ivermectin drug. Dog was treated for tick infestation by owner with 20 mg Ivermectin. Acute onset of clinical symptom were observed by owner after 12 hr of ivermectin therapy. Initially, dog seemed to be blind, cloudiness of eye with severe lacrymation, absence of papillary light reflex, mydriasis, partial blindness, hypothermia, ataxia and certain behavioral changes. On the basis of acute clinical signs therapy started with neostigmine @ 0.05mg/kg BW SC repeated 6 hourly, atropine sulphate @ 0.02mg/kg b. wt. *iv*, dexamethasone @ 0.5 mg/kg b. wt., and neurobion 1ml *im* with infusion of 250 ml NSS *iv*. After three days of follow-up, the dog recovered from clinical condition.

Key words: Apparent blindness; ivermectin toxicity; lacrimation

Ivermectin belongs to the family avermectin produced by actinomycetes, specifically *Streptomyces avermitilis* and is a semi-synthetic macrocyclic lactone having a wide range of antiparasitic activity (Panigrahi *et al*., 2016). This is one of the most potent drug in ruminants having high margin of safety (Reinemeyer and Courtney, 2001). However, an extra-label use is common and has heen documented for the treatment of parasites in various other animal species. It has broad-spectrum efficacy against plant and animal arthropod and nematode infections (Omura, 2008).Ivermectin acts by selectively binding to glutamate-gated and gamma-aminobutyric acid (GABA)-gated chloride channels in the nervous system of insects, resulting in hyperpolarization of cell, paralysis and finally death. Safety in mammals is due to the lack of glutamate gated chloride channels in the peripheral nervous system and restriction of GABA to a central nervous system (Macdonald and Gledhill, 2007). Trematodes and cestodes are having the natural resistance against ivermectin because they do not use GABA as a PNS neurotransmitter. Ivermectin toxicity has been reported in several species of animals including dogs, cats, cattle, horses, pigs, frogs and chelonians (Dey *et al.,* 2017). Ivermectin has been demonstrated as an extremely safe drug in dogs, an increased susceptibility to the toxic effects is evident in a subpopulation of collies and collie-type dogs (Paul and Tranquilli, 1998). Clinical signs initially include salivation, vomiting, ataxia, tremors and disorientation, but these progress to weakness, recumbency, non-responsiveness, stupor and coma in some dogs (Dey *et al.,* 2017). Present report deals with a case of ivermectin toxicity and its therapeutic management.

Case History and Observations

A 10 year old bitch (nondescript), weighing about 10 kg was presented at TVCC, DUVASU, Mathura with the history of acute illness of apparent blindness after being exposed with high dose of ivermectin drug along with depression, cloudiness of eye with severe lacrimation, ataxia and certain behavior changes. Dog was treated for tick's infestation by 2 tablets of 10 mg ivermectin drug. Clinical examination revealed hypothermia (99.6^{0}F), tachycardia (140 beats/min) and oligopnea. Close physical examination revealed absence of pupillary light reflex (PLR), partially dialated pupil with severe lacrymation from protruded eye ball.

On the basis of history and clinical symptom the case was highly suggestive of ivermectin toxicity. Therapy of dog started with symptomatically with atropine sulphate @0.02mg /kg bw iv and dexamethasone @ 0.5 mg /kg bw, neurobion 1ml i/m with infusion of 200ml normal saline I/V and suitable antidote like neostigmine @

*Corresponding author: arvindvet04@rediffmail.com

0.05mg/kg BW SC with follow-up schedule of 3 days. After treatment, dog was presented in clinics with reduced symptoms of toxicity and normal body condition.

Discussion

Ivermectin have wide range of efficacy in animals for internal and external parasites. Dosage regimens vary depending on the species and parasite treated. The margin of safety for ivermectin in most breeds of dog is well over 100 times the recommended dose but in Collies it is about 16 times the usual dose(Dey *et al.,* 2017). Occurrence of toxicity in selective breeds may be due to the reason that these breeds have comparatively more permeable blood brain barrier to the drug (Houston *et al*., 1987) or due to an autosomal recessive trait (MDR-I) gene that causes a defect in the p-glycoprotein, which is a multidrug transporter in the blood brain barrier and it helps in passage of ivermectin into the brain at low dosages and thus causes toxicity (Macdonald and Gledhill, 2007). Similar clinical toxicity findings had been reported by Veena *et al*.(2016) in adult German Shepherd dog and Sheikh *et al*.(2017) in German Shepherd cross breed dog. In dogs, an oral preparation of ivermectin in sesame oil induced mydriasis at a dosage of 2.5 mg/kg, tremor at a dosage of 5 mg/kg, severe tremor and ataxia at a dosage of 10 mg/kg, and death at a dosage of 40 mg/kg (Campbell and Benz, 1984). Depression, ataxia, coma and death have followed treatment of dogs with products intended for use in horses or cattle, at a dosage of 0.2 mg/kg (Sivine *et al.,* 1985). Ivermecrtin toxicosis was observed in dogs in many studies. Hopkins *et al.,* (1990) showed tremors, dilated pupils and blindness in male Doberman pinscher dog administered ivermectin orally in a dose of 115 mg. Very low test doses are often recommended at the starts of a treatment to identify these individuals regardless of their breed. Alternatively, a blood test is now available to test for the genetic sensitivity. This genetic test (DNA test using an oral swab) for P-glycoprotein mutation will identify ivermectin sensitive dogs as also suggestive by Houston *et al*. (1987) ; Hadrick *et al*. (1995).

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Received : 07.12.2022
Accepted : 29.05.2023