

Case Study

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Ivermectin Toxicity in a German Shepherd Cross Breed Dog: A Case Study

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ABSTRACT

A German Shepherd cross male dog one year old weighing 12 kg was presented to Teaching Veterinary clinics complex, International Institute of Veterinary Education and Research (IIVER), Rohtak Haryana for treatment. The dog was treated for tick infestation by owner. History revealed that about 1.5 ml of ivermectin (I-mac) was injected intramuscularly. Abnormal clinical signs were observed by owner 12 hours after injection. Clinical examination revealed hypothermia (98.5°F), ataxia, partial blindness, dilated pupil, negative papillary light reflex, weakness, incoordination and behavioural changes. Therapeutic management was done with the administration of atropine sulphate @ 0.02-0.04 mg/kg BW IV stat, neostigmine @ 0.05mg/kg BW SC repeated 6 hourly and dexamethasone @ 0.25-0.5mg/kg BW IM BID and optineuron @ 1 ml total dose with infusion of 200 ml dextrose (5%) IV. The dog recovered uneventfully after treatment.

Keywords

Dogs, Ivermectin,
Toxicity, Therapeutic
management.

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Introduction

Ivermectin is an antiparasitic drug belonging to the avermectin family of compounds. Ivermectin is a mixture of 80% or more of an analog of avermectin B_{1a} (AB_{1a}) and 20% or less of an analog of avermectin B_{1b}. These compounds are 2 of 4 avermectins produced by the actinomycete *Streptomyces avermitilis*. Although similar in structure to the macrocyclic lactones, avermectins have no antibacterial or antifungal activity. They do have a broad spectrum of activity against nematode and arthropod parasites of both plants and animals Campbell (1983). Ivermectin has been widely used in veterinary

medicine and is approved for use in dogs as a heartworm preventative at a dosage of 6 µg/kg PO once a month. Off-label use of the drug in dogs for ectoparasites and endoparasites is common, with dosage recommendations ranging from 50 to 300 µg/kg PO or subcutaneously Plumb *et al.*, (1995).

The median lethal dose (LD₅₀) of ivermectin for beagle dogs has been reported to be about 80 mg/kg, and the highest single oral dose in beagle dogs without an adverse clinical effect was 2 mg/kg Campbell (1989). Some Collies

are extremely sensitive to ivermectin, with notable individual variation. A dose of 50–60 µg/kg ivermectin was found to be safe in Collies known to be susceptible to the drug Fassler *et al.*, (1991) and Pulliam *et al.*, (1985). Ivermectin is widely used endectocide in canines and toxicity is seen when excessive dose is administered in pets that are sensitive to drugs. Toxicity results in any clinical signs ranging from mild to severe and death may occur.

Some breeds are sensitive to lower doses of ivermectin such as Collie, Australian Shepherd and Shetland Sheepdogs. 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 Houstonet *et al.*, (1987).

History and Clinical observations

A German shepherd cross male dog one year old weighing 12 kg was presented to Teaching Veterinary clinics complex, International Institute of Veterinary Education and Research (IIVER), Rohtak Haryana for treatment with complaint of depression (Figure 1a), ataxia, partial blindness, dilated pupil (Figure 1b), negative pupillary light reflex, weakness, incoordination and behavioural changes. The dog was treated for tick infestation by owner for tick infestation.

The dog was injected 1.5 ml of ivermectin intramuscularly 24 hours before to treat ectoparasites. Clinical examination revealed hypothermia (98.5°F), mydriasis, tachycardia (110 beats per minute), dyspnea with respiration rate of (17 breaths per minute), incoordination, seizures and unable to stand properly. Hematobiochemical parameters were found normal (Table 1) and on the basis of anamnesis and clinical observations the case was diagnosed as ivermectin toxicity.

Treatments and Discussion

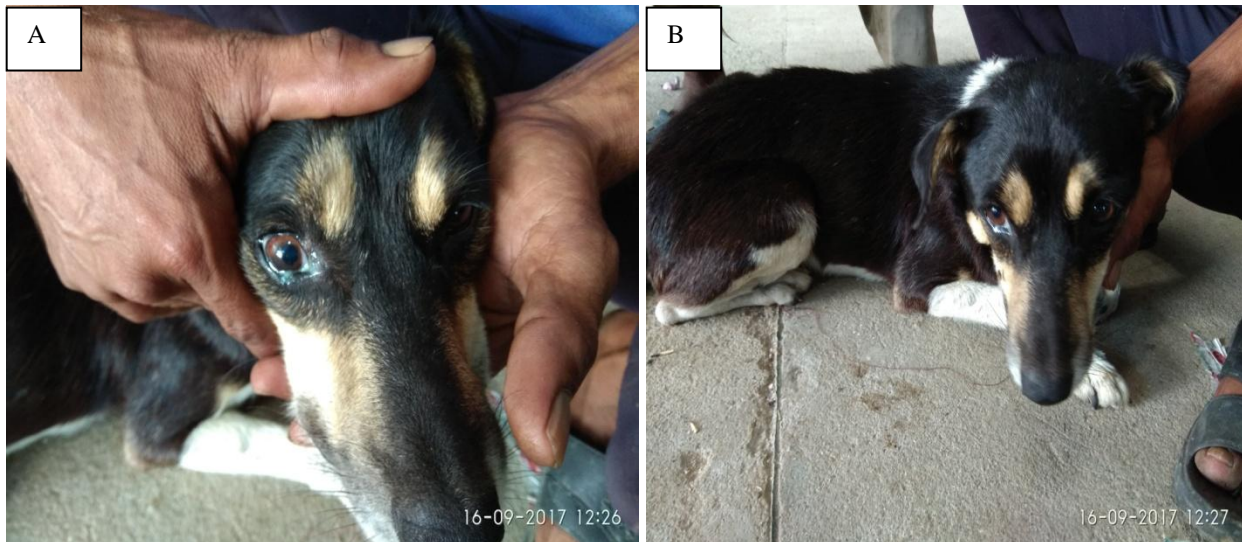
Therapeutic protocol for ivermectin toxicity is only managerial care, supportive therapy and symptomatic treatment as there is no specific antidote for ivermectin toxicity. The dog was treated with the administration of atropine sulphate @ 0.02-0.04 mg/kg BW IV stat, neostigmine @ 0.05mg/kg BW SC repeated 6 hourly and dexamethasone @ 0.25-0.5mg/kg BW. IM BID and optineuron @ 1 ml total dose with infusion of 200 ml dextrose (5%) IV. The dog recovered uneventfully after treatment.

Collie breed of dogs are more susceptible to ivermectin and tolerate only up to 0.1 mg/kg dose rate of ivermectin Paul *et al.*, (1987). 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. Clinical signs of toxicity were reported in two Australian shepherds receiving ivermectin at oral dosage of 0.17 mg/kg and 0.34 mg/kg respectively Hadrick *et al.*, (1995). 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 Houstonet *et al.*, (1987) or due to an autosomal recessive trait (MDR-1) gene that causes a defect in the p-glycoprotein, which is a multidrug transporter in the blood brain barrier and this leads to passage of ivermectin in to the brain at low dosages thus causing toxicity Kant (2007). In present case, the animal was young and the blood brain barrier might not have been fully developed leading to toxicity. Side effects of urgent concern are dilated pupils and drunken gait which can progress to respiratory paralysis and death if medication is not withdrawn and supportive care is not initiated. Unfortunately, ivermectin toxicity cannot be reversed and therefore, it is wise to treat the symptoms to the best our potential and ability.

Table.1 Showing normal hematobiochemical parameters of dog affected with ivermectin toxicity

Parameters	Day 0	Reference values
RBC ($\times 10^3/\mu\text{L}$)	5.3	5.5-8.5
WBC ($\times 10^3/\mu\text{L}$)	5.9	6-17
Hemoglobin (g/dl)	12.4	12-18
PCV (%)	37	37-55
Monocyte (%)	5	3-10
Neutrophil (%)	72	60-76
Basophil (%)	2	00-11
Eosinophil (%)	1	2-10
Lymphocyte (%)	23	12-30
AST (U/L)	31	9-49
ALT (U/L)	37	10-100
Creatinine (mg/dl)	0.7	0.5-1.6
BUN (mg/dl)	25	18.8-55.4
Albumin (g/dl)	2.6	2.6-4.0
Globulin (g/dl)	2.8	2.1-3.7

Fig.1 Showing mydriasis of eye bilaterally (A) and depression (B) of dog affected with ivermectin toxicity



Physostigmine is an anticholinesterase agent that results in the accumulation of increased amounts of acetylcholine (ACh) at the synapse. This increase in ACh increases the conductance of sodium ions into the postsynaptic membrane, causing depolarization to occur. In an uncontrolled trial, Collies dosed with ivermectin were treated with physostigmine if they showed

severe lethargy or coma. Improvement in clinical signs occurred within minutes of physostigmine administration, but the effect only lasted 30–90 minutes. It was not possible to determine if physostigmine administration in these animals hastened their recovery Tranquilli (1987). Increased limb movements also were reported after physostigmine administration to 1 of 2 Australian Shepherds

suffering from ivermectin toxicity Hopkins *et al.*, (1990). A Collie with ivermectin toxicity was treated with physostigmine. The dog was in sternal recumbency before therapy and was able to stand and walk unaided 15 minutes after treatment. The improvement only lasted 45 minutes, after which the dog was recumbent again Smith *et al.*, (1990).

Management of ivermectin intoxication may be aided by an understanding of the action of the drug and its interaction with other therapeutic agents. After these considerations, the prognosis for complete recovery from ivermectin toxicity is good.

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