



## Clinical Management of Ivermectin Toxicity in Dog

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## Abstract

The recklessness with which important yet menacing (if not used cautiously) drugs being used in veterinary medicine creating more harm than benefit. Be it Nsaid's, the overdosage of which causes acute kidney failure or be it ivermectin which if given in quantity more than recommended will result in multiple harmful signs such as tremors, incoordination, ataxia, transient blindness etc. Similarly, here the case of dog was presented at VCC, COVAS, Parbhani. The history of administration of ivermectin, more than 3 times of ideal dosage and the corresponding signs exhibited by dog were self-evident of the toxicity. The haematological and biochemical parameters were ideal and no abnormality was observed in them. As a result, after taking into account all the differentials and history taking, the present case diagnosed as case of ivermectin toxicity. Since there's dearth of antidote against ivermectin, supportive and symptomatic treatment was carried out. The dog was administered with anticholinesterase medication (neostigmine), acetylcholinergic antagonist (atropine sulphate), neuroprotectants and intravenous dextrose infusions twice in period of 12 hrs. Animal showed signs of recovery within 2 hrs of end of first treatment, however it took 2 days for complete recovery of dog.

**Keywords:** Ivermectin; Neostigmine; Atropine Sulphate; Sialorrhea

## Abbreviations

GABA: Gamma-Aminobutyric Acid; Hrs: Hours; Kg: Kilogram;  
mg: Miligram; BPM: Beats Per Minute

## Introduction

## Background: Origin of Ivermectin

Ivermectin has been one of the most effective medicinal treatments since it was first introduced more than 20 years ago as well as the foundation of one of the most effective public health initiatives of the last century and medications used in veterinary medicine. The drug was the result of a singular multinational public-private partnership. The Tokyo-based Kitasato Institute is well known throughout the world for its proficiency in identifying bioactive substances generated by microorganisms that are mostly present in the environment.

## Developmental history: Ivermectin [9]

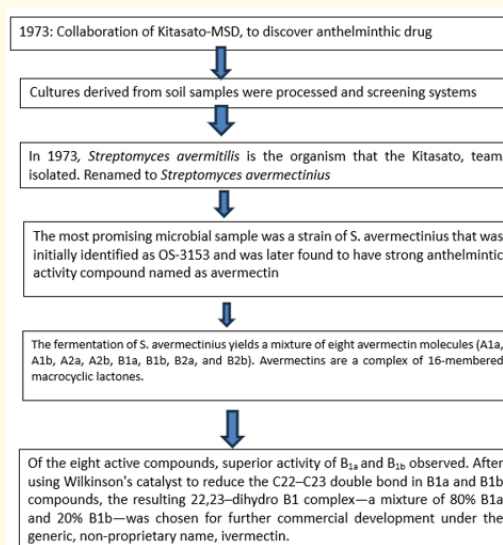


Figure 1

Ivermectin mode of action [3,4]

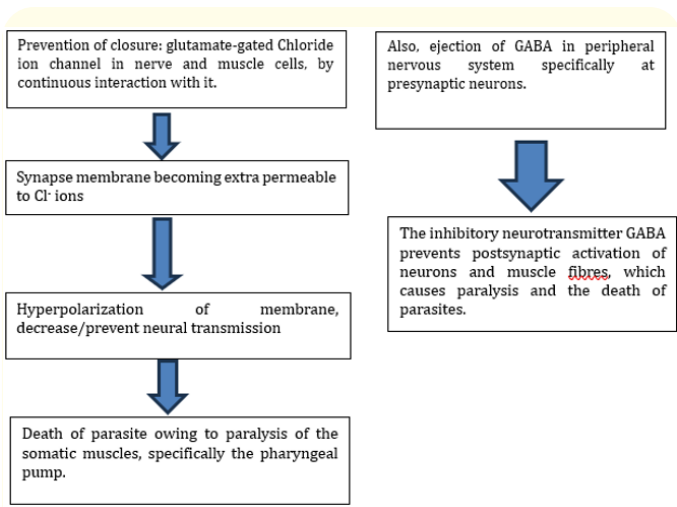


Figure 2

Materials and Methods

Case presentation

“Orian” a 2-year-old dog, sex-Male, breed- Doberman, unvaccinated weighing 10 kg with complaint of incoordination, sialorrhea, depressed for 8 hours was presented to TVCC, Covas, Parbhani-431401.

History taking- The appetite of dog remained normal throughout day. The dog was active alert. As per at bed time the dog was administered with 2 tablets containing 10 mg of ivermectin this was done as against the treatment of ectoparasites over body of dog. The dog after 5 hours initiated to show signs such as sialorrhea and tremors.

The body temperature was 101.1°F. Heart rate of 50 BPM and Respiration rate was 15 BPM. The lymph node on palpation were of normal size and shape and some of ticks were present on body of animal. CBC, serum chemistry profile, and blood glucose were within normal limits (Table 1).

Since as per history provide by owner, the dog has been administered with 20 mg of ivermectin and that is, 3 and half times more than maximum dose recommended. Signs such as incoordination, mydriasis, sialorrhea were evident on observation as s result it was diagnosed as case of ivermectin toxicity.

Parameters	Test values
Haemoglobin	11.3 mg/dL
Total erythrocyte count (TEC)	4.3×10 <sup>6</sup> /μl
Total leucocyte count (TLC)	7.2×10 <sup>3</sup> μl
PCV	32.8 %
Platelets	167×10 <sup>3</sup> / μl
Blood urea nitrogen (BUN)	25 mg/dL
Creatinine	0.9 mg/dL
ALT	56 U/L
AST	45 U/L
Blood glucose	110 g/dL

Table 1

Treatment and basis

Since, Ivermectin doesn’t have any antidote the line of treatment is supportive care and intravenous infusions and use of such medication who can stimulate excretion of ivermectin from faeces (since ivermectin mostly excreted in the faeces).

Inj. Neostigmine @ 0.05 mg/kg SC repeated after 8 hours.

Neostigmine inhibits the acetylcholinesterase enzyme by forming an oxy-diaphoretic bond with its anionic site, thereby binding and inhibiting the enzyme through acid-transferring (Neely, *et al.* 2023). An anticholinesterase medication called neostigmine works by competitively preventing acetylcholine (ACh) from binding to acetylcholinesterase (AChE) binding sites. This prolongs the half-life of ACh and improves impulse transmission across neuromuscular junctions, improving mental alertness momentarily [7].

The main excitatory neurotransmitter in the gastrointestinal (GI) tract is acetylcholine. Neostigmine and other acetylcholinesterase inhibitors boost GI motility by increasing acetylcholine availability.

Inj. Atropine sulphate @0.03 mg/kg IV in dilution of Inj. NS 250 ml IV.

To treat sialorrhea and bradycardia

Atropine works as a nonselective muscarinic acetylcholinergic antagonist, increasing firing of the sinoatrial node (SA) and conduction through the atrioventricular node (AV) of the heart, op-

poses the actions of the vagus nerve. Atropine sulfate blocks the muscarinic receptors in the salivary glands and leads to reduced saliva production.

Inj. Neurobion forte @ 1ml in dilution of Inj. Dextrose (5%) IV.

Mecobalamine Aids in the production of neuronal lipids, regenerates axonal nerves, and has neuroprotective properties, all of which support healthy neuronal function and ameliorate neuropathic syndromes, Alzheimer's disease, Parkinson's disease, and dementia [6].



Figure 3

## Result and Discussion

### Post treatment

The following treatment was again administered to dog after 12 hrs. Meanwhile after 2 hrs of first treatment the animal voided considerable amount of faeces. The sialorrhoea reduced considerably 2 hrs after treatment. The body temperature recovered to normal after 4 hrs of treatment while it took 24 hrs to water down ataxic and incoordination symptoms. The dog started eating food after 30 hrs after initiation of treatment. To sum up, the complete recovery from ivermectin toxicity occurred 2 days after initiation of treatment.

### Discussion

Veterinarians have long utilized ivermectin, which can be administered to dogs once a month at a dose of 6 µg/kg PO as a prophylactic against heartworms. The medication is frequently used off-label in dogs to treat ectoparasites and endoparasites; dosage suggestions range from 50 to 300 µg/kg PO or subcutaneously [2]. Ivermectin is a common endectocide used in dogs, and toxicity occurs when an excessive dosage is given to pets who are drug-sensitive. Any clinical symptom, from moderate to severe, is a result of toxicity, and death is a possibility [12]. One of the main causes of

drug toxicity in animals has been identified as management negligence when it comes to drug delivery [1].

Differences in ivermectin blood-brain barrier permeability have been proposed as the likely cause of the response variations observed between individual dogs that develop toxicity and the normal, non-susceptible animal [10]. By simple diffusion, lipid-soluble compounds can easily pass through the BBB.

Certain transport systems facilitate the entry of nonlipid soluble substances into the brain. There are also safeguards in place to keep undesired chemicals out. The mdr1a P-glycoprotein is one of these and it can be found in the brain among other tissues. One important factor influencing the concentration of some drugs, such as AB1a, vincristine, doxorubicin, morphine, and digoxin, that can be reached in the brain is the mdr1a P-glycoprotein [11,13]. It was discovered that mice deficient in the mdr1a P-glycoprotein were very vulnerable to ivermectin poisoning. It has been discovered that collies that are ivermectin hypersensitive had higher brain ivermectin concentrations than beagle dogs or other ivermectin-treated animals [10]. This finding raises the possibility that one of the mdr1-type P-glycoproteins may be lacking in Collies that are vulnerable to ivermectin [11]. Nonetheless, it hasn't been noted that collies are sensitive to drugs such as morphine.

## Conclusion

The present case precisely reflects the concern associated with misuse of drugs. The administration of ivermectin beyond recommended dose have tremendous repercussion. From incoordination, hypersalivation to nervous signs and transient blindness is range of repercussions. Since there is no antidote for ivermectin toxicity, symptomatic and supportive treatment is only viable option.

## Conflict of Interest

The author declares that they have no conflict of interest.

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