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# SUCCESSFUL MANAGEMENT OF A RARE CASE OF EMAMECTIN BENZOATE PESTICIDE POISONING IN A DOG

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**ABSTRACT**
Emamectin Benzoate (EB) is a novel pesticide designed for control of insects and mites in crops. It is a semisynthetic avermectin derivative, belonging to the 16 – membered macrocyclic lactones, has widespread application in agriculture for pest management (1). Avermectin, from which Emamectin Benzoate is derived, is produced through the fermentation of *Streptomyces avermitilis* (2). The safety of avermectin compounds for mammals, including humans, stems from their limited ability to cross the Blood – Brain Barrier (BBB), the absence of glutamate – gated chloride channels in mammals, and the reduced affinity of avermectins for other ligand – gated chloride channels in mammals (3). Emamectin Benzoate poisoning can present with severe symptoms, surpassing initial expectations, leading to manifestations such as altered consciousness, inhalation pneumonia and gastrointestinal (GI) symptoms (4). We present a rare case of Emamectin Benzoate toxicity in a puppy and its successful management with Intravenous Lipid Emulsion (ILE).

**KEYWORDS:** Emamectin Benzoate toxicity, Intravenous Lipid Emulsion (ILE), Avermectin toxicity, Blood – Brain Barrier

## INTRODUCTION

Emamectin Benzoate (EB) is a novel pesticide designed for control of insects and mites in crops. It is a semisynthetic avermectin derivative, belonging to the 16 – membered macrocyclic lactones, has widespread application in agriculture for pest management (1). Avermectin, from which Emamectin Benzoate is derived, is produced through the fermentation of Streptomyces avermitilis (2). The safety of avermectin compounds for mammals, including humans, stems from their limited ability to cross the blood – brain barrier, the absence of glutamate – gated chloride channels in mammals, and the reduced affinity of avermectins for other ligand – gated chloride channels in mammals (3). Emamectin Benzoate poisoning can present with severe symptoms, surpassing initial expectations, leading to manifestations such as altered consciousness, inhalation pneumonia and gastrointestinal (GI) symptoms (4). We present a case of Emamectin Benzoate toxicity in a puppy and its successful management with Intravenous Lipid Emulsion (ILE).

### History and Clinical Observation

A four months old female labrador puppy was presented to Small Animal Medicine Unit of Veterinary College and Research Institute, Theni, Tamil Nadu, India, with history of facial tremors and hypersalivation since morning of the day of presentation. The pet was vaccinated against rabies and canine distemper as per standard protocol, for the common disease in dogs which manifest with neurological signs. The rectal temperature was $39^0$C, heart rate was 90 beats per minute, and the respiratory rate was 25 breaths per minute and they were within the range of any healthy pup of that age. Ophthalmic examination had sluggish pupillary right reflex (both ipsilateral and contralateral) and decreased menace reflex. Detailed history regarding the frequency of tremors was collected. The owner reported that the tremors were observed only from early hours of the day of presentation. Inspite of the facial tremors the appetite was normal in the pet. Since the time of initiation of tremors, the pet had five to six episodes of vomiting. The vomitus had undigested food indicating a short transit in the stomach. There was no change in the food, fed to the pet since a week. The pet was not treated with systemic or topical parasiticides. The owner informed that the pet was playing with the empty pesticide plastic pack used in their terrace garden. The owner had no details of the name of the pesticide used, as it was over the counter purchase. The owner was asked to present the pack which was damaged and had distorted label on it with manufacturers name. The online search of the image with manufacturer's name correlated with the 5% Emamectin Benzoate soluble powder. This guided in initiating the treatment immediately. This was later verified with the seller and it was confirmed that it was the pack with 5% commercial Emamectin Benzoate soluble powder.

**Treatment And Discussion**

Intravenous administration of Normal Saline was initiated followed by ILE 20% @ 1.5ml / Kg as a bolus followed by ILE 20% @ 0.25 ml / Kg BW as Constant Rate Infusion (CRI) over a period of 30 minutes (6). Due to altered mentation gastric lavage was not attempted. Oral activated charcoal @ 2 g / Kg Bw PO was administered orally to enhance adsorption of unabsorbed Emamectin Benzoate in the stomach (7, 14). The pet recovered from tremors 30 minutes post treatment and the hypersalivation stopped completely. One week post treatment followup the pet had all vital parameters within the normal range including the mentation being normal.

The clinical presentation of Emamectin Benzoate poisoning involves Central Nervous System (CNS) dysfunction and Gastrointestinal (GI) upset. Mammalian species are less sensitive to it due to lower Gamma – Aminibutyric Acid (GABA) affinity and relative impermeability to BBB (1, 7). In animals there is substantial evidence of behavioural effects like change in motor activity (tremors, incoordination, ataxia and lethargy). These signs coincides with the present case.

Emamectin being Avermectin derivative (1) the mechanism of action (5) is by preventing the transmission of electrical impulse in the muscles and nerves similar to Ivermectin. The major toxic effects of Ivermectin observed in dogs were hypersalivation, ataxia, blindness, coma, respiratory compromise, tremors, mydriasis, anorexia and death (3). Hypersalivation and tremors were observed in the present case.

Emamectin Benzoate additionally enhances activity of Gamma Amino Butyric Acid (GABA) in the Central Nervous System (CNS) and increases inhibitory signal resulting in CNS depression (2, 3). Side – effects of EB poisoning can range from simple gastrointestinal distress to severe CNS manifestations, cardiac distress which might result in death in humans. Intravenous Lipid Emulsion (ILE) is widely used in poisoning with lipophilic drug such as ivermectin, and its ease of use in emergency cases has made it applicable (8) and hence used in the present case.

The mechanism of action is not understood. It is postulated that ILE therapy provides a lipid compartment within circulating plasma in which the toxic compounds become sequestrated, known as “lipid sink phenomenon” (9) thus reducing the lipophilic drug aqueous plasma concentration (10). In mammals, the administration of Ivermectin has a good safety margin in cases of a healthy Blood – Brain Barriers (BBB) and use of appropriate drug dose (11). Insufficient BBB development in immature puppies, may result in Ivermectin crossing the BBB and the development of neurological symptoms (12). High concentration of Ivermectin can cross the BBB without the aid of the gene mutation and still lead to toxicity in dogs (13). The Clinical sign in the presented puppy was probably due to Emamectin Benzoate crossing the BBB which would have poorly developed in the puppy.

As Emamectin Benzoate has no specific antidote the management of this poisoning is always supportive and symptomatic. As it possesses GABA mimetic activity, the drugs that enhance GABA activity like benzodiazepines, barbiturates and valproic acid should be avoided. Hence, inspite of tremors the pet was not treated for the tremors specifically and symptomatically with benzodiazepines and barbiturates.

There is paucity of literature regarding the complete spectrum of manifestation of Emamectin Benzoate poisoning in pets or other animals. There is no consensus recommendation for the management of Emamectin Benzoate poisoning. Emamectin Benzoate is available as 5% soluble granules. It is water soluble. It is important to label and store chemicals safely to minimise harm by accidental ingestion. Detailed literature search of case reports of Emamectin Benzoate poisoning in pets have not been found and no specific management or treatment of Emamectin Benzoate poisoning in pets are lacking. Hence, after informed consent from the owner of the pet and with available standard recommendations, the pet was treated with ILE and the treatment was successful. The pet survived uneventfully. Any clinical case presented with signs of toxicity a meticulous history will give vital details as an empty container in this case. The pet owners should be aware of the consequences and use the pesticides as per the manufacturer’s instructions. The safe disposal of all things utilised for insecticides or pesticides as per the manufacturer’s instructions plays a vital role in preventing toxicity.

Here we have reported probably the first case of Emamectin Benzoate poisoning in a pet presented with signs of gastritis, depressed mentation, hypersalivation, sluggish menace reflex managed successfully with activated charcoal, intravenous fluids and Intravenous Lipid Emulsion.

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