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Popular Article

Ivermectin Toxicity in Animals: Understanding the Dangers and Preventive Measures

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Introduction

Ivermectin is a medication derived from avermectins, produced by the soil bacterium *Streptomyces avermitilis*. Ivermectin is a widely used antiparasitic medication in both human and veterinary medicine. Despite of being effective in treating various parasitic infestations in animals, its misuse and improper administration can lead to potentially severe toxicity. This article explores the dangers of ivermectin toxicity in animals and offers insights into preventive measures to safeguard our beloved pets and livestock.

Common Animals at Risk

- Ivermectin is typically harmless for most species, but some are more sensitive to its toxicity than others. These consist of Dogs: Certain dog breeds, particularly Collies, Shetland Sheepdogs, Australian Shepherds, and similar crossbreeds have a mutation known as the MDR1 mutation that makes it difficult for them to properly remove resulting in severe toxicity.
- Cats: When compared to dogs and other livestock animals, cats are more sensitive to ivermectin. The drug must be administered with caution to feline patients.
- Ivermectin is frequently used in livestock to manage parasites, but if administered incorrectly, it can be harmful, especially to young or weak animals.



- Individual Variation and Dosing: Beyond breed-specific sensitivities, individual variation in drug metabolism and sensitivity can also influence an animal's response to ivermectin. The ability of an animal to process and tolerate the drug might be impacted by variables like age, health, and concurrent medications. To prevent toxicity, the precise dosage must be used and should be determined by the animal's weight and state of health.

Causes of Ivermectin Toxicity in Dogs:

Ivermectin toxicity in dogs mostly results from unintentional overdose. Some potential causes of the overdose include:

- Consumption of a livestock ivermectin product designed for large animals (i.e., at a dosage higher than advised for dogs).

- consumption of the excrement of cattle that received ivermectin treatment for parasite management. The medication (which is eliminated in faeces) nevertheless carries a risk of toxicity due to the significantly higher doses used in livestock compared to canines.
- Overdosing on a canine ivermectin product, either as a result of inappropriate weight/size range or simultaneous consumption of numerous monthly doses.

Mechanism of Toxicity

These medications are macrocyclic lactones and have numerous shared characteristics among them, including their mechanisms of action. By enhancing glutamate-gated chloride ion channels, these medicines render parasites neurotoxic. Increased permeability to chloride ions and hyperpolarization of nerve cells produces paralysis and death of the parasite. These medications additionally activate chloride channels that are GABA-gated. Since mammals lack glutamate-gated chloride channels and have a lesser affinity for other mammalian chloride channels, they are typically unaffected. GABA-gated channels in the mammalian CNS are unaffected by these medications because they typically do not cross the blood-brain barrier.

Ivermectin is effective against heartworm microfilaria, mites, bots, intestinal parasites, and growing larvae. GABA-mediated transmission occurs in peripheral synapses in nematodes and arthropods, but only in the central nervous system in mammals, where ivermectin would typically not be able to enter due to its large molecular size. Ivermectin binds to glutamate-gated chloride channels in peripheral neurons in nematodes and arthropods. Mammals do not have these channels. According to the widely recognized theory of action, ivermectin has toxic effects in mammals by enhancing GABA (g-aminobutyric acid) release and binding at specific neuronal synapses in the central nervous system. The fact that GABA-mediated neurotransmission is limited to the central nervous system in mammals and that ivermectin typically does not reach the mammalian central



nervous system may help to explain the wide margin of safety in mammal species.

Ivermectin concentrates in the liver and body fat. Its hepatic metabolism is minimal and it is eliminated in the faeces.

- **Cytochrome P450 Enzymes and Ivermectin Metabolism:** Ivermectin is metabolized in the liver by a family of enzymes called cytochrome P450. These enzymes are crucial in the breakdown of medications and poisons, enabling the body to get rid of them. Ivermectin metabolism is slowed down in some dog breeds, such as Collies, due to a genetic mutation that affects the activity of cytochrome P450 enzymes. As a result, the medication builds up to hazardous levels, raising the possibility of side effects.

Toxicity Symptoms of Ivermectin:

Ivermectin poisoning symptoms might differ depending on the species, the individual sensitivity, and the dosage administered. Typical signs include:

- **Neurological issues:** Ataxia (loss of coordination), tremors, and seizures.
- **Gastrointestinal issues:** nausea, diarrhoea, and appetite loss.
- **Respiratory distress:** Breathing that is rapidly or laboriously.
- **Visual impairment:** blurred vision, dilated pupils, and blindness.
- **Lethargy:** A lack of energy and weakness
- **Coma:** In serious cases, Ivermectin poisoning can result in a coma or possibly death.

Lesions:

1. **Gastrointestinal inflammation:** This condition results in damage to the stomach and intestines by inflaming the lining of the digestive tract.
 - **Erosion and ulcers:** In extreme cases, the intestinal and stomach mucosa may develop erosions and ulcers, which can lead to gastrointestinal bleeding, vomiting, and diarrhoea.
2. **Neurological Lesions:**
 - **oedema:** Areas of oedema (swelling) in the brain and spinal cord may be visible.
 - **Neuronal degeneration:** Long-term or high-dose ivermectin exposure may cause neuronal degeneration, resulting in irreversible neurological impairment.
3. Ivermectin poisoning can result in hepatotoxicity, which is characterised by alterations in liver cells, hepatocyte degeneration, and inflammation. Hepatic (liver) harm. Liver failure could occur in extreme circumstances.

Ivermectin can have an adverse effect on the kidneys, resulting in renal tubular injury, inflammation, and decreased kidney function.



4. Ocular Lesions: • Retinal Degeneration: In some animals, ivermectin can induce retinal degeneration, which can impair vision and, in severe circumstances, result in blindness.
5. Respiratory Lesions: • Pulmonary edoema, which causes breathing difficulties.

Treatment:

- Management of Liver and Kidney Impairment
- Monitoring and Symptomatic Treatment, Activated Charcoal Administration
- Isotonic dextrose normal saline, 1.0 mg/kg physostigmine and 3 mg/kg dexamethasone

Preventive Measures

To avoid ivermectin toxicity in animals, responsible pet owners and livestock managers should adhere to the following preventive measures:

- a) Veterinary Guidance: Always seek advice from a qualified veterinarian before administering any medication to your animals. Based on the animal's weight and condition, dosages should be carefully calculated.
- b) Be cautious of breed-specific sensitivity, particularly in dogs, and use alternative drugs if necessary.
- c) Prevent Off-Label Use: Because doses and tolerances can differ greatly between species, never use ivermectin formulations designed for one species on another.
- d) Separate Livestock from Dogs: Prevent accidental exposure to ivermectin by keeping treated livestock away from susceptible dog breeds.
- e) Secure Medications: Store ivermectin and other medications in a safe place, out of reach of animals and children.

Conclusion

Ivermectin is an essential tool in the fight against parasites in animals, but its misuse can lead to severe toxicity and potential fatalities. In order to protect our cherished animals, including pets and livestock, responsible usage, accurate dose, and knowledge of breed-specific sensitivities are essential.

In order to ensure safe and responsible use, it is essential to better understand the pathophysiology of ivermectin poisoning. The blood-brain barrier, cytochrome P450 enzymes, the interaction of the GABA receptor, and individual variance are all important factors in deciding how an animal will respond to the medication.

