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Fenpyroximate Poisoning: A Mini Review

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ABSTRACT

Fenpyroximate is an acaricide that acts by inhibiting the complex I of the mitochondria. It is a white crystalline powder with poor solubility in water. Fenpyroximate is absorbed from gastrointestinal tract following ingestion then metabolized and eliminated with a half-life of 8 to 49 hours depending on the dose. In acute toxicity fenpyroximate can cause metabolic acidosis, gastrointestinal irritation, neurotoxicity and CNS depression. There is no specific antidote for fenpyroximate, treatment is symptomatic and supportive. Decontamination should be considered, rinse contaminated eyes with water immediately, do not induce emesis. Activated charcoal should be considerable, management of hypotension, metabolic acidosis should be done carefully and monitored. Benzodiazepines may prevent neurotoxicity and seizure. Further studies are needed for more accurate diagnosis and treatment.

KEYWORDS: Fenpyroximate; Poisoning; Neurotoxicity

INTRODUCTION

Fenpyroximate is a phenoxypyrazole acaricide that acts by inhibiting the complex I of the mitochondria which also known as NADH-ubiquinone reductase [1]. It is widely used in agriculture and horticulture to eliminate insects, and can control all stages of mites [2]. Fenpyroximate has been associated with cases of life-threatening intoxication in humans [3,4,5].

Chemistry:

It is a white crystalline powder with molecular formula of C24-H27-N3-O4, it has poor solubility in water (2.31X10-2 mg/L at 25 °C, pH 7) and is soluble in solvents such as methanol (15.3g/l), acetone (150g/l) and chloroform (1197g/l) [6].

TOXICOKINETIC

Fenpyroximate relatively well absorbed from gastrointestinal tract following ingestion, it is absorbed and eliminated faster at lower doses, but at high doses its rate of absorption and elimination is reduced. In experimental animal half-life was 8.9 hours. At the high dose the half-life was 45-49 h [6]. In one study, rats were given 96 mg/kg fenpyroximate orally and half-life was 30.92±3.67h [7].

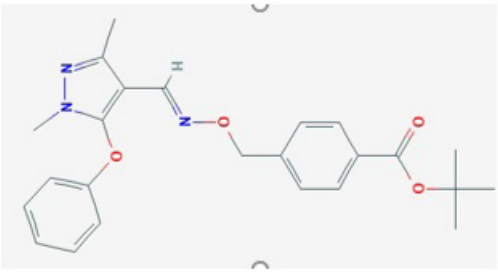

Figure 1: Fenpyroximate Structure

MECHANISM OF ACTION

The mechanism of action of this toxin has been investigated in a study by Motoba et al. in 1992, they reported fenpyroximate inhibits its electron transport from NADH or NADH-linked substrates as the electron donors, so it is inhibitor of NADH-ubiquinone reductase. With this mechanism fenpyroximate can decrease amount of ATP production and subsequently causes morphological changes in mitochondria [8].

CLINICAL MANIFESTATION

Acute Toxicity

In cases of human intoxication, decreased level of conscious, metabolic acidosis, hypotension, neurotoxicity, and even cholinergic symptoms have been reported [3,4,5]. In two of these three cases, metabolic acidosis was reported to be mild or absent [3,4], but in one case, severe metabolic acidosis was reported [5]. In experimental animal tests moderate oral toxicity was observed in mice and rats. Symptoms of acute toxicity in mice and rats included staining of urine and feces, decreased activity, and hypotension. Decreased food intake was observed in surviving animals one week after dosing. Necropsies of found dead animals were found to cause irritation and / or corrosive effects in the gastrointestinal tract. No signs of acute toxicity or skin irritation were observed after application of the fenpyroximate formulation on the skin. LD50 values in experimental animals ranging from 245 to 480 mg/kg for rat and 440 to 520 mg/kg for mice. Fenpyroximate LC50 values for rat ranging from 0.21 to 0.36 mg/liter air [9,10]. Inhalation of the active ingredient or formulation leads to respiratory symptoms of irritation (shortness of breath, fatigue and shortness of breath) [11].

Chronic Toxicity

In the report of the results of medical supervision on workers producing 5% fenpyroximate formulation eye and skin irritation were observed in July, November 1990 and March 1991[12]. Fenpyroximate caused decreases in hemoglobin and erythrocyte count in animal studies and also increase in aminotransferase [6].

Neurotoxicity

In 2018 Kim et al. reported a case of parkinsonism in a 58 years old man 2 years after fenpyroximate poisoning [13]. In another study KuruppuArachchi et al. Noted bilateral lower limb weakness, unsteady gate, and sensory was lost from T4 down. Their patients also had ptosis and loss of gag reflex which resolved in 24 hours [3]. Lee et al also reported toxic leukoencephalopathy in a patient with fenpyroximate intoxication [5].

Neurotoxicity of fenpyroximate could be because of neurons sensitivity to inhibition of a mitochondrial complex I [14], development of Parkinson disease also could be due to inhibition of mitochondrial complex I [15].

Treatment

Since there is no specific antidote for fenpyroximate, treatment of patients is symptomatic and supportive. Decontamination should be considered, rinse contaminated eyes with water immediately, do not induce emesis [16]. Activated charcoal seems to be effective in other studies so it is considerable, management of hypotension, metabolic acidosis should be done carefully and monitored [5]. Patients may benefit from benzodiazepines to prevent neurotoxicity and seizure [4].

Despite some studies recommending the use of N acetylcysteine in patients with complex 1 inhibitor poisoning [17], Lee et al.'s study noted that antioxidants alone effectiveness in severe poisoning is not sufficient [5].

CONCLUSION

Treatment of fenpyroximate intoxication is challenging and there are few studies about it. Lack of information may make it difficult to manage poisoned patients so we need further studies for more accurate diagnosis and treatment.

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