Case Report

Hepatotoxicity and neurotoxicity of Fipronil poisoning in human: A case report

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Abstract

Fipronil is an N-phenylprazole insecticide which is commonly used pesticide in south India. In animals it has been described to cause toxic manifestations mainly in the Gastro-intestinal (GI) and Central nervous system (CNS) and less commonly in kidney and liver. The available medical literature about toxic effects of Fipronil consumption in humans has been very little and mostly limited to acute GI and neurological manifestation mostly lasting for less than three days. We report the case of a 32-year-old gentleman who had consumed Fipronil (5%) in an attempt of deliberate self-harm. The patient had neurotoxicity features in the form of seizures and decreased sensorium requiring intensive medical care with mechanical ventilation and also had hepatotoxicity. Both hepatotoxicity and neurotoxicity lasted for nearly three weeks. The patient improved with supportive therapy and gradually overcame both the toxicities.

Keywords: Fipronil, hepatoxicity, insecticide, neurotoxicity

Introduction

Fipronil is an N-phenylprazole insecticide which is commonly used pesticide in south India. The available medical literature about toxic effects of Fipronil consumption in humans has been very little and mostly limited to acute GI and neurological manifestation mostly lasting for less than three days. We report the case of a 32-year-old gentleman who had hepatoxic (very rare) manifestation following Fipronil (5%) consumption. In addition to hepatotoxicity, he also had neurotoxicity both of which atypically lasted for nearly three weeks.

Case History

32-year-old gentleman presented to our hospital with an alleged history of consumption of an insecticide following domestic dispute with his wife. He had consumed 150 ml of five percent Fipronil (N-phenylpyrazole) identified by the container [Figure 1] brought by relatives.

The patient had consumed it two weeks prior to his presentation to our hospital and currently presented with history of altered sensorium with recurrent episodes of seizures and jaundice for past two weeks. After being treated for nearly 10 days, his symptoms and deranged liver function test were persistent and hence was referred to our hospital for further management.

At presentation to casualty, he was conscious, altered sensorium with a Glasgow Coma Scale GCS - 13/15 (E4V4M5). His pulse was 92/min, regular, blood pressure 110/70 mmHg and respiratory rate 18/min and afebrile. He had pallor and icterus. There were no focal neurological deficits. There was absence of hepatosplenomegaly or any signs of hepatic encephalopathy. His cardiovascular and respiratory examination was normal. He had three episodes of GTCS in the hospital.

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On initial evaluation, his blood counts and metabolic parameters except liver function test were all normal [See Table 1]. Ultrasound of the abdomen was normal. MRI brain images done outside were reanalyzed and found to be normal. CSF analysis and EEG was normal.

He was treated with antiepileptics (phenytoin, levetiracetam and clobazam) and atypical antipsychotics (Quetiapine). His levetiracetam levels were found to be 6.1 mg/ml and hence the dose was increased. His altered sensorium gradually improved to being normal. His liver function test showed a gradual declining trend with complete resolution by third week after being conservatively managed. A psychiatric consult was sought during hospitalization. He is on a regular follow-up and has been doing well.

Discussion

Fipronil ($C_{12}H_4Cl_2F_6N_4OS$) is a broad spectrum, first N- phenylpyrazole insecticide [see Figure 2].

It was first introduced with aim of controlling insect pest which had gained resistance to conventional pesticides. It is classified as WHO (World Health Organization) Class II moderately hazardous pesticide.

Fipronil blocks GABA (A) gated chloride channels in the central nervous system. Disruption of the GABA (A) receptors by

Table 1: Baseline investigations at admission

Haemoglobin (gm/dL)	14.3
WBC Counts (per cu. mm)	12,000 (N-77, L-13)
Platelets (per cu. mm)	2,53,000
Sodium/Potassium (mmol/L)	137/3.8
Calcium/Phosphorous (mg/dL)	9.9/3.5
Magnesium (mg/dL)	1.85
Urea/Creatinine (mg/dL)	29/0.99
Liver function test	3.18/0.85/7.6/4.1/41/84/112
PT/INR/APTT	10.5/0.96/27.5

Figure 1: FISTO - 5% Fipronil

Fipronil prevents the uptake of chloride ions resulting in excess neuronal stimulation and death of the target insect.[1] Fipronil exhibits differential binding affinity for GABA (A) receptor subunits, with a higher binding affinity for insect receptor complexes compared to mammalian complexes. The lower binding affinity for mammalian receptors enhances selectivity for insects and increases the margin of safety for people and animals.[2]

Fipronil also impedes the metabolic enzymatic systems that are often known to contain sulfhydryl groups and uncoupling of oxidative phosphorylation in the mitochondrial complex resulting in ischemia, hypoxia of vital organs and death.[3] Toxic effects in liver and kidneys have been described in animals.[4]

Kartheek *et al.* studied hepatotoxicity of Fipronil in wistar rats and found that Fipronil causes significant rise in levels of AST, ALT and ALP with hepatotoxicity effect lasting till 90 days at selected doses.[5] Recently, Pandit *et al.* demonstrated pulmonary toxicity in mice models secondary to chronic exposure to low dose Fipronil.[6]

However, there is limited information available in the current literature about clinical manifestations and management of Fipronil poisoning in humans. Two accidental cases of poisoning were reported.[7,8] A case series of seven patients from Srilanka was reported in 2004, wherein all the patients had vomiting and neurological manifestation and had shown clinical improvement and become asymptomatic within three days.[9] In a study by Lee *et al.*, 103 cases of Fipronil exposure had mild neurological complaints followed by ocular, respiratory, and dermatology complaints.[10] There was only one case report from India till date of Fipronil poisoning, wherein apart from the neurotoxicity (seizures), the patient also had acute kidney injury with mild hepatic dysfunction.[11]

Our patient had neurotoxicity features in the form of seizures and decreased sensorium requiring intensive medical care with mechanical ventilation and also had hepatotoxicity in the form of toxic hepatitis with jaundice with deranged liver function (hepatocellular pattern).

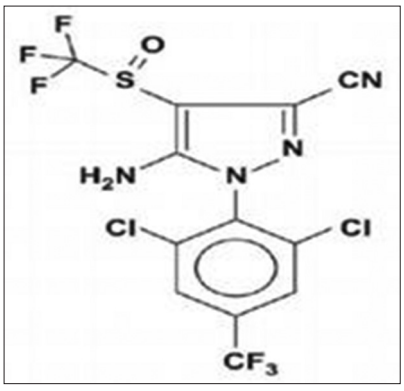

Figure 2: Chemical structure of Fipronil. (IUPAC name is 5-amino-1-[2, 6 dichloro-4-(trifluoromethyl) phenyl]-4-(trifluoromethyl sulfinyl)-1H-pyrazole-3- carbonitrile)

There has been only single case report till now describing mild liver dysfunction following Fipronil poisoning. However, in the case which we have described, the hepatoxicity was severe and longer in duration. Both hepatotoxicity and neurotoxicity lasted for nearly three weeks, which was much longer than the clinical profile (less than three days) described in the cases reported so far.[7-11] However, both these toxic manifestation required only conservative symptomatic treatment and the patient survived and gradually overcame both the toxicities with no long-term side effects of the toxin.

We hope this article helps the primary care providers to understand the clinical manifestations and management of Fipronil poisoning in humans especially considering the rise in use of Fipronil in agricultural sector.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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