CASE REPORT

Fipronil and Acetamiprid Poisoning: New Perils

Ramkumar Jayaprakash[1], Ashok Elangovan[2], Pradeep Nagaraju[3]

Abstract

Suicides due to insecticide poisoning represent a major public health concern. Introduction of newer synthetic pesticides like neonicotinoids and fipronil, with novel mechanisms of action, have led to widespread adoption of these in the agriculture industry. They act by altering the neuronal transmission mechanisms in the central nervous system, specifically of the invertebrates, and lead to death of the organism. Though they were perceived to be invertebrate-specific, there have been few case reports of these, leading to notable clinical adverse effects on human exposure. We present a case of acetamiprid and fipronil consumption, who presented to us with central nervous system manifestations and his clinical management. With increasing use of newer pesticides, clinical knowledge regarding the toxic effects of these seems indispensable.

Keywords: Acetamiprid, Fipronil, Poisoning, Seizure.

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Introduction

Deliberate self-harm with pesticides represents a major hidden public health problem, accounting for up to a third of all suicides worldwide. It is estimated that more than 300,000 people die from pesticide poisoning each year.[1] Concerns regarding human safety due to use of organophosphorus/organochlorine pesticides and the selection of resistant insect strains have provided new impetus to develop newer insecticides like neonicotinoids and fipronil. The relatively low risk for nontarget organisms and the environment and the high specificity for target insects have led to widespread acceptance of these novel insecticides in the farming community.

Neonicotinoids and fipronil exert their toxic effects by altering the mechanism of neural transmission in the central nervous system (CNS) of invertebrates. While neonicotinoids mimic the action of neurotransmitters, fipronil inhibits these receptors. By doing so, they ultimately lead to death of target invertebrates. Here, we present a case report of both acetamiprid (neonicotinoid) and fipronil poisoning.

Case Report

A 45-year-old man was referred to our hospital emergency department with alleged history of ingestion of pesticide, which contained a combination of acetamiprid 4% (w/w) and fipronil 4%. He had a generalized tonic clonic seizure (GTCS), while being transported to our hospital. On arrival, his GCS was E1V2M5. There was drooling of oral secretions. His heart rate was 45–55/minute, and blood pressure was 100/60 mm Hg. He was breathing at 20–25 breaths/minute and SpO_2 >94% on room air. He was intubated for airway protection and initiated on mechanical ventilation. He was commenced on midazolam for his seizure management. Gastric lavage was done, and activated charcoal was administered. Laboratory investigations revealed a normal hemogram, sodium of 135 mmol/L, potassium of 2.9 mmol/L, creatinine of 0.81 mg/dL, and urea of 24 mg/dL. ABG showed pH 7.30, PaO_2 172 mm Hg, $PaCO_2$ 36 mm Hg, HCO_3 17.7 mmol/L, and lactate 3.9 mmol/L. A plain chest radiograph was normal, and ECG showed sinus bradycardia.

He was transferred to the ICU for further management. Invasive ventilatory support and other supportive care were continued. Potassium was 4.5 mmol/L, post-IV correction. Over the next 24 hours, his sensorium improved and there were no focal neurological deficits. His muscle power was adequate, and he was successfully weaned off ventilatory support and extubated. He made an uneventful recovery and was discharged home after 3 days of hospital stay.

Discussion

Nicotine from tobacco extracts was used as plant-derived insecticide in 1600s. Later, synthetic organics, like neonicotinoids, replaced inorganics and botanicals. The neonicotinoids act as agonists at the postsynaptic nicotinic acetylcholine receptors (nAChRs) of insects and mammals. The neonicotinoids are not protonated but instead have an electronegative tip that imparts potency and selectivity. The low mammalian toxicity of neonicotinoids has also been explained by its inability to cross the blood–brain barrier because of lack of a charged nitrogen atom at physiological pH. The uncharged molecule, however, can penetrate the insect blood–brain barrier. These differences provide the neonicotinoids with favorable toxicological profile.[2] However, the desnitro breakdown product, which is formed in a mammal's body, postmetabolism has a charged nitrogen and shows high affinity to mammalian nAChRs.[3]

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The mechanism of action of organochlorine pesticides was discovered in the early 1980s. The antagonistic activity on the GABA receptors prevents the opening of chloride ion channels leading to lowering neuron's membrane potential. This results in CNS hyperstimulation. Fipronil, a N-phenylpyrazole insecticide, acts by binding to allosteric sites of GABAA receptors as an antagonist, but not to the GABAC receptor.[4] Of all GABA receptor-binding pesticides, fipronil has the highest specificity for insect GABA receptors with 150-fold–2,000-fold selectivity. Fipronil is metabolized in mammals to a sulfone compound, which binds to native human GABA receptors with around sixfold higher avidity.[5]

There is dearth of literature considering acetamiprid and fipronil poisoning. Lin et al., in their literature review regarding neonicotinoid poisoning, have noted that acetamiprid poisoning accounted for about 5% of neonicotinoid poisonings.[6] Seizures were seen in 5% of all cases. Coma was noted in 64% of cases. Apnea/dyspnea was seen in 73% of cases. Severe intoxication, characterized by apnea/dyspnea, GCS <8, tachy/bradycardia, and hypotension, was seen in up to 33% of cases. Todani et al. reported a patient who had coma, hypotension, nausea, vomiting, and hyperglycemia following intentional acetamiprid ingestion. The patient had paroxysmal atrial fibrillation for ~11 hours. Subsequently, the patient was discharged without any complications.[7] Imamura et al. have reported two cases with intentional acetamiprid ingestion who had CNS manifestation in the form of single self-limiting seizure. Both of them had muscle weakness, which resolved spontaneously. They were discharged without any complications.[8]

Mohamed et al. have presented a case series of seven patients with fipronil intoxication. Nonsustained GTCS was seen in two patients, both of whom were treated with diazepam and recovered without any neurological deficits. They also describe a patient who was unconscious on admission and had to be intubated. The patient had GTCS several times despite therapy with benzodiazepines and phenobarbitone. He subsequently developed pneumonia and died in ICU.[1] Yadla et al. have reported a case who had four episodes of seizures following fipronil poisoning. Subsequently, she developed acute kidney injury (AKI) needing renal replacement therapy.[9] Lee et al. have presented surveillance data from United States regarding acute illness associated with fipronil exposure. Neurological symptoms like headache, dizziness, paresthesia, muscle weakness, and confusion were most common (>50%) observed clinical manifestations. All of them improved with supportive care.[10]

Thus, management of both acetamiprid and fipronil intoxication remains predominantly supportive in nature, in the absence of any specific antidote. Appropriate timely resuscitation and supportive care lead to favorable outcomes. Seizure management with standard protocols with benzodiazepines, maintenance of oxygenation, ventilation, and circulation form the mainstay of therapy. Though acetamiprid and fipronil are generally considered to be less toxic to humans, the clinician should watch out for potential complications, which predominantly needs supportive care.

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