Case Report

Chlorantraniliprole: An unusual insecticide poisoning in humans

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Abstract

A 26-year-old female presented with deliberate self-harm using chlorantraniliprole, an unknown substance in human toxicology. She developed symptomatic Mobitz Type I atrioventricular block during observation, for which a temporary pacemaker was inserted. She reverted to sinus rhythm after 48 h and was discharged. Although claimed to be nontoxic to humans, chlorantraniliprole, an insecticide, could cause conduction defects by activating ryanodine receptors. To the best of our knowledge, this is the first case of chlorantraniliprole poisoning reported in the medical literature.

Keywords: Chlorantraniliprole, Mobitz Type I atrioventricular block, ryanodine

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Introduction

Insecticide poisoning is a common modality of deliberate self harm in India. The manifestations of commonly used insecticides are well studied and reported. Here we present a case of deliberate self harm with Chlorantraniliprole, a novel insecticide manifesting with cardiotoxicity and review the possible mechanisms behind the same.

Case Report

A 26-year-old female presented to the emergency department with alleged history of having deliberately consumed about 10 ml of a pesticide chlorantraniliprole [Figure 1]. She had no symptoms, following consumption of the poison. She had no previous medical comorbidities, and there was no family history of coronary artery disease or sudden cardiac death.

On examination, her temperature was 98.2°F, blood pressure was 100/70 mmHg, and heart rate was 70 beats/min. Her respiratory rate was 18 breaths and saturation was 99% in room air. Her cardiac examination and other systemic examination were normal. She was given a gastric lavage in emergency and transferred her to the ward for observation. She had normal complete blood counts and metabolic parameters. Her coagulation parameters, thyroid functions, and chest X-ray were also normal.

During observation, the cardiac monitor revealed intermittently dropped P-wave with a rate of 58/min. Subsequently, she complained of lightheadedness and her heart rate was found to be 47/min, with a systolic blood pressure of 90 mmHg. Electrocardiogram (ECG) showed the presence of a Mobitz Type I atrioventricular (AV) block - progressively prolonging PR interval -

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followed by an unconducted P-wave, corrected QT interval of 384 ms, and a QRS interval of 86 ms [Figure 2].

She was administered 1.2 mg of atropine as an intravenous bolus to revert to sinus rhythm. In spite of multiple doses of atropine, she continued to have bradycardia with repeat ECG showing persistence of AV block. She underwent temporary transvenous pacemaker placement through femoral approach. A transthoracic echocardiogram showed normal ejection fraction and no evidence of regional wall motion abnormalities. Subsequently, her symptoms and hemodynamic parameters improved. Pacemaker was removed after 48 h when her ECG showed normal sinus rhythm, with a baseline heart rate of 66 beats/min, normal sinus rhythm, PR interval of 138 ms, QRS interval of 90 ms, and a QT interval of 431 ms. She was discharged subsequently after a counseling session.

Figure 1: Container of the pesticide alleged to have been consumed by the patient

Discussion

Chlorantraniliprole is structurally 3-bromo-4′-chloro-1-(3-chloro-2-pyridyl)-2′-methyl-6′-(methylcarbamoyl) pyrazole-5-carboxanilide and belongs to the chemical group diamides. It has a different mode of action compared to other common insecticides and acts as a ryanodine receptor modulator.[1]

Structure of Chlorantraniliprole is depicted in Figure 3.[1]

Chlorantraniliprole activates ryanodine receptors through stimulation of the release of calcium stores from the sarcoplasmic reticulum of muscle cells causing impaired regulation, paralysis, and ultimately death of sensitive species. The differential selectivity of chlorantraniliprole toward insect ryanodine receptors explains its low mammalian toxicity. It is active on chewing pests primarily by ingestion and secondarily by contact and shows good ovi-larvicidal and larvicidal activity. Chlorantraniliprole was of low acute toxicity by the oral, dermal, and inhalation routes in a rat. Chlorantraniliprole is applied for use in apples and acts

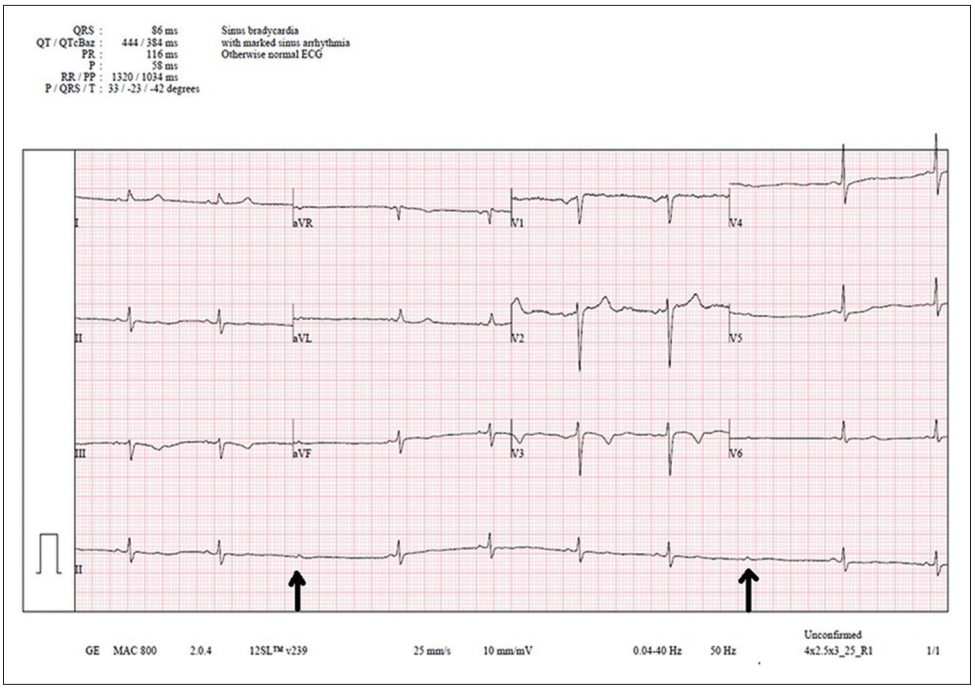

Figure 2: Electrocardiogram of the patient showing the presence of a Mobitz Type I atrioventricular block with a heart rate of 48/min, progressively prolonging PR interval, followed by an unconducted P-wave (arrows), corrected QT interval of 384 ms, and a QRS interval of 86 ms

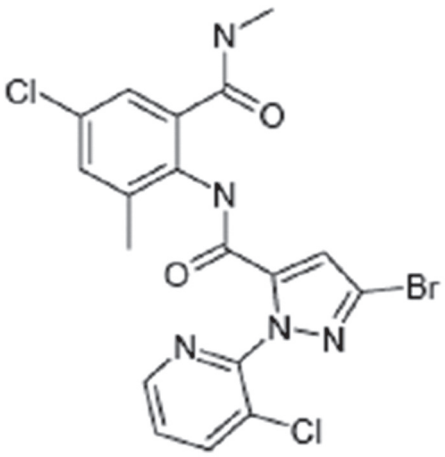

Figure 3: Structure of chlorantraniliprole

against caterpillars of *Lepidoptera*, codling moth (*Cydia pomonella*), apple fruit moth (*Argyresthia conjugella*), and free leaf living larvae.[2]

There are multiple isoforms of ryanodine receptors: RyR1 is primarily expressed in skeletal muscle, RyR2 in myocardium, and RyR3 in the brain.[3] The primary mechanism in cardiac muscle is calcium-induced calcium release from the sarcoplasmic reticulum.[4] RyR2 mutations play a role in stress-induced polymorphic ventricular tachycardia and arrhythmogenic right ventricular dysplasia.[3] Animal experimental studies have demonstrated cRyr2KO mice to exhibit a significantly lower rate of heart contraction by echocardiography when RYR2 protein levels were 50% reduced. ECG wave patterns have indicated that this decreases in heart rate as sinus bradycardia. Instances of mice exhibiting a secondary AV block were also observed. This indicates that RYR2 ablation is sufficient to decrease heart rate at both contractile and signaling levels.[5]

Chlorantraniliprole has been an unknown substance in human toxicology. It is presumably the mechanism elaborated above, which has been responsible for the cardiac manifestations in our patient. We ruled out all possible cardiac causes such as rheumatic heart disease, ischemic heart disease, heart failure, and previous cardiac surgery along with metabolic abnormalities such as hypokalemia, hyperkalemia, calcium and magnesium abnormalities, hypothermia, azotemia, and hypothyroidism. She had no medications such as digoxin, beta-blockers, and calcium channel blockers. As we excluded all the other causes of AV block, the association of the above cardiac findings was attributed to consumption of chlorantraniliprole. To the best of our knowledge, there have been no previous case reports of chlorantraniliprole poisoning in humans. We presume that AV block leading to symptomatic bradycardia might be one of the various manifestations of chlorantraniliprole. We suggest reporting of the various clinical manifestations of this compound in future for further understanding of its effects.

Conclusion

There is a quest among researchers to discover pesticides with high selectivity so that it is nontoxic to humans. Although it can be claimed that they are partly successful based on animal experiments, one cannot be sure of its absolute safety in humans. Chlorantraniliprole is one such compound with such claims, which has presented with significant toxic manifestations though not lethal in this present case. This emphasizes the need to approach any unknown poisoning holistically to identify subtle manifestations which have not been reported by experimental studies.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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