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Acetamiprid Poisoning: A Case Report of Self- Poisoning with an Acetamiprid-Containing Insecticide

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A B S T R A C T

Insecticides play an important role in controlling as well as in preventing the transmission of insect-borne diseases. However, insecticides exposure can result in harmful off-target effects. Over the past few decades, numerous classes of insecticides have been introduced. Neonicotinoids means "new nicotine-like insecticide", were developed to replace older and more harmful insecticides. Acetamiprid is a new-generation chloronicotinyl insecticide target nicotinic acetylcholine receptors. The majority of studies have endorsed the use of neonicotinoids as a safer alternative to other insecticides. However, a few studies have associated neonicotinoid exposure in mammals with adverse reproductive and developmental outcomes, such as embryo death, premature birth, reduced pregnancy rates, impaired sperm function, decreased offspring weight, and stillbirth. Understanding the risks across these classes is crucial for developing safer strategies. Here, we present a case report of a 32-year-old male who self-poisoned with an acetamiprid- containing insecticide. Upon presentation, he exhibited abnormal vital signs, which ultimately led to cardiac arrest despite resuscitation efforts. Treatment involved supportive measures with intravenous fluids and vasopressors, administering atropine and performing endotracheal intubation. After four days, the patient showed signs of improvement, eventually being successfully extubated, and discharged 13 days later in stable condition.

Introduction

Insecticides are vital for controlling insect damage to crops, livestock, and pets, as well as for disease prevention. Unfortunately, they also have toxic effects that can harm other species, including humans. Certainly, insecticides predominantly affect the nervous system, and the resemblances between insect and human nervous systems frequently result in cross-toxicity. As a result, both experimental animal research and epidemiological evidence emphasize the health risks linked with exposure to all these insecticide classes [1]. Neonicotinoids have emerged as the fastest-growing class in conventional crop protection, broadly used against a broad spectrum of sucking and chewing pests. Their popularity stems from their high toxicity to invertebrates, ease of application, flexibility, long-lasting effects, and systemic nature, which ensures widespread distribution throughout the target crop [2]. The seven neonicotinoids authorized for global commercial use are imidacloprid, thiacloprid, clothianidin, thiamethoxam, acetamiprid, nitenpyram, and dinotefuran, comprise the most extensively employed class of insecticides worldwide. These neonicotinoids are broad-spectrum insecticides, a factor that has facilitated their successful market entry. Acetamiprid, (E)-N′-[(6-Chloro-3-pyridyl) methyl]-N2Cyano-N′- methylacetamidine, a new-generation chloronicotinyl insecticide, is widely utilized as an alternative to organophosphates and carbamates for insect pest control. It has been employed worldwide for the management of various pests, including sucking insects, aphids, leafhoppers, moths, beetles, hemipterans, and lepidopterans, affecting commercial crops as well as fruits, flowers, and ornamental plants. It is designed to target nicotinic acetylcholine receptors in insects, it's extensive use has led to adverse effects in non-target organisms, including mammals. Traces of acetamiprid have been found in various food products, water sources, and soil. Moreover, the metabolism of acetamiprid produces toxic metabolites detected in the brain, liver, plasma, and urine of rodents [3]. Compared to other insecticides, neonicotinoids have lower mortality rates than organophosphates (12.3%) and carbamates (7.3%), with imidacloprid frequently associated with mortality, while death from acetamiprid has not been documented [4].

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Case Report

This case involves a 32-year-old male with no known prior medical history who arrived to the emergency department approximately one hour after ingesting 30-40 ml of pesticide liquid in a suicide attempt. He experienced multiple episodes of vomiting during his transfer to hospital. Upon arrival, he complained of dizziness and exhibited recurrent episodes of nonbilious and nonprojectile vomiting. His roommate provided the pesticide bottle he consumed which contains Acetamiprid as a main component at a concentration of 20%. The patient denied chest pain, shortness of breath, throat discomfort, abdominal pain, diarrhea, urinary incontinence, or blurred vision.

Physical examination revealed a patent airway with normal breath sounds with clear chest on auscultation, with no signs bronchorrhea, crackles, or wheezes upon chest examination. Despite an increased respiratory rate to 35 breaths per minute, his oxygen saturation was maintained at 96% on room air. Initial vital signs revealed hypotension with blood pressure readings of 75/42 mmHg and tachycardia with a heart rate of 140 beats per minute. The patient also showed signs of fatigue and dry mucous membranes, while maintaining a GCS score of 15/15. Pupillary examination showed bilateral constriction (miosis), in the absence of signs such as oral drooling, lacrimation, or excessive salivation. Cardiovascular assessment revealed normal heart sounds without audible murmurs or additional sounds. His abdomen was soft and nontender. The peripheries revealed normal pulses and warm skin. The ECG displayed sinus tachycardia with ST depressions in V4-6, flattening of P waves and normal QT intervals as shown in (Figure 1). Initial venous blood gas (VBG) demonstrated metabolic acidosis with respiratory alkalosis and high lactate of 9.10 mmol/L, a pH of 7.44, PO_2 of 48 mmHg, PCO_2 of 18 mmHg, HCO_3 of 12.3, Na of 136 mmol/L, K of 2.4 mmol/L, Cl of 104 mmol/L, blood glucose of 11.5 mmol/L, beside normal ranges of CO and methemoglobin levels.

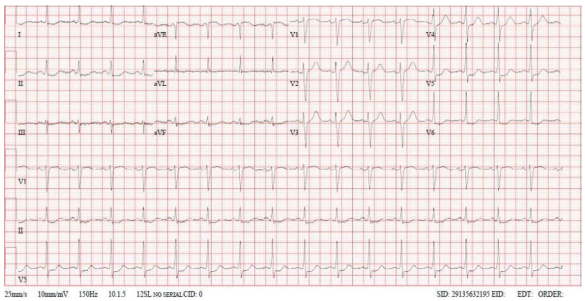

Figure 1: ECG shows sinus tachycardia with ST depression in lead V4-6, flattening of P waves and normal QT intervals as shown.

The patient received intravenous (IV) fluids and antiemetics upon arrival and was promptly connected to a continuous cardiac monitor in the resuscitation bay. The toxicology team was consulted. Despite the administration of 2 L of normal saline and ringer lactate, the patient's blood pressure did not improve, prompting the initiation of norepinephrine infusion, which resulted in a slight improvement in blood pressure. However, the patient deteriorated shortly afterward and experienced cardiac arrest with an initial rhythm of asystole. Immediate cardiopulmonary resuscitation (CPR) was initiated as per ALS guideline, and the ECMO team was called in. Return of spontaneous circulation (ROSC) was achieved after two cycles of CPR and administration of single dose of epinephrine 1:10000 IV and AV ECMO was terminated. The patient remained unconscious, and extensive secretions were noted from the nares and mouth, urging to the administration of repeated doses of IV atropine (Total of 4 mg). Subsequent VBG analysis revealed worsening acidosis with PH of 7.01 and further elevation in lactate levels to 12.1. The patient was subsequently intubated and placed on mechanical ventilation in controlled mode setting as follows: TV 420, RR 30, PEEP 8, FiO_2 60%. Patient developed a pulseless ventricular fibrillation while attempting to insert a central venous line, and ROSC was achieved after single DC shock. A chest X-ray revealed patchy infiltrates in the right lung, likely due to aspiration (Figure 2).

The patient was then admitted to the Intensive Care Unit (ICU) for further management, where he received sedation with fentanyl and midazolam infusions, as well as vasopressin and noradrenaline infusions initially, which were later switched to phenylephrine and vasopressin for mean arterial pressure (MAP) support. Supportive management for acetamiprid toxicity was continued by the toxicology team, and the patient received ampicillin-

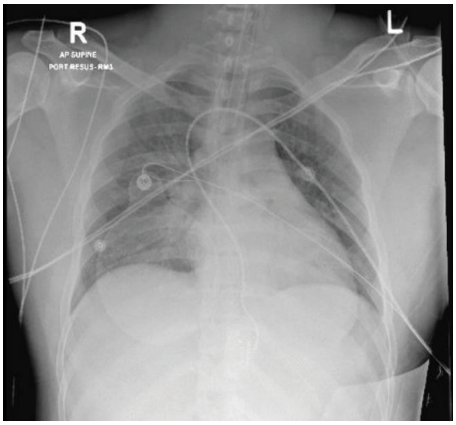

Figure 2: Chest XR shows infiltrate in the lower lobe of the right lung.

sulbactam and heparin prophylaxis during his ICU stay. After four days, the patient was weaned off sedation and vasopressors and he was successfully extubated and showed gradual signs of improvement, including improved mental status and oral feeding tolerance, prompting transfer to the medical ward for ongoing care.

Throughout his hospitalization, the patient developed odynophagia and dysphagia that requiring ENT fiberoptic assessment, which revealed mucosal ulceration over epiglottis that was managed conservatively with subsequent improvement. His clinical course was complicated by the development of diabetic ketoacidosis (DKA), necessitating initiation of intravenous insulin infusion as per DKA management guidelines. In addition, he suffered from elevated troponin levels, initially measured at 318 ng/L (NR 3-15) and escalating to 3,697 ng/L, demanding cardiology assessment. Echocardiography findings revealed moderately reduced systolic left ventricular function, with a calculated biplane left ventricular ejection fraction (LVEF) of 37%, grade 1 diastolic dysfunction, and regional wall motion abnormalities as shown below (Figure 3). These cardiac abnormalities were suspected to be a result of cardiac injury following chemical ingestion (Acetamiprid). However, further investigation with a CT cardiac angiogram unveiled a short segment subtotal occlusion of the proximal left anterior descending (LAD) artery, mid LAD soft plaque with positive remodeling causing mild stenosis, and minimal stenosis in the right coronary artery (RCA) (Figure 4). Though percutaneous coronary angiography was planned, the patient declined the procedure.

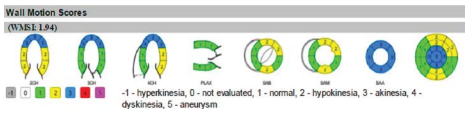

Figure 3: A diagram showing the regional wall motion abnormality in echocardiography.

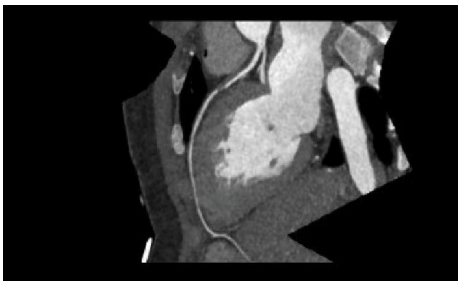

Figure 4: A section of the CT angio-coronary showing LAD stenosis.

Subsequent follow-up assessments demonstrated a declining trend in troponin levels to 18 ng/L, improved LVEF to 60% on echocardiography. His lactate levels decreased from 14.90 mmol/L to 0.90 mmol/L, accompanied by an improvement in pH from 6.789 to 7.407. Ultimately, following the psychiatry team evaluation, the patient was discharged 13 days later in stable condition.

Discussion:

The use of neonicotinoid insecticides in U.S. agricultural production and worldwide has grown dramatically in the past decade. Upon initial approval by the U.S. Environmental Protection Agency (EPA) for commercial use, neonics were deemed less hazardous to wildlife and humans due to their greater chemical affinity for insect nicotinic Ach receptors and their inability to penetrate the mammalian blood-brain barrier. More recent in vitro and in vivo studies as well as ecological field studies suggest adverse effects may occur in mammals at sublethal doses of neonicotinoids. In a systematic review, the review incorporates eight studies focusing on the relationship between neonics and human health. These studies are categorized by the type of exposure whether it is acute or chronic [5].

Among the four studies focusing on acute exposure to neonicotinoids, only one study documented fatalities, with two reported deaths following acute exposure reported to the Taiwan National Poison Center between 1987 and 2007. Out of 70 reported cases, 46 involved neonic ingestion alone, while the remaining 24 cases were co-exposed to different pesticides and/or ethanol. Ten out of the 46 neonic-only cases developed severe symptoms requiring intubation and intensive care, whereas 36 cases were asymptomatic or had mild to moderate symptoms requiring only supportive care. Among the severely ill group, two individuals died of respiratory failure, all of whom had ingested only Imidacloprid. The study found no significant difference in the amount ingested between the severe/fatal poisoning group and the non-severe group (p=0.938), indicating potential exposure misclassification or other contributing factors to fatality. Additional four studies examined the link between chronic environmental exposure to IMI, THX, or N-desmethyl-acetamiprid (DMAP) and adverse human health. Three studies investigated developmental health outcomes such as congenital heart defects (CHDs) and neural tube defects (NTDs). Two of these focused on maternal proximity to pesticide use during periconception, while the third examined maternal use of flea and tick medication containing Imidacloprid [5].

A study involving Wistar rats exposed to acetamiprid (ACP) multiple times found significant liver damage, as evidenced by increased levels of AST, ALT, ALP, and ACP in the plasma, indicating widespread tissue damage. Additionally, there was a dose-dependent impact on glucose metabolism and cholesterol synthesis. Histopathological examinations revealed specific organ lesions, such as lung congestion and hemorrhages, kidney tubular epithelial degeneration, spleen lymphoid cell depletion, and mild to moderate degenerative changes in the heart, female reproductive tract, and brain. Overall, the study concluded that acetamiprid exposure led to substantial harm to multiple organs in rats, advocating potential neurotoxic effects and emphasizing the need for further research to establish safe exposure levels [6].

In vitro testing on human peripheral blood lymphocytes examined the genotoxicity of a commercial acetamiprid formulation. Results indicated decreased the proliferation index (PI), mitotic index (MI), and nuclear division index (NDI) compared to controls. These effects mirrored those induced by the positive control, mitomycin C (MMC). This study provides the first evidence of acetamiprid's genotoxicity in human lymphocytes *in vitro* [7]. At the cellular level, research has shed light on Acetamiprid's molecular genotoxicity and introduced innovative methodologies for analyzing oxidative damage. This study, conducted on Acetamiprid exposure, revealed increased reactive oxygen species (ROS) levels, DNA damage, and elevated concentrations of oxidized nucleotides, including 8-oxo-G in tRNA. Moreover, the study identified altered tRNA fragments in cells following Acetamiprid treatment, indicating potential genotoxic effects [8].

The literature suggests that ingesting large amounts of insecticides can induce a central nervous system response, leading to symptoms such as dizziness, drowsiness, and disorientation. Conversely, autonomic nervous system stimulation can manifest as sweating, dilated pupils, rapid heartbeat, and increased blood pressure. However, not all findings were observed in this case [9].

Few published cases have explored acetamiprid toxicity. A case report published in 2023 conveyed a similar case to ours, involving a 74-year-old woman who ingested a pesticide containing acetamiprid in combination with pyridaben. She experienced symptoms such as nausea, vomiting, and unconsciousness upon arrival at the hospital, with a GCS score of 6 and tachycardia. Treatment involved gastric lavage, intubation, and mechanical ventilation in the ICU. Subsequent tests revealed metabolic acidosis and elevated lactate levels, prompting hemoperfusion and continuous renal replacement therapy. Over 24 hours, the patient gradually recovered, with normal neurological function restored after 23 hours. She was discharged after one week without delayed neurological impairment. This case underlines the challenges in managing acute acetamiprid and pyridaben poisoning due to the absence of a specific antidote, highlighting the possible importance of prompt gastric lavage to decrease absorption and blood purification techniques like hemoperfusion and CRRT to mitigate toxicity and prevent organ damage. In contrast to our case report, where lactate levels continued to decrease without supportive elimination, the patient's outcome was also similar without required intervention [10].

Imidacloprid, a type of neonicotinoid, has been associated with cases of self-poisoning, with rapid absorption and persisting elevated plasma levels for up to 10-15 hours post-ingestion. Mild symptoms are common, but more severe effects including respiratory failure, seizures, and death have been reported. Over a 5-year period, 68 patients presented to study hospitals with imidacloprid exposure, of which 56 were included in the study. The median ingested volume of 15 mL, which is half the amount ingested by the patient in the case report. However, the volume ingested was unknown in 23 cases. Most patients experienced only mild symptoms such as nausea, vomiting, headache, dizziness, abdominal pain, and diarrhea during their hospital stay, which were mostly self-resolving. Although there were no deaths reported, two patients developed more severe symptoms requiring management in an ICU. One patient, who ingested an unknown amount, presented with tachycardia and agitation. At 16 hours post-ingestion, she developed respiratory arrest requiring endotracheal intubation. She received an atropine infusion and was extubated on her 4th day in ICU. The other patient presented to a peripheral hospital after ingesting an unknown amount of imidacloprid while intoxicated. He received forced emesis and atropine before being transferred to a study hospital. Upon admission (4.5 hours post- ingestion), he exhibited vomiting, a regular pulse rate, stable blood pressure, dilated pupils, rapid respiratory rate, normal oxygen saturation, and decreased GCS score. He was later transferred to the ICU for closer monitoring. Treatment included nebulized salbutamol and intravenous antibiotics for aspiration pneumonia. The patient's condition improved within 24 hours, and he was discharged three days later. Although the two cases were treated with pralidoxime, the use of oximes like pralidoxime may be ineffective or even contraindicated, as they can exacerbate nicotinic effects such as tachycardia, hypertension, and muscle weakness, particularly in the absence of organophosphorus pesticides [11].

Another study documented the case of a 56-year-old man with a protracted history of depression who attempted suicide by consuming around 40 ml of pesticide containing 9.6% imidacloprid. The patient illustrated similar findings to those in our case report, including vomiting, dyspnea, diaphoresis, and severe lactic acidosis, alongside comparable vital signs. The patient required mechanical ventilation and admission to the intensive care unit, followed by experiencing significant recovery and ultimately being discharged four days later [12].

In conclusion, most reported cases of acetamiprid poisoning have involved mild symptoms, with only a few occurrences showing notable morbidities, similar to our case. This suggests that while acetamiprid may be a safer alternative to organophosphates and carbamates, it may not be as safe as previously considered. Additionally, the mainstay of treatment currently relies on supportive and resuscitative measures, as no antidote has been discovered yet.

Summary:

Neonicotinoids represent a novel class of potent insecticides with high selectivity for insect nicotinic receptors over those in mammals. Acetamiprid, a prominent neonicotinoid insecticide, has been linked to acute pesticide poisoning with potentially severe health consequences. While various studies have implied at adverse effects associated with exposure, it's crucial to note that the majority of these studies were not conducted on human subjects, requiring caution in extrapolating these findings to human health outcomes. Although most cases of acetamiprid exposure result in only mild symptoms, a few cases stated significant mortalities and morbidities.

Currently, there are no specific antidotes available for neonicotinoid poisoning in mammals, leading to recommendations primarily focused on symptomatic and supportive care. Atropine is recommended in the presence of bronchorrhea.

Further exploration is warranted to ascertain whether substituting older anti-cholinesterase pesticides in agriculture with newer, lower-fatality pesticides will indeed lead to a net reduction in fatalities resulting from self-poisoning.

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