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Acetamiprid and pyridaben poisoning: A case report

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ABSTRACT

Background: The agricultural industry has experienced beneficial outcomes by implementing contemporary synthetic pesticides, specifically, the mixture of acetamiprid and pyridaben. However, concerns regarding public health have arisen due to the increased number of suicides caused by insecticide poisoning. Nevertheless, limited reports of human exposure to these pesticides have reported various adverse clinical effects. In this study, we present the case of an individual who consumed the acetamiprid and pyridaben mixture for suicidal purposes, and subsequently developed central nervous system depression, hyperlactacidemia, and metabolic acid poisoning, which thus required clinical management.

Case report: A 74-year-old woman was transported to our hospital after ingesting a combination of 30 mL of acetamiprid 5 % and pyridaben 5 %. The patient displayed nausea and vomiting symptoms, followed by confusion. An arterial blood gas analysis revealed metabolic acidosis and hyperlactacidemia. The patient was carefully monitored for vital signs and treated with gastric lavage, purgation, and proton pump inhibitors to reduce gastric acid, blood volume, and electrolyte resuscitation. In addition, the patient received 24 h of hemoperfusion (HP) and continuous renal replacement therapy (CRRT). As a result of these interventions, the patient had a speedy recovery and was discharged 10 days later.

Conclusion: This case report provided the details of a rare instance of acute poisoning in humans resulting from exposure to newer synthetic pesticides, specifically acetamiprid and pyridaben. The report described the clinical manifestations and effective supportive therapy management. Future clinicians may find the results of this report valuable for identifying clinical symptoms and treating acute poisoning caused by newer synthetic pesticides.

1. Introduction

Introducing novel synthetic pesticides with stronger insecticidal effects, such as acetamiprid and pyridaben, has expanded the spectrum of control and led to their widespread adoption in the agriculture industry.

The increased number of suicides caused by insecticide intoxication has prompted public health concerns. Although adverse clinical effects have been observed in humans exposed to these chemicals, still their occurrence is infrequent. This report presented a case of central nervous system depression, hyperlactacidemia, and metabolic acid poisoning from consuming acetamiprid and pyridaben. Given the increasing use of novel pesticides, it is imperative to have clinical expertise regarding the toxicological effects of these compounds.

2. Case report

A 74-year-old female with a history of ingesting pesticide was referred to our hospital's emergency department after consuming 30 mL of pesticide containing acetamiprid 5 % and pyridaben 5 % (Fig. 1) approximately 3 h before her arrival. The patient presented symptoms of nausea, vomiting, and unconsciousness during transportation to our facility. Upon arrival, the patient displayed a Glasgow Coma Scale (GCS) score of 6, with normal pupillary light reflexes of both eyes measuring 2 mm in diameter, without convulsions, and with negative pathological indications. The patient's heart rate, blood pressure, and temperature were 154 beats/min, 172/83 mmHg, and 35.7 ℃, respectively. The patient had a respiratory rate of 28 breaths per min, and SpO_2 levels exceeded 96 % while breathing room air. A significant amount of gastric contents emitting a strong pesticide odor was suctioned from the

Abbreviations: GCS, Glasgow Coma Scale; ABG, arterial blood gas; CT, computed tomography; ECG, Electrocardiography; PPI, proton pump inhibitors; NAChRs, nicotinic acetylcholine receptors; HP, hemoperfusion; CRRT, continuous renal replacement therapy; CVVH, continuously venovenous hemofiltration.

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patient's mouth and nose. Notably, liver and kidney functions, cardiac troponin, coagulation function, and C-reactive protein showed inapparent abnormalities. Laboratory results indicated leukocytosis of 13.81 * $10^{\wedge 9}$/L and 3.2 mmol/L of potassium levels. The arterial blood gas (*ABG*) analysis revealed the following values: pH 7.42, PaO_2 112 mmHg, HCO_3^- 16.2 mmol/L, lactate 7.4 mmol/L, and BE − 6.3 mmol/L. However, CT scans of the brain and abdomen were unremarkable, identifying a small bilateral pleural effusion with atelectasis.

The electrocardiogram demonstrated tachycardia. The patient was intubated for airway protection, and mechanical ventilation was initiated. The gastric lavage was performed with 9000 mL of water, and the patient was admitted to the intensive care unit. Furthermore, rechecking arterial blood gases revealed metabolic acidosis and elevated lactate levels of 14.4 mmol/L, pH of 7.19, HCO_3^- of 11.8 mmol/L, and BE of −17.6 mmol/L. The patient's leukocyte count increased to 24.75 * $10^{\wedge 9}$/L, possibly indicating stress syndromes or inflammatory processes. The patient received hemoperfusion (HP) with continuous renal replacement therapy (CRRT) through an indwelling dual-lumen catheter in the right femoral vein. The CRRT was administered continuously using venovenous hemofiltration (CVVH) for 24 h, using a Prismaflex M150 set membrane hemofilter (Germany; synthetic high flux membrane, with a membrane area of 1.5 m^2), which was installed on a Prismaflex machine (Jinbao, Germany). After 2 h of HP treatment, the arterial blood gas (ABG) measurements were repeated, indicating lactate levels of 11.7 mmol/L, a pH of 7.2, HCO_3^- levels of 12.3 mmol/L, and a BE of −16.4 mmol/L. After 5 h, the patient's lactate level was 4.9 mmol/L, with a pH of 7.36, HCO_3^- at 19.9 mmol/L, and BE at −5.6 mmol/L. The patient displayed gradual recovery, and after 13 h, ABG analysis revealed normal lactate levels and pH (The *ABG* parameters are listed in Table 1). By 23 h, the patient had regained consciousness and displayed no signs of abnormal neurological function. The patient's oxygenation and circulation remained stable the following day, nevertheless, she developed a fever with a maximal body temperature of 38.9 °C. A repeat chest CT scan revealed left bronchus obstruction, pulmonary atelectasis of the left lower lobe, and bilateral pleural effusion. The left lower lobe discharged a significant amount of yellowish-white, adhesive sputum during bedside bronchoscopy. It was hypothesized that the documented loss of consciousness resulted in aspiration, which led to pneumonia. After receiving treatment with piperacillin-tazobactam for three days, the patient's temperature returned to normal. The patient was extubated on November 15, transferred to the general ward the following day, and ultimately discharged on November 22. During the one-month follow-up, no delayed neurological impairment was observed.

3. Discussion

Acetamiprid, a neonicotinoid with the chemical formula $C_{10}H_{11}ClN_4$ and the molecular weight 222.68 (Fig. 1), is one of nine neonicotinoids including imidacloprid, lothianidin, nitenpyram, thiacloprid, hiamethoxam, dinotefuran, sulfoxaflor, and cycloxaprid [1]. Since 1990, insecticide's use has increased globally, particularly in Japan, resulting in increased toxicity cases[2]. Neonicotinoids, as postsynaptic agonists of nicotinic acetylcholine receptors (nAChRs), exhibit low toxicity in humans due to their reduced interaction with postsynaptic nAChRs and limited ability to cross the blood-brain barrier in comparison to insects [3,4]. 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. The literature reports that excessive consumption of these insecticides can lead to adverse effects [3,5,6]. According to the literature, consuming significant quantities of insecticides can cause a central nervous system reaction characterized by dizziness, drowsiness, and disorientation. However, autonomic nervous system stimulation is characterized by diaphoresis, mydriasis, tachycardia, and elevated blood pressure [7]. Pyridaben, a heterocyclic acaricide with a molecular formula of $C_{19}H_{25}ClN_2OS$ and a molecular weight of 364.9 (Fig. 1), is a broad-spectrum and highly efficient pesticide that controls numerous food plant mites [8]. The mode of action of pyridaben involves inhibiting glutamate dehydrogenase synthesis in muscle and nerve tissues and electron transport system chromosome I, thus exhibiting insecticidal properties [9]. Although residual values of pyridaben detected in food items are within the maximal limit of the current standard [10,11], the increasing use of pesticides necessitates that the potential exposure effects of these compounds on human health be considered. Despite a limited number of reported cases

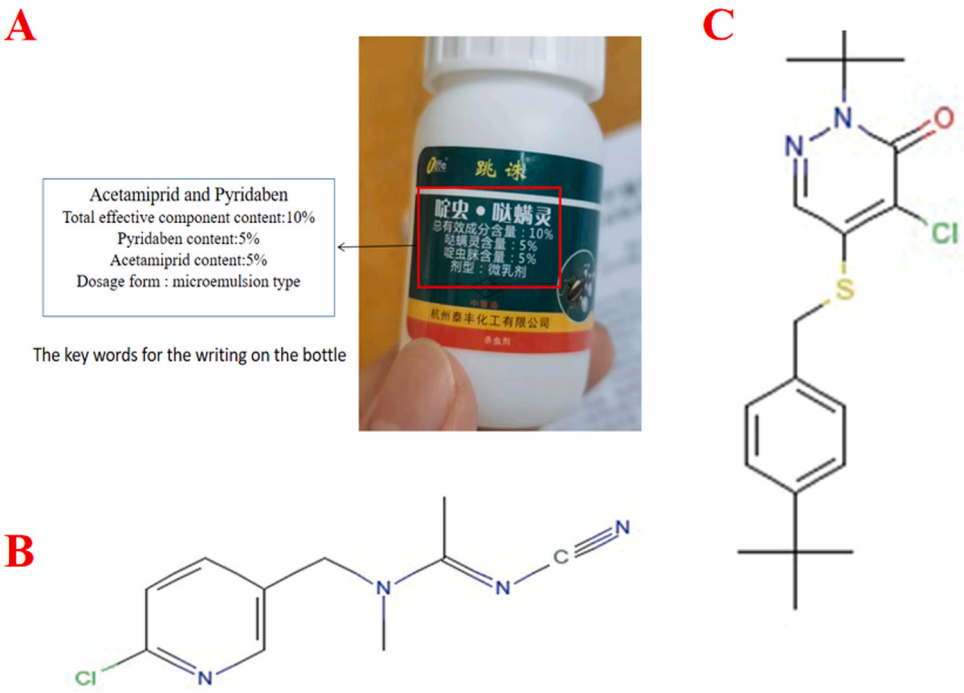

Fig. 1. The instructions of Acetamiprid and Pyridaben on the pesticide bottle(A), Molecular structure of Acetamiprid(B) and Pyridaben(C) were shown.

Table 1
The ABG parameters.

Time Parameters	Admitted to emergency (09:00)	Admission to ICU (12:00)	After 2 h of HP treatment (15:00)	After 5 h of HP treatment (18:00)	After 13 h of HP treatment (02:00 next day)
PH	7.42	7.19	7.2	7.36	7.4
Lac(mmol/l)	7.4	14.4	11.7	4.9	2.7
HCO_3^-(mmol/l)	16.2	11.8	12.3	19.9	23.7
BE(mmol/l)	-6.3	-17.6	-16.4	-5.6	-0.8
PaO_2(mmHg)	112	122	128	115	96
$PaCO_2$(mmHg)	25.3	26.1	27	34.2	38.4

Abbreviations:ABG: arterial blood gas; HP: hemoperfusion; Lac: lactate.

of pyridaben poisoning in China, there are few international publications on the subject. Exposure to low doses of pyridaben may result in gastrointestinal symptoms, such as nausea and vomiting. In contrast, exposure to high doses may result in intracellular respiratory dysfunction, tissue hypoperfusion, hyperlactacidemia, and ultimately metabolic acidosis. Pyridaben is promptly absorbed via the gastrointestinal tract and subsequently circulates throughout the body, affecting vital organs such as the heart, brain, lungs, liver, and kidneys. The occurrence of tissue hypoperfusion contributes to organ dysfunction, which can lead to myocardial ischemia and necrosis, reduced myocardial contractility, hypotension/shock, and renal dysfunction [12]. The co-administration of acetamiprid and pyridaben has been shown to increase toxicity; however, no specific antidote is available for treating acute poisoning caused by these agents, and symptomatic measures are employed instead. The patient initially presented with nausea and vomiting, followed by a gradual onset of consciousness disorders and hyperlactacidemia. The patient's rapid recovery was attributed to the low concentration and toxicity of the pesticides. However, it is crucial to note that the prompt removal of the toxic substances played a significant role in the patient's rescue.

The clinical characteristics of pesticide poisoning differ among various categories of pesticides [13,14]. Organophosphate and carbamate poisoning have been associated with respiratory failure as a frequent complication [15,16]. The pathophysiology of respiratory failure in these cases can be explained by mechanisms such as the suppression of the respiratory center in the ventrolateral medulla, resulting in a decrease in central respiratory drive, leading to respiratory muscle weakness. Additionally, organophosphate-induced bronchospasm can occur through local and vagal mechanisms [17]. In this study, it was revealed that of the mixture pesticide of acetamiprid and pyridaben poisoning is characterized by metabolic acidosis as compared to organophosphate and carbamate.

The patient's successful rescue experience can be summarized as follows: First, gastric lavage should be considered immediately to prevent further systemic absorption. Second, initiating blood purification techniques such as HP and CRRT can quickly eliminate toxins and prevent organ damage. Lastly, crucial interventions such as fluid resuscitation, organ support, and nutritional management are required to maintain oxygenation and tissue perfusion and ultimately improve clinical outcomes in these patients.

3.1. Why should an emergency physician be aware of this?

Newer synthetic pesticides such as acetamiprid and pyridaben have been widely used in agriculture due to their potent insecticidal effects. These pesticides have expanded the range of agricultural control. However, rare and serious complications such as acute toxicity resulting in severe metabolic acidosis and decreased consciousness have not been reported. and also, there is a lack of literature describing the clinical consequences of these newer synthetic pesticide poisoning. Therefore, it is imperative that clinicians and regulatory agencies are informed about this. Furthermore, the lack of an antidote requires reliance on prompt identification and proactive supportive care to achieve favorable clinical outcomes.

CRediT authorship contribution statement

All authors collected and analyzed data. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

Acknowledgements

None.

Declarations

Ethical approval and consent to participate (No 2022-Z-100).

Data Sharing Statement

All data generated or analyzed during this study are included in this manuscript, and the database is available from the first author upon reasonable.

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