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Fatal pesticide intoxication - case report of a 2 patients

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Abstract

Pesticides is a collective term for a group of chemicals used predominantly in agriculture and against vectors in vectorborne diseases such as malaria, filariasis, etc. Organophosphates (OP) have become nowadays the most widely used pesticides among the world. However, they are very highly toxic to humans. Poisoning with OP is a life - threatening condition. It is responsible for the symptoms due to a cholinergic effects. The Acetylcholinesterase (ACHE) enzyme inhibition leads to an acetylcholine accumulation, which causes symptoms such as diarrhea, sweating, vomiting, small pupils, muscle tremors, increased saliva and tears production and confusion. Other type of pesticides are also common used in agriculture. Glyphosate is a broad-spectrum systemic herbicide used to kill weeds. It is promoted by the manufacturer as having no risks to human health.
We present two patients with a fatal pesticide poisoning. First patient drank OP agent, which was decanted in a non-original bottle. Despite the intensive treatment, including high doses of atropine, and toxogonine, patient died after 6 days due to acute respiratory failure. The second one, tried to commit suicide by drinking 2 glasses of a pesticide called 'Roundap' (glyphosate). Short time after admission to a hospital, a myocardial infarction occurred. The patient died the same day, due to a cardiac arrest.

Key words: organophosphates, intoxication, toxicology

Introduction

Pesticides are a group of chemicals, used in agriculture, that have become essential over the last five decades and are used predominantly in agriculture and against vectors in vectorborne diseases such as malaria, filariasis, etc [1]. The term 'pesticide' is used for a wide array of products that can be classified by target organism (eg. insecticides, pesticides), chemical structure (eg. organic, inorganic), and chemical state. The universe of pesticide types and products is broad, and a comprehensive review of all active ingredients is beyond the scope of this report. Despite many benefits of using pesticides, there are certain undesired and harmful effects, that cannot be ignored [1]. Based on 1984 research, carried out in Sri-Lanka, Jeyaratnam estimated there were 220,000 pesticide related deaths every year worldwide [2]. World Health Organisation (WHO) reports show, that the pesticide poisoning may be the most common method of committing suicide worldwide [3].
Organophosphates (OP) are widely used as insecticides due to their widespread availability, low cost, and relatively rapid degradation [4]. OP poisoning is a life-threatening condition, which may causes death. Deaths from intentional poisoning are more common, than from unintentional poisoning [5]. This method is especially popular in a developing countries. OP pesticides inhibit esterase enzymes: especially acetylcholinesterase in synapses and on a red cell membranes [6]. That leads to accumulation of acetylcholine and overstimulation of acetylcholine receptors in synapses of the autonomic nervous system, central nervous system and neuromuscular joints [6]. The clinical features of OP pesticide poisoning are shown in the table 1 [5,7] Most of the patients show the symptoms of parasympathetic overstimulation [5]. Typically, the patients with OP poisoning present with pinpoint pupils, excessive sweating, reduced consciousness and poor respiration [5]. Diagnosis can be made, basing on a data from the anamnesis, characteristic clinical symptoms and reduced acetylcholinesterase in the blood [6].
Glyphosate is a broad spectrum, systemic herbicide used heavily in agriculture, as well as domestic and urban settings [8]. Nowadays, it is the most common post-emergent non-selective herbicide used in agriculture in the United States and worldwide [9]. Glyphosate targets the synthesis of chlorophyll-related molecules by competitive inhibition of the enzyme enolpyruvylshikimate phosphate synthase. This enzyme is present in plants but not in animals [10].Glyphosate is promoted by the manufacturer as a safe, and not affecting human health. However, some severe intoxications and deaths, often associated with a suicide attempts were reported [11]. Glyphosate-poisoning is characterized by various symptoms such as gastrointestinal symptoms, altered consciousness, hypotension, respiratory distress, metabolic acidosis and renal failure [12]. No specific, antidotal therapy is available, however hemodialysis was used to treat patients with acute glyphosate poisoning [13].

Table 1. Clinical features of OP poisoning.

Clinical features of OP pesticides poisoning due to overstimulation of :			
Muscarinic acetylcholine receptors in the parasympathetic system	Nicotinic acetylcholine receptors in the sympathetic system	Nicotinic and muscarinic acetylcholine receptors in the CNS	Nicotinic acetylcholine receptors at the neuromuscular junction
• Bronchospasm • Bronchorrhea • Miosis • Lachrymation • Urination • Diarrhea • Hypotension • Bradycardia • Vomiting • Salivation	• Tachycardia • Mydriasis • Hypertension • Sweating	• Confusion • Agitation • Coma • Respiratory failure	• Muscle weakness • Paralysis • Fasciculations

Case report

We present two cases of patients, hospitalized in the Department of Toxicology, that ended up with death.

First of them, was a 62 years old man, who had a history of alcoholism. He probably drank OP agent, that was decanted into a non-original bottle. The patient was brought to the ER because of the convulsion seizure. Head CT didn't showed any pathologies. Lab tests showed low activity of cholinesterase (<99U/L). The patient was admitted to the Department of Toxicology. He remained in a severe condition, conscious, but in a difficult contact. The patient had excessive salivation and a fever. Blood oxygen level was 75-80 %. Doctors decided to treat the patient with high doses of atropine (8mg/h) and toxogonine. They also started antibiotic therapy. Despite the treatment, the patient's condition got worse. Lab tests showed increasing parameters of kidney failure. After six days, his condition got worse rapidly. He showed signs of respiratory failure, the blood oxygen level decreased to 60%. Patient was intubated. The next day, patient had a cardiac arrest. Despite the resuscitation, the doctors were unable to rescue the patient.

Second patient was a 73 years old man, with a history of coronary disease and myocardial infarction, who tried to commit suicide using pesticides. At the day of admission, he drank two glasses of a pesticide agent 'Roundup' (glyphosate). As the Emergency Medical Team arrived, the patient was aggressive and refused examination. At the time of the admission to the ER, the patient

remained conscious and in logical contact. He was vomiting, had diarrhea and an episode of apnea. The doctors decided to admit the patient to the Department of Toxicology. Patient's condition was getting worse and it was no longer possible to make logical contact with him. He had a peripheral cyanosis, HR - 55/min. , and a blood oxygen level 80-85 % while he received oxygen therapy. Arterial blood gas test showed acidosis (pH=7,18). In ECG there was a ST segment elevation in V4-V6 leads. Doctors decided to intubate the patient. Soon after that, he had a cardiac arrest, but the doctors performed successful resuscitation. The episodes of cardiac arrest repeated several times. The patient was qualified to the urgent coronarography, where the three-vessel coronary disease was diagnosed. Doctors also implanted endocavitary electrode. Not long after the coronarography, the patient had again a cardiac arrest. This time, despite the resuscitation, doctors were unable to rescue the patient.

Discussion

In 1990, the WHO estimated that there are around 3 million hospital admissions, because of pesticide poisoning each year. 2 millions were the result of intentional ingestion. 220,000 cases resulted in death. [1]. Nowadays, probably the problem is larger - there have been some well recognised increases in pesticide poisoning, e.g. in a South Asia. [14].
In 2000, in Poland there were 107 cases of pesticides poisoning. The most cases (19) were registered in Lubelskie region. 74,8 % of cases, were result of oral ingestion. 28 % were suicide attempts, and 43 % coincidental. 15,9 % of patients were poisoned, during agricultural work [15]. At The Clinical Department of Toxicology in Lublin, between 2007 and 2016, there were 259 hospital admissions for pesticide poisoning (average 25,9 per year).

Study held in Poland in 2000 showed, that from 107 patients, admitted to the hospital, because of the pesticide poisoning, 7 died (6.5%). The study held at the Chonnam National University Hospital, on the group of 42 patients, showed that for OP poisoning the mortality
rate is 9,5 % [16]. For glyphosate, the mortality rate, based on a study, that included 601 patients is reported at 3,2% [17].
Respiratory failure is a very dangerous complication following OP poisoning. There are several explanations, for respiratory failure in OP poisoning. These include central and peripheral mechanisms, with central mechanisms predominating [18]. It can be categorized into two types, depending on the time onset from the OP ingestion. Early form, that presents within 24 hours, can be effect of three mechanisms: depression of central respiratory drive, weakness of the respiratory muscles and bronchospasm and bronchorrhea, via local and vagal mechanisms [6,17]. Late form, that is caused by peripheral dysfunction due to the sustained overstimulation of the neuromuscular junction [17]. It can be a part of a intermediate syndrome - clinical phase of OP poisoning, in which we observe cranial and respiratory muscle weakness which occurs 1–4 days after poisoning, following the cholinergic phase [19].
In a several studies, there were described the clinical and laboratory parameters for glyphosate intoxication, that could serve as predictive factors associated with mortality. They included: age >40 y.o., amount ingested, HR >100/min, pulmonary infiltration, acidosis, potassium >5.5 mmol/L, suicide attempt and creatinine >1,4 mg/dl [12]. Patient described in this case had 4 risk factors

from the above. He had a history of coronary artery disease and myocardial infarction, therefore he was vulnerable for a further cardiac complications.

Both cases, described in this article despite the different type of pesticide used and a difference in mechanism, ended up with death. One of the patients died from the respiratory failure, that occurred few days from OP ingestion. Although the treatment of OP poisoning is usually effective and allows to save the patient, still doctors are unable to rescue some of them. The second patient, despite using potentially less harmful substance, died because of his health burden, and using a very large amount of a pesticide (two glasses). That shows us, that while managing pesticide poisoning we must remember about rare symptoms, and late complications, that may happen while the patient's state seems to improve. We must also remember that substances ostensibly less harmful for our health, may be equally dangerous, when the dosage is high.

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