











# Severe carbamates intoxication of 43-year-old farmer – case report

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## Abstract

**Introduction.** Carbamate insecticides are methyl carbamic acid esters and reversible cholinesterase inhibitors. In contrast to the long-term action of organophosphate insecticides, this complex undergoes rapid hydrolysis.

**Case report.** A suicidal poisoning by exposure to carbofuran in a 43-year-old farmer is reported. The patient had a sudden respiratory and cardiac arrest in the mechanism of bradycardia asystole. He was additionally diagnosed with metabolic acidosis and massive aspiration pneumonia. After applied treatment, the patient's general condition improved – alignment of efficiency of both respiratory and circulatory efficiency were reached.

**Conclusion.** Carbofuran is one of the most toxic carbamate insecticides. It is therefore important to react quickly and choose the right treatment. Differentiation between organophosphate and carbamate intoxication is essential.

## Key words

poisoning, carbamates, intentional poisoning

## INTRODUCTION

Carbamate insecticides are methyl carbamic acid esters and reversible cholinesterase inhibitors. The most popular carbamates include methomyl, carbamyl and aldicarb, with the most toxic being aldicarb, carbofuran, carbosulfane and methomyl. The combination of carbamates with acetylcholine causes inactivation of the enzyme. In contrast to the long-term action of organophosphate insecticides, this complex undergoes rapid hydrolysis (usually 24 hours). According to physical features carbamates are colourless crystalline substances or liquids. They dissolve weakly in water but dissolve well in organic solvents, and after absorption into the body they undergo rapid biotransformation. They undergo 1<sup>st</sup> phase reaction such as hydrolysis by non-specific tissue carboxylesterases and oxidation by cytochrome P450 oxidase, as well as 2<sup>nd</sup> phase reaction such as coupling with sulfuric acid and glucuronic acid. The majority of carbamates is excreted with urine [1].

This case report concerns suicidal poisoning by exposure to carbofuran – one of the most dangerous and toxic carbamate insecticides. Carbofuran is a substance used to control insects in a wide multiplicity of field crops, such as soybeans, corn, and potatoes. Carbofuran also has contact activity against pests [2]. Such poisoning is relatively common in the rural population.

Inhibition of acetylcholinesterase (AChE) activity in nerve synapses within the central and peripheral nervous system is associated with the accumulation of acetylcholine, and may lead to excessive cholinergic stimulation because

of binding to muscarinic and nicotinic receptors. AChE activity increases spontaneously as a result of the separation of the carbamate from AChE, or as a result of the subsequent enzyme resynthesis [3].

## CASE REPORT

A 40-year-old farmer was hospitalized at the Toxicological and Cardiological Department in Lublin because of intentional consumption of a toxic pesticide – carbamate derivative. Initially, the patient was admitted to the district hospital in Kraśnik with suspicion of alcohol intoxication, due to the presence of 2.67g/L of ethanol in the blood. At that time, his general condition was very severe with persisting deep unconsciousness. Computed Tomography (CT) was performed, the result of which excluded head injury or a vascular cause of loss of consciousness. Neurological examination of the patient was also performed.

The severe general condition and awareness of carbamate intoxication necessitated the transportation of the patient to the Toxicological and Cardiological Department in Lublin. The patient's family complemented the interview and provided information about consumption of Furadan (carbofuran). At the moment of admission to the Toxicological and Cardiological Department he was conscious, with blood pressure 183/110 mmHg and heart rate 100/minute.

The patient had a sudden respiratory and cardiac arrest in the mechanism of bradycardia asystole. Due to indirect heart massage and respiratory therapy, these functions returned to normal; however, respiratory disorders persisted in a variable range and attempts to take him off the respirator were ineffective. The patient required respiratory therapy up to the sixth day of hospitalization. Additionally, he was

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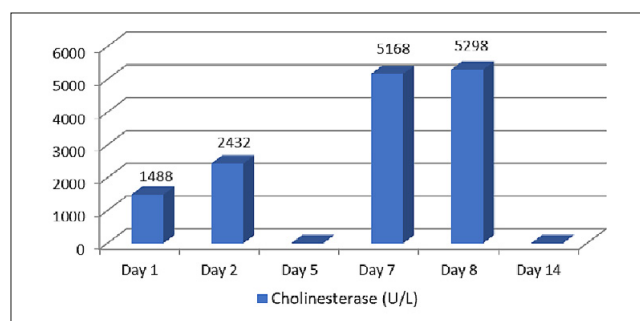
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**Table 1.** The results of laboratory tests from the first to the fourteenth day of hospitalization

Laboratory Parameters	Day 1	Day 2	Day 5
pH	7.117; 7.509	7.506; 7.464	7.463
pO <sub>2</sub> [mmHg]	76.6; 86.1	83.1; 109.4	77.7
pCO <sub>2</sub> [mmHg]	65.7; 28.5	29.0; 33.2	33.0
BE(B) [mmol/l]	-9.8; 0.5	0.5; 0.3	0
HCO <sub>3</sub> <sup>-</sup> [mmol/l]	20.7; 22.2	22.4; 23.3	23.1
CRP [mg/l]	169	85	181
Procalcitonine [ng/l]	0.05	0.04	-

unconscious till the 5<sup>th</sup> day of hospitalization and his general condition remained very serious.

After analysis of laboratory parameters (Tab. 1) at the beginning of hospitalization, the patient presented metabolic acidosis, ethanol intoxication and decreased level of cholinesterase (Fig. 1). Metabolic acidosis appeared as the effect of respiratory insufficiency, activity of carbofuran and ethanol.

**Figure 1.** Graph showing variation in cholinesterase activity during hospitalization

After examination of the results of laboratory and imaging tests the patient was diagnosed with massive aspiration pneumonia, presumably caused by aspiration of a chemical substance or food, due to the depressive effect of Furadan and ethanol.

The observed abnormalities in the patient required not only respiratory therapy but also pharmacological treatment, including specific treatment. A complex, multi-drug antibiotic therapy had to be implemented. As a result of the applied treatment, the patient's general condition improved – alignment of efficiency of both respiratory and circulatory efficiency were reached. The patient was extubated and no organ damage was observed.

During further hospitalization the patient was consulted psychiatrically, and discharged from hospital in good general condition, with the recommendation of addiction treatment.

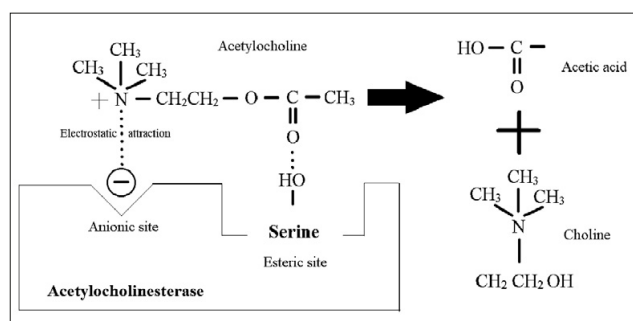
## DISCUSSION

**Epidemiology.** Poisonings occur among people exposed to contact insecticides and sometimes in households by accidental ingestion. However, there can also occur intentional consumption, as in the presented case, which was suicidal poisoning.

The World Health Organization (WHO) estimates that at least one million unintentional poisonings and two million suicide attempts occur annually worldwide from these

insecticides. However, these figures undoubtedly omit numerous unreported and possibly unrecognized illnesses resulting from lower-level environmental exposure to these chemicals [4]. The American Association of Poison Control Centers (AAPCC) data, collected between 2002 – 2006, showed carbamate poisonings accounted for 14,000 reported exposures and incurred a case fatality rate of 10% – 20%. In 2008, the United States reported 8,000 cases to the AAPCC, accounting for 14 fatalities [5].

**Mechanism.** Carbamate insecticides enter the body through the skin, digestive and respiratory tracts. They are metabolized quite quickly and excreted in the urine [6]. The mechanism of action of toxic carbamates is similar to the mechanism of action of organophosphorus compounds (Ops, which involves blocking the activity of cholinesterase by binding to it [Fig. 2]. Most authors believe that the observed symptoms of poisoning indicate the existence of yet other, unexplained mechanisms of toxic action of this group of compounds [7].

**Figure 2.** Mechanism of combining carbamate to acetylcholinesterase at the ester and anionic site

Organophosphorus compounds increase cholinergic transmission, both in the central and peripheral synapses. Systemic exposure to these compounds induces effects resulting from stimulation of the muscarinic receptor, such as hypersalivation, lacrimation, pupil constriction and bronchoconstriction. Increased activation of nicotinic receptors leads to a block of depolarization of the neuromuscular plate and muscle weakness. Convulsions, respiratory depression, and coma may occur as a result of activating acetylcholine receptors in the central nervous system. All of these symptoms are components of the cholinergic syndrome [8].

A resemblance can be seen between the pathophysiology of carbamate poisoning and organophosphorus compounds intoxication; however, carbamates are less toxic than the others because the binding of carbamate insecticides to the active site of the enzyme is reversible; therefore, the enzyme may return to its original activity relatively quickly. Symptoms are analogous to phosphate ester poisoning, but less intense and less dangerous. Delayed neuropathies are not usually associated with carbamate insecticides. One reason for this difference is presumed to be that aging of the neuropathy target esterase insecticide complex is a requirement for neuronal degeneration. Paradoxically, one study has suggested that subgroups of carbamates may bind neuropathy target esterase and exert a protective effect against more toxic OPs. However, several cases of delayed neuropathy associated with carbamates have been reported [1].

**Table 2.** Summary of management of anticholinesterase intoxication

Procedures	Emergency treatment
Decontamination	Removal of all clothing wearing personal protective equipment in order to avoid self-contamination of medical personnel
Specific treatment	The main antidote was atropine
General support	Intubation Low molecular weight heparin Benzodiazepines Anesthetics Corticosteroid Catecholamine Antibiotics Anxiolytic drug

The diagnosis of such intoxication is based on an interview and analysis of the clinical symptoms – it is important to identify features of the cholinergic syndrome. The differential diagnosis may sometimes be difficult. A drop in the activity of blood cell acetylcholinesterase in the first phase of intoxication may be deceptive and make it harder to distinguish between carbamates and organophosphorus compounds poisoning; however, a rapid increase in the activity of AChE confirms carbamate intoxication.

The earliest cause of death in most anticholinesterase pesticide poisonings is extreme weakness and paralysis due to cholinergic motor neuron stimulation leading to respiratory arrest. Copious pulmonary secretions from muscarinic stimulation can lead to pulmonary oedema, aspiration and hypoxia, that can also be fatal [4].

The most important part of the treatment of a patient exposed to these compounds is proper mechanical ventilation to ensure a clear airway. Due to reverse excessive muscarinic effects, especially bronchorrhea, pharmacotherapy should be borne in mind. The main antidote used in carbamates intoxication is atropine. Studies suggest that it is essential to maintain general support, especially diazepam and other benzodiazepines, because they may improve the outcome in anticholinesterase pesticide poisoning [4].

## CONCLUSIONS

Carbofuran is one of the most toxic carbamate insecticides. Therefore, it is important to react quickly and select the right treatment. It is crucial to take into consideration the differential diagnosis, which includes three broad categories of cholinergic toxicity – cholinomimetics, nicotine alkaloids, and cholinesterase inhibitors [5]. It is then essential to differentiate between organophosphate and carbamate intoxication. Patients who have attempted suicide with carbamates may have a long hospitalization and severe health complications, whereas patients intoxicated by accident are much less likely to suffer life-threatening consequences.

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