Carbamate Poisoning

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Introduction

- **Carbamates also inhibit acetylcholinesterase and produce similar clinical effects.**

- **However, reactivation occurs much more quickly than with OPs**

Fatal Dose

- **The following are extremely toxic (LD50: 1 to 50 mg/kg), or highly toxic (LD50: 51 to 500 mg/kg)—**

Aminocarb, Bendiocarb, Benfuracarb, Carbaryl, Carbofuran, Dimetan, Dimetilan, Dioxacarb, Formetanate, Methiocarb, Methomyl, Oxamyl, Propoxur

Fatal Dose

- **The following are moderately toxic (LD50: 501 to 5000 mg/kg), or slightly toxic (LD50: more than 5000 mg/kg)—**

Aldicarb, Bufencarb,
Isoprocarb, MPMC,
MTMC,
Pirimicarb.

Mode of Action

- **Inhibits acetylcholinesterase, but carbamylate the serine moiety at the active site instead of phosphorylation.**
- **The carbamate–acetylcholinesterase covalent bond is not as strong as that produced by OPs.**
- **Because of this, spontaneous hydrolysis or decarbamylation occurs more readily, usually reactivating acetylcholinesterase within 24 hours.**

- **This is a reversible type of binding and hence symptoms are less severe and of shorter duration**

- **Carbamates do not penetrate the CNS to the same extent as organophosphates, Hence CNS toxicity is much less**

- **Some Carbamates may take longer to spontaneously hydrolyze**

Toxicokinetics

- **Most carbamates are poorly absorbed across the skin compared with organophosphates**
- **Carbamates have rapid onset but are less fat soluble**
- **Carbamates are rapidly hydrolysed by liver enzymes to methyl carbamic acid and a variety of low toxicity phenolic substances**
- **Metabolites may sometimes be measured in urine as long as 2 to 3 days after absorption**

Clinical Presentation

Muscarinic, Nicotinic and CNS symptoms can be seen

Miosis, Sinus tachycardia, Sinus tachycardia with ST segment depression Repolarisation abnormalities Dyspnoea Chest tightness, bronchospasm, increased pulmonary secretions, and rales Acute lung injury (pulmonary oedema Hypoxia	Headache, dizziness, blurred vision, tremor, paresis, mental depression, coma, delayed neuropathies, various dystonias, weakness, muscle twitching, convulsions CNS depression, hypotonia, peripheral neuropathies, Acute pancreatitis

Diagnosis

- History of exposure to a particular carbamate
- N-methyl carbamate specific phenolic metabolites in urine, e.g. carbaryl (alpha-naphthol), carbofuran (carbofuranphenol) propoxur (isopropoxyphenol).
- Chest X-ray
- Cholinergic signs and symptoms
- Note: Measurement of cholinesterase activity in blood may be misleading due to in vitro reactivation of carbamylated enzyme due to dilution of the sample

MANAGEMENT

- **Airway, Breathing and circulation stabilization**
- **Specific Decontamination based on route of exposure**
- **Use activated charcoal within one hour of an ingestion**

Antidote

- **Oximes are generally not recommended, while atropine can be given**

- **In carbaryl poisoning, oxime therapy can lead to the production of a carbamylated oxime which may be a more potent acetylcholinesterase inhibitor than carbaryl itself.**

- **carbamate insecticides particularly aldicarb, oximes may be a useful adjunct to atropine**

Pralidoxime can be used in conjunction with atropine for specific indications as follows:

- **Life-threatening symptoms such as severe muscle weakness, fasciculations, paralysis, or decreased respiratory effort.**
- **Continued excessive requirements of atropine.**
- **Concomitant organophosphate and carbamate exposure.**

Atropine

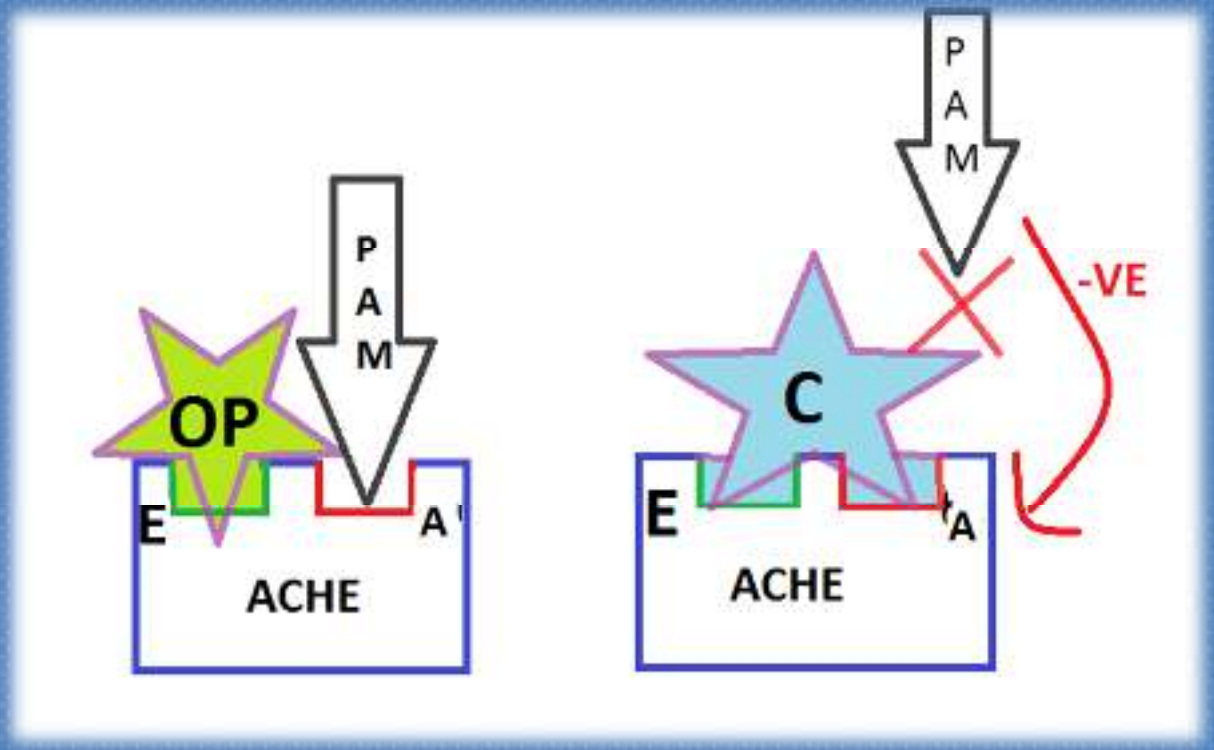
- **Administer atropine in repeated doses intravenously until atropinisation is achieved (indicated by drying of pulmonary secretions).**
- **Adult dose—2 to 4 mg IV every 10 to 15 minutes.**
- **Paediatric dose—0.05 mg/kg IV every 10 to 15 minutes.**

Benzodiazepines

- **Convulsions can be controlled with a benzodiazepine (diazepam or lorazepam).**
- **If they persist or recur, administer phenobarbitone**

Pralidoxime

- Pralidoxime is used in Organophosphate poisoning and not carbamate poisoning.
- Cholinesterase reactivating agent that are effective in treating both muscarinic and nicotinic symptoms
- Oximes also have weak ACHE inhibitory action.



PAM -PRALIDOXIME
OP - ORGANOPHOSPHATE
C - CARBAMATES
E - ESTERIC SITE
A - ANIONIC SITE
ACHE - ACETYL CHOLINE ESTERASE
OP - ESTERIC SITE ONLY
C - ESTERIC + ANIONIC

The American Journal of Emergency Medicine
Volume 27, Issue 9, November 2009, Pages 1117-1124

Review

Carbamate poisoning: treatment recommendations in the setting of a mass casualties event

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https://doi.org/10.1016/j.ajem.2009.01.035

Abstract

The threat of using chemical compounds by terrorists as weapons of mass casualties has been a rising concern in recent years. Carbamates, a group of reversible acetylcholinesterase inhibitors, could be potentially involved in such toxic mass casualty events because they can cause cholinergic crisis that could lead to fatality, similar to that of organophosphate poisoning. The medical management of carbamate poisoning consists of supportive measures and specific antidotal treatment, that is, the anticholinergic compound atropine. The administration of oximes, acetylcholinesterase reactivators, in carbamate poisoning is controversial because of the potential toxicity of oximes in conjunction with carbamate especially in the case of the carbamate—"carbaryl" poisoning. However, recent data suggest that this concern may be unwarranted. In this article, we review the current data regarding the pros and cons of using oximes against carbamates poisoning in a mass casualties event scenario. We also propose a new decision-making algorithm for the medical first responders in a mass casualties event suspected to be caused by a cholinergic substance (organophosphate or carbamate). According to this algorithm, treatment should consist of atropine and oxime regardless of the exact toxic compound involved. We speculate that in a mass casualties event, the benefits of using oximes outweigh the low level of potential risk