

INTRODUCTION

Organophosphorus insecticides (OPI) are the pesticides most often involved in serious human poisoning (*Pajoumand et al., 2004*).

The use of OPI as insecticides in the agricultural and urban settings is still high and is expected to remain so, at least in the near future. While other classes of insecticides are gaining market share (e.g., pyrethroids) and new classes have been developed (e.g., neonicotinoids), the efficacy of OPI, their relatively low cost and their lack of bioaccumulation in the ecosystems, would support this prediction. The early discovery of acetylcholinesterase (AChE) enzyme inhibition by organophosphorus compounds (OPCs) has led to their development primarily as insecticides, but also as nerve agents and to a limited extent, as drugs. OPCs are potent and effective insecticides and still represent the largest group of insecticides sold worldwide. Due to the strong similarities of the insect and mammalian cholinergic nervous system, these compounds are, however, responsible for the millions of poisonings and thousands of deaths occurring annually as a result of pesticide exposures, particularly in third world countries (*Costa, 2006*).

Organophosphorus poisoning is a worldwide health problem, with around 3 millions poisonings and 200,000 deaths annually according to a World Health Organization report (WHO) (*Karalliedde and Senanayake, 1999*).

Organophosphorus insecticides are responsible for a large number of accidental and/or suicidal exposures and have been used also for warfare and terrorism (*Petroianu et al., 2004*).

The toxicity of these pesticides is due to the irreversible inhibition of AChE leading to accumulation of acetylcholine and subsequent over-activation of cholinergic receptors in various parts of the body. Acutely, these patients present with cholinergic crisis; intermediate syndrome and delayed polyneuropathy are other sequel of this form of poisoning (*Paudyal, 2008*).

Acute cholinergic syndrome is characterized by a variety of symptoms including rhinorrhea, salivation, lacrimation, tachycardia, headache, convulsions and death (*Karalliedde et al., 2001*).

The intermediate syndrome is considered to be a delayed complication of severe acute poisoning, and organophosphorus induced delayed polyneuropathy (OPIDP) may be the consequence of both acute and chronic poisoning with some OP-neuropathic agents, the typical biochemical sign of their action being inhibition of the so called neurotoxic target esterase (NTE) (*Kolodkin and Ruck, 2006*).

Organophosphorus (OP) poisoning is associated with a high mortality rate due to respiratory failure, dysrhythmias, and multi-organ failure (*Schrickel et al., 2008*). The diagnosis depends on the history of exposure to these pesticides, characteristic manifestations of toxicity and improvements of the signs and symptoms after administration of atropine (*Paudyal, 2008*).

Erythrocyte AChE is found in nervous tissues and skeletal muscle, its activity reflects peripheral tissue, muscle, and brain acetylcholinesterase activity. Plasma cholinesterase, butyrylcholinesterase (BuChE), is a liver protein found in plasma, heart, and brain. Its endogenous function is unknown (*Kwong, 2002*).

Determination of AChE and BuChE activity in blood remains a mainstay for the fast initial screening of OPCs but lacks sensitivity and specificity. Quantitative analysis of organophosphorus compounds and their degradation products in plasma and urine by mass spectrometric methods may prove exposure but is expensive and is limited to specialized laboratories. However, history of exposure to OPCs and clinical manifestations of a cholinergic syndrome are sufficient for management of the affected patients (*Balali-Mood and Balali-Mood, 2008*).

Treatment of intoxication with organophosphorus chemicals (OPs) conventionally involves atropine for reduction of muscarinic signs and oximes that increase the rate of hydrolysis of the phosphorylated enzyme AChE. Although atropine and oximes (pralidoxime or obidoxime) are traditionally used in the management of such poisoning, their efficacy remains a major issue of debate (**Pajoumand et al., 2004**).

Recent advances on treatment of OP pesticides poisoning revealed that blood alkalinization with sodium bicarbonate and also magnesium sulfate as adjunctive therapies are promising. Patients who receive prompt proper treatment usually recover from acute toxicity but may suffer from neurologic complications (*Balali-Mood and Balali-Mood, 2008*).

Many studies have shown that the administration of phosphotriesterases (enzymes that detoxify OPs through hydrolysis) is a promising treatment of persons poisoned with these substances. Such as enzyme- based treatment might introduce important improvements in the treatment of patients having ingested large amounts of OPs (*Sogorb et al., 2004*).