Review Article

Dangers of Organophosphate Pesticide Exposure to Human Health

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Abstract

Organophosphate pesticides are used in agriculture to protect plants and livestock from pests so as to increase food yield. They are also used to control household and structural pests. Organophosphate pesticides inhibit acetylcholinesterase, preventing the break-down of acetylcholine in the nervous system which leads to the accumulation of acetylcholine in nerve endings resulting in paralysis. Information on organophosphate pesticides, mechanism of action of organophosphate chemicals, organophosphate toxicity, biological monitoring, and regulation of pesticides was obtained from other published articles, textbooks, and relevant internet sites. Studies have shown that there is a link between sensorimotor and cognitive impairments to organophosphate exposure as well as a link between affective disorders, depression, and suicide to the acute and chronic exposure to organophosphate insecticides in humans. Although being used as a pesticide and an insecticide, organophosphate chemicals pose a huge danger to health and as such, there should be general public awareness on its health risk with continuous and unguarded exposure to it.

Keywords: Chlorpyrifos, insecticides, organophosphate, pesticides

Introduction

Organophosphates are chemicals that are produced by a process of esterification between alcohol and phosphoric acids.[1] They are widely used in agriculture as well as in buildings to control pests.[2] Organophosphates form the basis from which most pesticides and insecticides are produced.[3]

The chemical structure is composed of a phosphate group which forms the basic structural framework,[4] as shown in Figure 1.

Classification of Organophosphates

Examples of organophosphates classified based on structure include phosphates, phosphonates, phosphinates, and phosphorothioates (S=), phosphonothioates (S=), phosphorothioates (S substituted), phosphonothioates (S substituted), phosphorodithioates, phosphorotrithioates, and phosphoramidothioates.[5] As shown in Figure 2.

History of Organophosphates

As early as the 19th century, there has been a synthesis of organophosphate compounds.[6] Gerhard Schrader, a German chemist at company IG Farben, synthesized organophosphate, which was used as a chemical agent of war,[7] although he initially aimed his work in developing insecticides. In 1936, he synthesized a very toxic compound known as ethyl-N, N-dimethylphosphoramidocyanidate (tabun), and in 1937, isopropyl methylphosphonofluoridate (sarin) was synthesized.[8]

The synthesis of these compounds caused the German military to apply them in warfare thereby directing Gerhard Schrader research from an insecticidal to a warfare agent.[9] Although an inexpensive compound knows as dichlorodiphenyltrichloroethane an organochlorine was synthesized in 1939 to be used as an insecticide,[10] they were found to bio accumulate unlike organophosphates which do not accumulate in the environment and are rapidly hydrolyzed when exposed to air, sunlight, and soil.[11] This led to many

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European countries as well as the USA banning the use of organochlorines.[12] Organophosphate use as a pesticides was then exploited and therefore became widely used in controlling agricultural and household pests.[13]

Uses of Organophosphates

There are numerous organophosphate chemicals which are widely used as insecticides and pesticides in various parts of the world.[14,15]

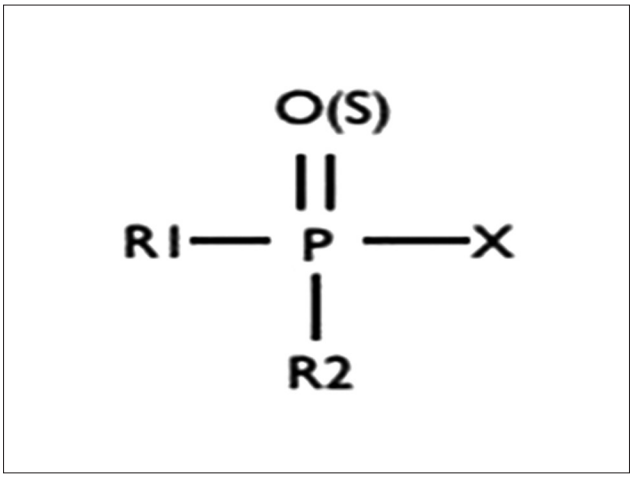

Figure 1: Chemical structure of organophosphate[5]

Organophosphate pesticides such as terbufos, chlorpyrifos, diazinon, parathion among others are generally used as an agricultural and a household insecticide.[16] Some organophosphate chemicals such as glyphosate and tribufos are used as herbicides, while trichlorfon is used as an anthelmintic agent.[17]

Mode of Action of Organophosphates

Organophosphates generally by inhibiting acetyl cholinesterase enzyme which hydrolysis acetylcholine and excitatory neurotransmitter in vertebrates and insets.[18] As shown in Figure 3.

The acetylcholinesterase inhibition and consequent synaptic junction accumulation of acetylcholine, results in a continuous stimulation of the postsynaptic tissue.[19]

When inhibited, acetyl cholinesterase is reactivated rapidly depending on the chemical structure of the organophosphate used, and because of this rapid or spontaneous reactivation, organophosphates are therefore classified into reversible and no-reversible acetyl cholinesterase inhibitors.[20] The inhibition of acetyl cholinesterase by organophosphates possessing dimethyl-and diethyl phosphate structure is most of the time not.[21,22] For organophosphate chemical warfare agents such as tabun and sarin, there is usually no rapid/spontaneous acetylcholine reactivation due to their branched radicals.[9]

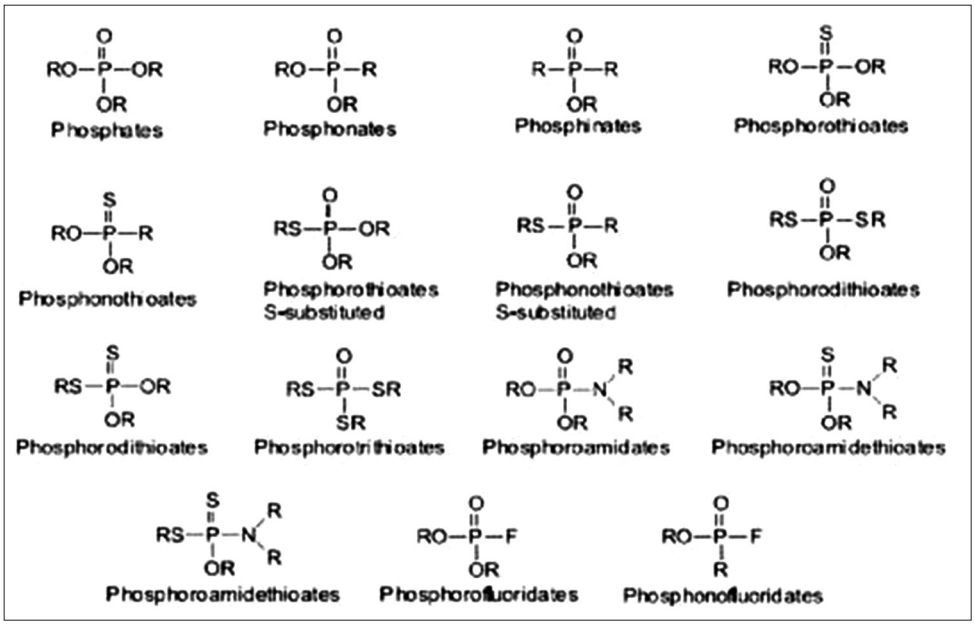

Figure 2: Structural classification of organophosphates[5]

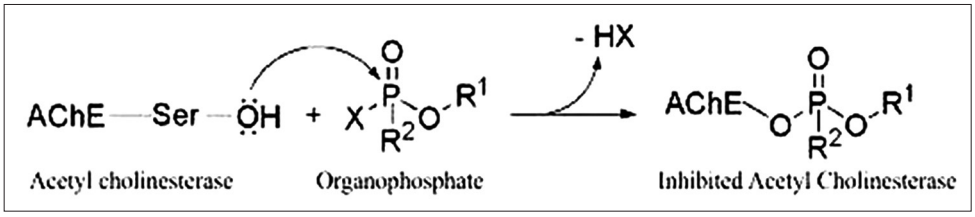

Figure 3: Inhibition of acetyl cholinesterase by organophosphates[18]

Organophosphate Toxicity

Widely used globally, organophosphate pesticide exposure poorly control especially in cases when personal protective equipment are not used.[23]

There are however two types of toxicity: acute and chronic organophosphate toxicity.

Acute organophosphate toxicity

Even though it was widely claimed that organophosphate has an advantage over the more popular organochlorines, it has, however, been found that organophosphate causes far greater acute toxicity and are as such, far more hazardous than the later.[24] Suicide attempts are one of the consequences of the classical syndromes of acute toxicity in humans exposed to organophosphate.[25,26] There are three different forms in which acute toxicity from organophosphates can be expressed, and these are cholinergic syndrome, intermediate syndrome (IMS), and delayed polyneuropathy.[27]

Cholinergic syndrome

This occurs when acetyl cholinesterase is inhibited following accumulations of acetylcholine at synaptic and neuromuscular junctions in the cholinergic pathways, which results in the overstimulation of the postsynaptic muscarinic and nicotinic receptors. The physiological actions of these receptors are therefore said to be exaggerated.[28] Cholinergic syndrome being a consequence of organophosphate exposure, within minutes or hours after exposure.[26] Some of the symptoms of cholinergic syndrome are sweating, lacrimation and salivation, respiratory difficulties and cough, miosis, dyspnea, wheezing, bradycardia, cyanosis, nausea, vomiting, involuntary defecation and urination, headache, dizziness, confusion, and ataxia among others.[29] Some patients who survive the first day may experience or exhibit personality changes, psychotic episodes, paranoia, and existing psychiatric problems may be exacerbated. There could be hallucinations and nightmares as well as attention and memory disorders.[30,31] It has also been shown that death caused by organophosphate poisoning could be centrally mediated,[32] as death would occur because of respiratory failure (resulting from the depression of the respiratory center of the brain and respiratory muscle paralysis).[31,33]

Cholinergic syndrome is usually diagnosed based on the history, situation regarding exposure, clinical presentation, and laboratory tests are used to confirm diagnosis by assaying blood acetyl cholinesterase or plasma/serum cholinesterase activity.[34]

Intermediate syndrome

This was first described by Senanayake and Karalliedde[35] as a distinct clinical entity. Intermediate syndrome is so termed since it starts around 24–96hrs after initial exposure[36] and could last from 5 to 18 days and in very rare cases can last to 21 days according to Das *et al*.,[37]

The characteristics of IMS are acute respiratory insufficiency as a result of the respiratory muscles being paralyzed.[37,38] Other symptoms of IMS are weakness of neck flexion, weakness of the proximal limb muscle that manifests as shoulder abduction, and hip flexion weaknesses.[36,39]

Usually followed organophosphate metabolites excretion in urine and a marked reduction in cholinesterase level, IMS could be said to either be a decline in the number of functional cholinergic receptors at postjunctional membrane or a failure in the release of acetylcholine.[31] Diethyl organophosphates are less likely to produce IMS than dimethyl organophosphates.[40]

Organophosphate-induced delayed polyneuropathy

Organophosphateinduced delayed polyneuropathy (OPIDP) is rare and manifests between 10 and 20 days after a single exposure to organophosphate insecticide.[31] It is basically an axonopathy of the distal sensory-motor where the long axons of the central and peripheral nervous systems are degenerated which may result in paralysis about 2 or more weeks after organophosphate exposure.[41] Lotti and Moretto[42] reported organophosphate induced delayed polyneuropathy outbreaks in humans in some countries such as Morocco and the USA while it has also been observed in some animals such as sheep and chickens[43] and Husain[4] reported it in some experimental rodents. Parathion, leptophos, methamidophos, malathion, and some other organophosphates have also been found to induce OPIDP.[44]

Although the mechanism in which OPIDP develops is not fully understood, it is however thought that target esterase activity in the nervous system is gradually lost thereby membrane phospholipid and the functions of the endoplasmic reticulum which includes axonal transpots as well the interaction between glial and axons is supposedly disrupted.[4,45] It has however been observed that OPIDP may be caused by exposure to organophosphate compounds in large toxic doses, which may result in acute neuronal cell death in the brain.[46] Masoud and Sandhir[47] through their rat models, observed that the development of OPIDP may be mediated partly with an increase in oxidative stress.

Chronic Toxicity

Neurodegeneration may occur from exposure to organophosphates at small subclinical does and may be referred to as organophosphate-induced chronic neurotoxicity or OPICN.[46] Another chronic toxicity develops from exposure to large doses of organophosphates and usually proceeds acute toxicity, this is named chronic organophosphate-induced neuropsychiatric disorder or copind.[48]

Anxiety, apathy, confusion, disorientation, impaired memory and concentration, irritability, speech difficulties, delayed reaction times, dizziness, and insomnia are some of the signs and symptoms. Others include decreased verbal attention, decreased academic skills, short-term memory deficits, increased social isolation, fatigue, impaired vigilance as well as slow reaction time.[46] There have also been studies to show

that there could be a correlation between subclinical doses and diabetes among Indian farmers.[49]

Improvement is usually slow due to the fact that central and peripheral nervous systems have a greater damage.[46]

Conclusion

Organophosphate chemicals despite being used as pesticides and insecticides pose a huge risk to human health. There is the need for general public sensitization on the dangers of exposure to organophosphate pesticides be it for agricultural or household use. The use of protective equipment by pesticide applicators as well as other risk populations should be encouraged. Individuals who are frequently exposed to low doses of organophosphates should periodically evaluate their health status to enable them to seek professional help and counseling.

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Conflicts of interest

There are no conflicts of interest.

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