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Chronic Effects Of Organophosphates On Human Health And Ecosystem: A Systematic Overview

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Abstract:

Uses of pesticide have been increased from year to year for enhancement of crop and control of pests. Organophosphates are the class of pesticides which are widely used among all agricultural chemicals. Most OP's are used as insecticides, rarely purposed as fungicides or herbicides. Factors like farm pesticide drift, mixing and spraying pesticides, use of personal techniques, water floods from sprayed areas, wearing contaminated clothes, eating, and drinking, smoking, and hot weather are common in our countries. Such factors increase the risk of administration of OP's into the human body and their relatives. The continuous exposure of these OP's to humans results in lethal and mortal effects on the body. Highly intensified exposures may result in various dysfunctions and disability in human regulatory systems (neurological, respiratory, digestive, circulatory and tissues). In this paper we are going to review the chronic diseases/dysfunctions that are caused due to ingestion of organophosphate inside the human regulatory system. We will understand the scenario of the havoc that can be caused by such pesticides. The objective of this paper is to brief the ancient as well as current risk that has influenced the normal bodily working of humans. It is also focused on pesticide as suicidal as well as homicidal weapons in society.

Keywords: pesticides, poisoning, organophosphate, chronic effects, dysfunctions.

1. Introduction-

A pesticide can be generally defined as a chemical compound, biological agent, antimicrobial or disinfectant used against pests including insects, plant pathogens, weeds, molluscs, birds, mammals, fish, nematodes and microbes that compete with humans for food, destroy property, have a propensity for spreading or are a vector for disease or simply a nuisance (Goel & Aggarwal, 2007) [2]. These are the chemical compounds which control or inhibit the growth of microorganisms that are a risk to the proper nourishment of crops.

Pesticides are biodegradable as well as persistent. i.e. these are converted into harmless compounds by microbes, and it may also take years to years to break down.

Pesticides are not recent inventions. Many ancient communities used such remedies to protect their crops from insects and pests. Sumerial civilization used elemental sulfur to protect their crops from insects. Medieval farmers used arsenic, lead on common crops.

Pesticides can be classified on the basis of chemical components as-

1. Organophosphate
2. Carbamate
3. Organochlorines
4. Pyrethroids
5. Substituted urea

- **Organophosphates:**

OP pesticides are the most commonly available over-the-counter insecticides in India for agricultural and household use. They are responsible for the largest number of deaths following pesticide ingestion (Goel & Aggarwal, 2007) [2]. Some of the main examples of these OPs can be listed as parathion, paraoxon, malathion, diazinon, fenthion, dichlorvos, chlorpyrifos, ethion. monocrotophos, coumaphos, and chloropyrifos [3]. The majority of OPs fall into two categories.: diethyl (e.g. chlorpyrifos, diazinon, parathion, phorate and dichlorfenthion) and dimethyl (e.g. dimethoate, dichlorvos, fenitrothion, malathion and fenthion).

In earlier decades ops were used as chemical warfare agents. The majority of organophosphate insecticides block the function of acetylcholinesterase, which impacts the neurological systems of both aquatic and terrestrial animals. OP's are also linked to increased bladder cancer and leukemia in farmers followed by genotoxic effects (4). They are widely used all over the world because they are attractive alternative to persistent organochlorine pesticides and possess ability to rapidly degrade under natural conditions sunlight, air, and soil **(Stephen M & Meera, 2010)** [24]**.** Chemical compositions: (molecular levels) Organophosphate pesticides (OPs) are organic ester derivatives of phosphorous, generally thiol or amide derivatives of thiophosphoric, phosphinic, phosphonic, phosphoric acids with additional side chains of phenoxy, cyanide and thiocyanate group. Organophosphorus compounds are organic substances which contain a phosphoryl (P=O) or a thiophosphoryl (P=S) bond. They are essentially esters, amides or thiolic derivatives of phosphoric, phosphonic or phosphinic acids, with different arrangements of attached oxygen, carbon, nitrogen or sulfur atoms. The classification of OPCs is quite ambiguous due to random probability of attachment of side chains.

Ways of exposure: Humans can be prone to these chemicals through direct and indirect routes. Personal pesticide exposure in both occupational and residential settings is influenced by both the pesticide application characteristics and personal behaviour. Spills and other accidental events also contribute to an individual's pesticide exposure [12, 13]

Direct exposure occurs to individuals who personally apply pesticides in agricultural, occupational, or residential settings and thus leads to the highest levels of exposure, whereas indirect exposures occur through drinking water, air, dust, and food and represent routes of long-term, generally low-level exposures. Indirect exposures may occur more frequently than direct pesticide application [10]. These do occurs through social meetings within the people of same farming occupation. Risk increases when pesticide applicant comes in contact with family members and relatives. Some ways of pesticide exposure described in figure 1.

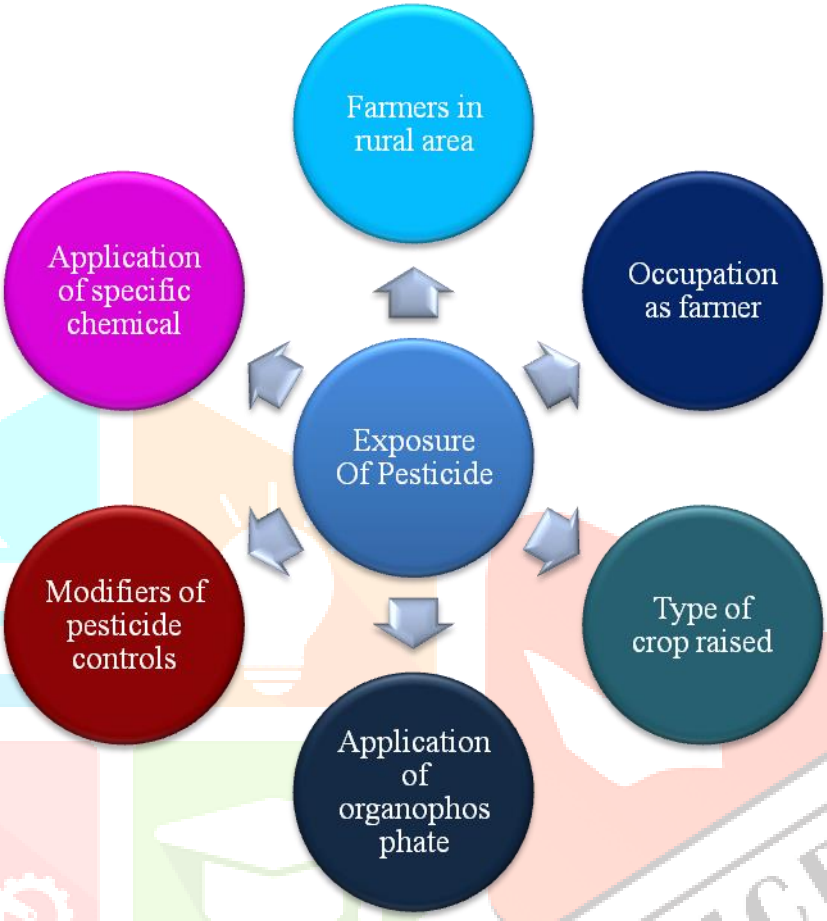


Figure 1: Routes of Pesticide Exposure

Statistics of WHO: Death polls by organophosphate poisoning- The worldwide consumption of OPs rose to an amount of 5 million and reached 6.8 million from 2011 to 2015[24]. Abiding the fact, not every exposure leads to death but the impact of these events on total pesticide exposure, although hard to quantify, needs to be overviewed since they may represent the bulk of an individual's lifetime exposure to pesticides. The World Health Organization reports about three million cases per year of intoxication with Organophosphorus pesticides, causing about 220.000 deaths, in the world. These intoxications usually result from wrong manipulation of pesticides and suicidal attempts [15, 16] Over a decade ago, it was estimated that as many as 25 million agricultural workers worldwide experience unintentional pesticide poisoning each year [11]

Mechanism of toxicity

OP compounds inhibit acetylcholinesterase (AChE) which hydrolyses acetylcholine. Acetylcholine is a neurotransmitter at many nerve endings. These include the postganglionic parasympathetic and cholinergic sympathetic nerves, and both sympathetic and parasympathetic preganglionic fibres.

Acetylcholine is also released at the myoneural junctions of skeletal muscle and functions as a neurotransmitter in the central nervous system. Inhibition of AChE by OPs results in accumulation of acetylcholine at various sites. Acetylcholine released from postganglionic parasympathetic and cholinergic sympathetic nerves acts on the muscarinic receptors present on various smooth muscles and glands. The postsynaptic sites of preganglionic fibres and neuromuscular junctions have nicotinic receptors while the central neurons have both muscarinic and nicotinic receptors. A difference in toxicity has been found between individual OP poisons, but the cause of this difference has not been clearly identified.(Eddleston M et al 2005) [3].

Binding of OP with AChE leads to phosphorylation of the enzyme and this reaction is not easily reversible. The rate of spontaneous reactivation of AChE is very slow with diethyl Ops while it is relatively fast with dimethyl OPs. Further, there is ageing of the phosphorylated enzyme after which the enzyme cannot be reactivated by oximes. The half-life of ageing of dimethlyphosphorylated and diethylphosphorylated AChE in vitrois 3.7 hours and 33 hours, respectively, and the therapeutic windows therefore are 13 and 132 hours, respectively (4 times thehalf-life). (Worek F et al 2000) [31].

Case study

In 2002, 1035 cases of poisoning were recorded; 653 patients were reported, or presumed from clinical signs, to have ingested OP pesticides, 213 had ingested organochlorines (one patient ingested OP and organochlorine), and 170 had ingested other pesticides The most commonly consumed OPs were monocrotophos (257 patients), chlorpyrifos (114), and quinalphos (78) (Table 2). The most commonly consumed organochlorines were endosulfan (139) and endrin (74). The other commonly ingested pesticide was cypermethrin (58). Carbamates were uncommon with only six identified admissions. Some patients consumed an unknown pesticide – 144 patients were treated for OP poisoning because of the clinical signs at presentation and are counted above; in 83 cases, no clinical diagnosis was made

Examples of organophosphates

Diazinon (O,O-diethyl O-[4-methyl-6-(propan-2-yl)pyrimidin2-yl] phosphorothioate), is an organophosphate insecticide which acts by inhibiting acetylcholinesterase. Propoxur (Baygon) (2-isopropoxyphenyl N-methylcarbamate) is a carbamate insecticide with a similar mechanism of action through acetylcholinesterase inactivation. Both insecticides have been extensively used in Greece with proven acute and chronic adverse effects on health.They both accumulate in various tissues, such as hair, and analysis of these tissues enables the determination and establishment of long-term exposure.[34][35]

Diazinon exposure has been linked to the development of serious histopathological lesions in the liver, the kidneys and the brain. On the other hand, propoxur exposure has only been linked to the decrease in weight

of several organs. Pesticide exposure has been linked to oxidative stress. Indeed, it has been established that both propoxur and diazinon induce oxidative stress and studies have shown that oxidative stress contributes to diazinon-induced toxicity. Telomerase is an enzyme, which adds DNA sequence repeats to the ends of eukaryotic chromosomes, called telomere regions. This addition prevents the constant loss of important DNA from chromosome ends. Alterations in telomerase activity have many clinical implications, such as aging, cancer, diabetes mellitus and many more. Due to its central role in the maintenance of steady state telomere length, telomerase is a principal target for regulatory mechanisms, while simultaneously being highly susceptible to oxidative stress[34]

Long term exposure of rabbits to propoxur and diazinon caused histopathological lesions (focal inflammation and fibrosis) in kidneys and liver. Oxidative stress and genotoxic effects were also induced, documented through changes in TAC, GSH and oxidative DNA damage. Systemic inflammation has also started to accumulate, whereas the observed increase in telomerase activity in liver and kidneys probably counteracts for local tissue damage.

Chronic effects of organophosphate poisoning-

Organophosphate (OP) compounds are extensively used as pesticides and industrial chemicals. They are primarily neurotoxic and produce well-defined muscarinic, nicotinic, and cholinergic neurosymptoms involving both central and peripheral nervous systems.Increases in both central and peripheral neurologic symptoms are also found in many studies on moderate exposure [18]. Increased symptom prevalence may provide early evidence of neurologic dysfunction, before clinically measureable signs are evident. High-level exposure has both acute and long-term neurologic effects, and adverse effects have been reported in most type of pesticides, including OP, carbamate, herbicides, and fungicides. OPs have been studied in great detail. Most previous studies of pesticides and neurologic symptoms have focused on OP pesticides. Farm workers, greenhouse workers,[20] and pesticide factory workers exposed to OPs reported more neurologic symptoms than unexposed workers. Similarly, farmers and farm workers who applied OPs had higher symptoms prevalence than did nonapplicators.

- **Symptoms:** OP's posed potential risk to endocrine, metabolic, neurological, hepatorenals disorders, psychiatric manifestations and neuritis(Kumar et al., 2015).

Acute effects- The acute features of poisoning generally develop within 1–2 hours of exposure and can be grouped as those related to the muscarinic, nicotinic and central nervous system.

Muscarinic acetylcholine receptors in the parasympathetic system-

Bronchorrhoea,Miosis,Lachrymation,Urination,Diarrhoea,Hypotension,Bradycardia, Vomiting, Salivation.

Nicotinic acetylcholine receptors in the sympathetic system- Tachycardia, Mydriasis, Hypertension, Sweating

Nicotinic and muscarinic acetylcholine receptors in the CNS-Confusion, Agitation, Coma, Respiratory failure

Nicotinic acetylcholine receptors at the neuromuscular junction-Muscle weakness, Paralysis, Fasciculation [3]

- **Environmental factors affected by organophosphate**

Keeping human health aside , ops are threat to many other habitats in the environment like plants , animals, soil cultures too. Although these contamination indirectly affects the cycle of human health too.

Effects on plants :

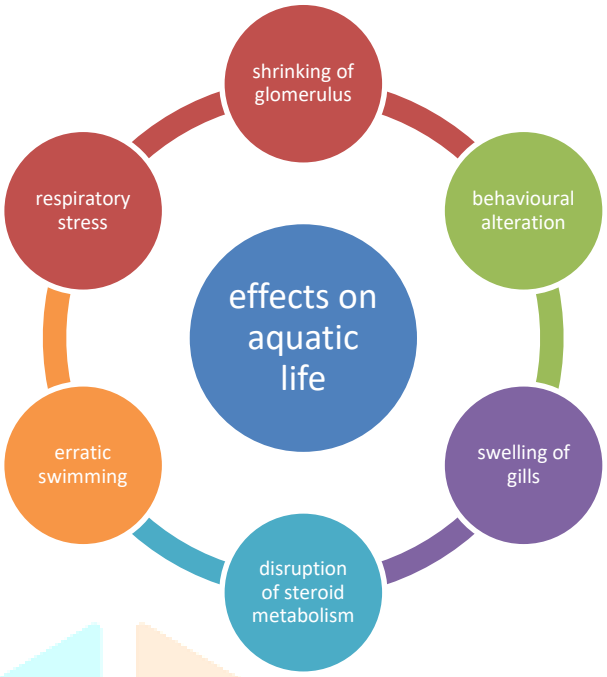
Organophosphate pesticides have been shown to adversely affect the photosynthesis

plant mineral nutrition (Zobiole et al., 2011)[37]. OPs prevent the biosynthesis of catalase, perioxidase and d-aminolevulinic acids (ALA) which are the major component of chlorophyl biosynthetic pathway by inducing Fe deficiency in plants (Barcelos et al., 2012) [25]. In India, OPs (glyphosate) were also reported to reduce the soluble sugar content in Pisum sativum along with the alterations in potassium and sodium tissue concentrations. The most commonly used OPs that have been found to have deleterious effects on non-target photosynthetic organisms include glyphosate, phorate, chloropyrifos, dimethoate, imidacloprid, chlorosulfuran, metasulfomethyl, dichlorovos, trichlorfon, etc. OPPs endanger biodiversity and acidify the soil. Air deposition, water from application locations, and direct application can all contaminate soil. OPs affect the biochemistry of plants by influencing photosynthesis at various levels by altering inorganic and the organic intermediates(Mondal, Kumar, Haque, & Kundu, 2017) [26].

Glyphosphate: Glyphosate inhibits the synthesis of aromatic amino acids by blocking the shikimate pathway and hence has direct influence on the PSII associated proteins – D1-D2 and finally leads to the inhibition of ATP synthesis.

Dimethoate is a thio-organophosphate insecticide which is reported to show toxic effects on algae. It results in growth reduction, inhibits chlorophyll biosynthesis, protein synthesis and carbohydrate synthesis in algae (Pandey & Gopal, 2011)[28].

Effect on aquatic life:



Most of the Ops are persistent in the ecosystem through many modes which induces sub-fatal or fatal effects in both aquatic and terrestrial organisms. It is, therefore a matter of concern to monitor the organophosphate pesticides in humans and food residues to check the population exposure size. Moreover, for safer use of organophosphate pesticides more research work should be performed to monitor the time of exposure and concentration that will not simulate sub-lethal or lethal effects on aquatic and terrestrial biota.

According to a review done by Singh(2007) for organophosphate pesticide poisoning dimethoate on common carp Cyprinus carpio. The LC50 after 24, 48, 72 and 96 hr of exposure was found to be 84, 1.78, 1.68 and 1.61 mg/L respectively. Increase in dose exhibits erratic swimming, low rate of opercular movement, inability to maintain balanced and normal posture with increase in time.[32]

Acetylcholinesterase (AChE) activity significantly decreased in the gill tissues of Pacific oyster Crassostrea gigas when exposed to dichlorvos at concentration of 0.1–200 lM Anguiano (2010) studied the toxicity of organophosphate pesticide to assess the acetylcholinesterase activity in Clariasga riepinus and found significant decrease in AChE activities in eye homogenate by 50% and plasma by 84%. The Acetylcholinesterase (AChE) activity was evaluated in plasma, eye and brain homogenates of unexposed and exposed fish. The concentration of pesticide that inhibited 50% (IC50) of AChE activities in brain homogenates was found to be 0.003, 0.03, 0.15, 190, 0.2, 0.003 and 0.002 mM for carbaryl, chlorfenyinphos, diazinon, dimethoate, fenitrothion, pirimi phosmethyl and profenofos respectively. Significant inhibition of AChE activities in plasma (84%) and eye homogenate (50%) was observed[33].

Conclusion :

Due to the detrimental impact that pesticides have on both humans and the ecology, environmental contamination by these chemicals is currently a global problem. In order to remove these contaminants from the contaminated environments, ecologically friendly and sustainable procedures must be used. Technological progress has made it possible to not only break down organophosphate pesticides in various environmental compartments, but also to improve the efficiency of existing technologies for this purpose and to develop new ones that will remove these pollutants entirely from environmental compartments. The current investigation demonstrated the increase in these pollutants' levels in a number of environmental compartments, many of which are beyond maximum residue limits and so endangering the dynamic balance of the ecosystem.

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