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Review Article

Organophosphorus Poisoning: An Overview

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ABSTRACT

Organophosphorus pesticides are used widely for agriculture, vector control, and domestic purposes. Despite the apparent benefits of these uses acute organophosphorus pesticide poisoning is an increasing worldwide problem, particularly in rural areas. Their toxicity has been recognised since the 1930s, when they were also developed for use as chemical warfare agents. Our aim is to provide an evidence based review of the pathophysiology, diagnosis and management of acute organophosphorus pesticide poisoning. We emphasize that in future, especially in developing countries, Government authorities should be encouraged to control organophosphate product licensing, manufacture, storage, import, methods of use and delivery, food contamination and disposal.

***Key words**:* Atropine, Organophosphorus poisoning, Pesticide, pralidoxime

***Key Messages**:*

In developing countries, especially in India, organophosphorus pesticide use is widespread as most population is mainly rural with farming as a major occupation. Acute poisoning is a medical emergency. It is important to know the nature, severity and outcome of acute poisoning cases in order to take up appropriate planning, prevention and management techniques.

INTRODUCTION

Organophosphorus (OP) compounds have been widely used for a few decades in agriculture for crop protection and pest control, thousands of these compounds have been screened and over one hundred of them have been marketed for these purposes. [1] Some have also been used in the medical treatment of myasthenia gravis, e.g. diisopropyl phosphorofluoridate (DFP), tetraethyl pyrophosphate (TEPP) and octomethyl pyrophosphotetramide (OMPA). [2-4] Some OP esters are still used to treat glaucoma (Ecothiopate). In addition to these beneficial agricultural, veterinary, and medical uses, some highly potent OP anticholinesterase compounds, including tabun, sarin, soman, and VX have been used as "nerve gases" in chemical warfare. They are also been used as plasticizers, stabilizers in lubricating and hydraulic oils, flame retardants, and gasoline additives. [5]

Acute poisoning is an important cause of morbidity and mortality in developing countries like India. In medical emergency 10% of admissions are due to poisoning and organophosphorus poisoning contributes to nearly 50% of it. [6]

Acute poisoning with organophosphate compounds is common in northwest India and is generally as a result of suicidal ingestion. In India, Organophosphorus compounds (OPCs) are freely available in shops and widely used as insecticides in agriculture and at home. In the past, a high mortality was reported but in recent years, with intensive care, mortality has considerably declined. [7]

Organophosphates cause poisoning by inhibition of the enzyme cholinesterase with subsequent accumulation of acetylcholine and symptoms relating to overactive cholinergic action. The mechanism of inhibition is phosphorylation of the esteratic locus on the enzyme with the formation of a stable chemical complex which is biologically inactive.

In parts of developing world pesticide poisoning causes more deaths than infectious diseases. [7] Organophosphate insecticides account for more than 50% of all acute poisoning in hospital practice, the majority of patients are younger than 30 yrs. [8] In teenagers and adults the poisoning is generally due to suicidal intention although accidental poisoning during spraying can also occur. [9]

Mortality ranges from 4% to 38% in Indian studies. The most common cause of death is respiratory failure. Early recognition and prompt ventilator support may improve the survival rate. The common use of insecticides in public health and agricultural schedules has caused severe environmental pollution and potential health hazards including severe acute and chronic cases of human and animal poisonings. [10] So our aim is to discuss the clinical features and management of organophosphorous poisoning with emphasis on optimization and monitoring of usage of OP compounds.

Epidemiology:

The organophosphate compounds are most commonly associated with serious human toxicity, accounting for more than 80% of pesticide-related hospitalizations. [11] In contrast to the past, when chlorinated hydrocarbon compounds such as DDT were commonly used, organophosphate insecticides have become increasingly popular for both agricultural and home use because their unstable chemical structure leads to rapid hydrolysis and little long-term accumulation in the environment. [12] A recent national survey in Bangladesh showed that 14% of all deaths (3971 of 28,998) of women between 10 and 50 years of age were due to self-poisoning, the majority with pesticides. [13]

The importance of pesticides in India can be understood from the fact that agriculture is a major component of the Indian economy: It contributes 22% of the nation's GDP and is the livelihood of nearly 70% the country's workforce. Globally, due to consolidation in the agrochemical industry, the top five multinational companies control almost 60% of the market.

Overexposure to pesticides can occur before spraying– because of easy access for children, lack of adequate labeling and during mixing – during spraying and after spraying operations. Spray operators and bystanders can be affected. Having cheap and easily available highly hazardous pesticides at hand increases the incidence of intentional pesticide poisonings. [14]

The effective number of cases of pesticide poisoning occurring in India annually has been estimated by G. Ravi et al 2007 to be up to 76 000, much higher than the figure of NCRB. Furthermore, Gunell et al, 2007 calculate that the number of

intentional cases alone reaches some 126,000 cases annually. [15] The reasons for the suicide in males may include lack of employment, poverty, urbanization and various other stress related factors. In females, it may be due to marital disharmony. [16]

CLASSIFICATION AND BIOLOGICAL ASPECTS OF ORGANOPHOSPHORUS COMPOUNDS:

Classification [9,17]

Organophosphorus compounds are classified as

I. By chemical structure:

A. Alkyl phosphates: HETP (Hexaethyl tetra phosphate)**,** TEPP (tetraethyl pyrophosphate) tetron, fosvex etc

B. Aryl phosphates : Paroxon (0,0, diethyl-o-p-nitrophenyl phosphate) –E 600-mintacol**,** Parathion (0,0, diethyl-o-p-nitrophenyl thiosulphate or diethyl thiophosphoric ester of p-nitrophenol-folidol (bayer), Eketox (sandoz), kilphos, niran, rhyntox, oriental Bug's bait etc.

II. By toxicity [18]

Highly toxic (< D50 < 50mg/kg): Azinophos-methyl (Cruthion)**,** Bomyl (Swat)

Carbophenthion (Trithion) etc.

Moderate Toxicity (αD50 = 50-1000mg/kg): Acephate (Orthene)**,** Bensulide (Betasan)**,** Chloropyrofos (Durshan, Lorsban) etc.

Low toxicity (αD50 = > 1000mg/kg) : Bromophos (Nexagan)**,** Etrimfos (Ekanet)**,** Iodofenphos (Nuvanol N) etc.

(αD50 = lethal dose in experimental animals)

MECHANISM OF ACTION:

Organophosphate compounds avidly bind to cholinesterase molecules and share a similar chemical structure. In human beings, the two principal cholinesterases are RBC, or true cholinesterase (acetylcholinesterase), and serum cholinesterase (pseudocholinesterase). [19]

Normally the cholinesterases rapidly hydrolyze the neurotransmitter acetylcholine into inactive fragments of choline and acetic acid after the completion of neurochemical transmission. The neurotransmitter acetylcholine is present in the terminal endings of all postganglionic parasympathetic nerves, at myoneural junctions, and at both parasympathetic and sympathetic ganglia. The major toxicity of organophosphate compounds is the covalent binding of phosphate radicals to the active sites of the cholinesterases, transforming them into enzymatically inert proteins. [19,20] Organophosphates thus act as irreversible cholinesterase inhibitors because the organophosphate-cholinesterase bond is not spontaneously reversible without pharmacological intervention. The inhibition of cholinesterase activity leads to the accumulation of acetylcholine at synapses, causing overstimulation and subsequent disruption of transmission in both the central and peripheral nervous systems. Exposure to organophosphate compounds will, therefore, interfere with synaptic transmission peripherally at muscarinic neuroeffector junctions and nicotinic receptors within sympathetic ganglia and at skeletal myoneural junctions. This is accomplished by an overstimulation of acetylcholine receptor sites that leads to a variety of physiologic and metabolic derangements. Disruption of transmission also will occur at the acetylcholine receptor sites within the central nervous system. [20]

MODE OF INTOXICATION: [18,20,21]

Most OP compounds are extremely lipophilic. They are therefore readily absorbed by passive diffusion across lung and gastrointestinal system or skin.

Deliberate ingestion is common with suicidal intensions in developing countries,

where they are readily available and cheap. Dermal and mucous membrane absorption is slower but clinical poisoning can occur after prolonged exposure. Inhalation by accident may occur during spraying in improper conditions. Intoxication by inhalation may occur during chemical warfare and following accidents during storage particularly when stock catch fire.

Kora etal 2011 found that The commonest route of poisoning was oral in the suicidal cases and there were 6 accidental poison cases with 3 cases of inhalational OP poisoning, in which one required ventilator support. The reasons for the suicide in males may include lack of employment, poverty, urbanization and various other stress related factors. In females, it may be due to marital disharmony. [16]

Distribution and Storage:

Following absorption, OP compounds accumulate rapidly in fat, liver, kidneys and salivary glands. The phosphorothioates (P=S), for example diazonin, parathion, and bromophos, are more lipophilic than phosphates (P=O), for example dichlorvos, and are therefore stored extensively in fat which may account for the prolonged intoxication and clinical relapse after apparent recovery which has been observed in poisoning from these OP insecticides. OP compounds generally are lipophilic and therefore cross the blood / brain barrier in most cases. [22]

ORGANOPHOSPHORUS COMPOUND METABOLISM: [8,18,20,23,24]

After absorption in skin, GI tract or inhalation, the insecticides and their metabolites gets distributed quickly especially in liver kidneys, adipose tissue and tissues rich in lipids. The plasma half life after a single administration is from few minutes to several hours which depends on type of compound and rate and amount of administration. Metabolism is mainly due to oxidation, by cytocrome-p-450 system and hydrolysis of ester bonds mediated by various esterases or paroxonases. Elimination mainly occurs via urine and faeces.

Urinary and faecal elimination is usually rapid, 80-90% of most compounds being eliminated within 48 hrs.A very small proportion of OP compounds and their active forms are excreted unchanged in urine. Some compounds remain longer in body like fenthion and Fenithrothion.

These compounds and their active metabolites cause toxicity by inhibiting the function of acetylcholinesterase, the enzyme responsible for hydrolysing and inactivating the neurotransmitter acetylcholine. They also inhibit number of enzymes belonging to the group of carboxyl-esterases. The biological effects of OP compounds are a result of accumulation of endogenous acetyl choline at sites of cholinergic transmission.

Ion binding is by which enzyme AChE is inhibited, but eventually progressively phosphorelated by covalent bonding a process normally takes 24-48 hrs.

This process is called “Ageing” and this period is known as the “critical interval” because during this time administration of antidote is still effective in reversing the process. Once ageing is completed the enzyme cannot be reactivated. Plasma AChE recovers quickly within 4 weeks. Red cell AChE takes longer and may not be restored. Affected AChE recovers at the rate of ~ 1% per day.

Restoration of AChE activity occurs by slow denovo synthesis of free enzyme and also to some extent as a result of spontaneous dephosphorylation of the inhibited enzyme. The inactivation (phosphorylation) and reactivation (Dephosphorylation) vary considerably with different OP compounds, which accounts for differences in toxicity. Ageing has an

important bearing on toxicity and treatment outcome. Organophosphorus compounds inhibit number of other enzymes such as lipases, trypsin and chymotrypsin which are phosphorylated by these compounds. The rate of reaction is slower compared to AChE and clinical consequences are not known. They also affect, central nervous system, cardiovascular system, metabolic and endocrine system including reproduction and neuromuscular system.

The acceptable daily intake:

The amount of chemical which can be consumed every day for an individual life span with the practiced certainty based on valuable evidence that no harms will result for humans. This is 0.02 mg/kg for malathion, and 0.004 mg/kg for parathion. [20]

CLINICAL MANIFESTATIONS:

The clinical manifestation of OP poisoning depends on the agent, quantity and route of entry. Ingestion and inhalation result in more rapid development of symptoms than dermal exposure. After ingestion symptoms appear within 30-90 minutes and a maximum of 24 hrs in case of compounds which are highly lipophilic and which require metabolic bioactivation. [18]

Local Effects:

GI symptoms appear first before the onset of systemic symptoms. In inhalation typically exhibits respiratory effects. After ocular exposure symptoms generally begins in the eyes.

Systemic Effects:

Three well defined clinical phases are observed-

1) Initial cholinergic phase.
2) The intermediate syndrome (IMS)
3) Delayed polyneuropathy

THE CHOLINERGIC PHASE [25-31]

It is mainly due to accumulation of Ach at the cholinergic synapses and may be classified into

1) Muscarinic (all postganglionic nerve endings)
2) Nicotinic (Autonomic ganglia and skeletal muscle end plates).
3) CNS manifestations (synapses in CNS)

1) Muscarinic manifestations

Anatomic site of action	Physiological effects
a) Bronchial tree	Dyspnea, increased bronchial secretions, cough, wheezing and tightness in chest
b) GI system	Vomiting, diarrhoea, nausea abdominal tightness, cramps tenesmus, faecal incontinence.
c) Sweat glands	Increased sweating
d) Pupils	Miosis, occasionaly unequal
e) Lacrimal glands	Increased lacrimation
f) Salivary glands	Increased salivation
g) Cardiovascular system	Hypotension, Bradycardia
h) Bladder	Frequency, urinary incontinence
i) Ciliary body	Blurring of vision

2) Nicotinic manifestations :

Of sympathetic ganglia	Pallor, Tachycardia Hypertension
Of striated muscle	Muscle twitchings Cramps Weakness Fasciculation

3) Central nervous system manifestations:

Anxiety, restlessness, giddiness, emotional liability, slurred speech, ataxia, seizures, drowsiness, confusion, difficulty in concentration, headache, nightmare, insomnia, excessive dreaming, apathy, tremor, depression, generalized weakness, coma, absence of reflexes, Cheyne – Stokes

respiration, depression of respiratory and circulatory centres with Dyspnea, Hypotension, cyanosis. The combination of symptoms may vary.

The predominant clinical finding are usually muscurinic which is followed by CNS and then nicotinic manifestations GI symptoms are first to appear after ingestion. [28]

The intermediate syndrome (IMS):

After apparent recovery from cholinergic crisis muscle paralysis occurs, but before the expected onset of the delayed polyneuropathy has been identified as "Intermediate syndrome (IMS). This is type II paralysis first described by Wadia et al. [21] In 1974 and later christened as "Intermediate syndrome" (IMS) by Senanayake, Karalliedde L. [22] The syndrome is of Acute onset, seen within 24-96 hrs (1-4 days) after poisoning, affecting conscious patients without fasciculations or other cholinergic manifestations. The cardinal features of this syndrome is muscle weakness affecting predominantly proximal limb muscles and neck flexors. [24,25]

Delayed polyneuropathy [8,20,25,27]

Though uncommon in India the neuropathy develops following a latent period of 2-4 weeks after the cholinergic crisis. The main clinical features are weakness of distal muscles of feet and hand. The weakness is preceded by pain and parasthesia of limbs. Wasting of distal muscles of particularly small muscles of the hand and those of anterior and peroneal compartments of the leg is an inevitable consequence. In some patients pyramidal tract signs appear after a few weeks or few months. Recovery is variable.

The phosphorylation of an enzyme neuropathy target esterase in nervous tissue is considered to be responsible for the polyneuropathy.

OTHER EFFECTS OF OP POISONING

1. Cardiovascular system [29-32]

Tachycardia and increased blood pressure occurs in initial stage and Bradycardia and low blood pressure in the later stage. Commonest effect observed was tachycardia.

2. Respiratory system [33,34]

Respiratory arrest a common terminal manifestation of OP poisoning is produced by over stimulation of 3 types of receptors. It can be recalled that muscarinic action produces increased bronchial secretions, Bronchoconstriction leading to pulmonary oedema and chest tightness. On other hand nicotinic action produce intercostal muscle paralysis and respiratory muscle weakness leading to respiratory paralysis.

3. Altered immunity to infection [35]

The immunosuppression is associated with severe cholinergic stimulation either from a direct action of acetylcholine on the immune system or secondary to toxic chemical stress associated with cholinergic poisoning.

4. Gastrointestinal system [36]

After ingestion of organophosphate compound the initial symptoms may be increased salivation, nausea, vomiting, abdominal tightness and cramps are the commonest. Other muscarinic manifestations include diarrhea, tenesmus and faecal incontinence.

5. Effects on reproduction

Following organophosphorus poisoning in females abortions were being reported.

In late 20th century, several experimental and epidemiological studies regarding hormonal imbalance especially sex hormones leading to adverse developmental outcomes related to pesticide exposure, including foetal death, intrauterine growth restriction, congenital malformations and male / female fertility have been published.

6. Effects on temperature regulation [20]

It has been noted in several case studies with incidence of 7% of derangement of temperature regulation in the form of

hypothermia. Some may experience fever lasting for many days a biphasic response.

7. Vocal card paralysis [20]

In few patients vocal card paralysis was reported within 2 days.

8. Effects on other systems [20]

Eyes : myopia and pigmentary degeneration of retina.

Joints : arthritis, cerebellar ataxia.

Interference with mitochondrial oxidative metabolism.

9. Changes in metabolism and endocrine activity [37,38]

Transient hyperglycaemia and glycosuria are often found in severe OP poisoning. Absence of acetone bodies differentiates from diabetic coma, except for coma in diabetic patients due to hyperosmolarity from excessive blood glucose.

DIAGNOSIS

1) Acute cholinergic crisis [24,39-41] – made on

• History of ingestion of the compound

• Signs and symptoms

• Improvement after atropine and oxime therapy

• Inhibition of cholinesterase activity

Organophosphate poisoning is generally diagnosed clinically based on the characteristic symptoms and the history of exposure to OP agents. When diagnosis is not evident, a depressed serum or RBC cholinesterase level is helpful (<50%). If OP poisoning is suspected therapy should never be withheld pending confirmation of lab values.

2) Intermediate syndrome

The diagnosis is clinical and should be suspected when a patient who is recovering from the cholinergic crisis develops respiratory difficulty. The presence of muscle weakness in the absence of muscle fasciculations and other cholinergic features differentiates it from cholinergic crisis. The early onset of muscle weakness distinguishes the IMS from the delayed polyneuropathy, which appears 2-3 weeks after poisoning.

3) Delayed polyneuropathy

History of intoxication with OP agents and the time of onset and distribution of muscle weakness differentiate from other causes of acute polyneuropathy.

MANAGEMENT

1. ACUTE CHOLINERGIC CRISIS [20,24]

All patients should be managed as emergencies in hospital.

A. First aid

B. Prevent further absorption of insecticide

C. Specific antidote therapy

• Anticholinergic medication

• Reactivation of Acetylcholine-oximes

D. Benzodiazepines

A. *First Aid:*

a) Remove patient from the contaminated environment.

b) Remove contaminated clothing

c) Wash skin with soap and water and eyes with water

d) Assess breathing and circulation

e) Resuscitate if necessary

f) Support vital functions if necessary

• O2 inhalation

• Lung ventilation

• Ionotropes

g) Control of convulsions

h) Monitor ECG, blood pressure, O2 saturation, ventilation, level of consciousness.

B. *Prevent further absorption of insecticide:*

a) ***Gastric lavage:***

Gastric lavage is often the first intervention poisoned patients receive on presentation to hospital, sometimes at the expense of resuscitation and giving antidote. No evidence shows any form of gastric decontamination to benefit patients poisoned with OP. gastric decontamination should only be done after the patient has been

stabilized and treated with oxygen, atropine and an oxime. [42]

Performed using largest possible oro-gastric tubes with 50-100ml of fluid / lavage, preferably within one hour of ingestion protect airway in patients with impaired consciousness.

b) ***Administer activated charcoal:***

dose initial 60-100gms, followed by 0.25gms to 0.50gms/kg every 1-4 hrs.

C. *Specific antidotal therapy:*

Treatment aims:

a) Reversal of synaptic biochemical abnormalities

b) Reversal of cholinesterase blockade

This is achieved by administering sufficient quantity of two complimentary medications.

i) Anticholinergic medications – atropine or glycopyrrolate

ii) Reactivation of AChE – oximes

i) *Anticholinergic medications:*

Atropine [6,20,23,41,43,44,45,47]

It is a tertiary amine, a competitive antagonist of acetylcholine at muscuranic post synaptic membrane and in the CNS. In symptomatic poisoned adults, atropine is given as 1-2mg IV or IM (0.02 – 0.05mg/kg in children). If there is no effect within 10 minutes, the dose is doubled every 5 to 10 minutes, until muscurinic symptoms are relieved. The action of 2mg atropine sulphate begins 1 to 8 minutes after IV, IM, administration, respectively and it is maximal at 6 to 15 minutes. Half life elimination is 2-5 hrs.

Alternatively atropine can also be given by continuous infusion. Atropine 30mg in 200ml of NS-at the rate of 0.02-0.08 mg/kg/hour – titrate against the important parameters for adequate atropinization, supplemented by giving additional IV boluses of atropine 1-5mg to regain quick control of secretions or severe bradycardia when indicated.

Once signs of adequate atropinization occurs the dose should be adjusted to maintain this effect for at least 24-48hrs, carefully withdrawn once the patient is adequately stabilized, observed for 72 hrs following termination of atropine before discharge from the hospital.

The patient should be oxygenated prior to atropine administration in order to prevent ventricular dysarrhythmias associated with hypoxia. The end point of anticholinergic treatment is clearing of secretions from tracheobronchial tree and drying of most secretions.

Pupillary dilatation is an early response to atropine, but it is not a therapeutic end point. Tachycardia is not a contraindication to atropine. Diaphragmatic muscle weakness is important contributor to hypoventilation and it is not reversible with atropine.

Atropine crosses the blood brain barrier and may cause severe toxic effects such as confusion, psychosis, coma, seizures, delirium, hallucinations, fever tachycardia and ileus.

The studies concluded that patient who receive aggressive heavy dose of atropine, survived more frequently than those who received inadequate doses or none at all. Also studies observed that continuous high dose atropine infusion is more effective than intermittent bolus doses.

Glycopyrrolate [43,46,48,49]

It is a quaternary ammonium compound may be substituted for atropine in patients with a clear sensorium, with no evidence of central toxicity. It has many advantages over atropine such as Better control of secretions, Lesser tachycardia, Fewer CNS side effects and Fewer respiratory infections . Dose 0.05 mg/kg Or given at increments of 0.25mg repeated every 5-10 minutes until anticholinergic over activity is reversed or upto maximum of 2.5mg/d.

ii) *Reactivation of AChE – OXIMES* [20,23,50,51]

Derivatives of hydroxamic acid and a number of other oximes were shown to

reactivate cholinesterase inhibited by organophosprus compounds. WHO recommends that oxime is given to all symptomatic patients who need atropine.

Mode of action

1) Functions by nucleophilic attack on the phosphorylated enzyme, removing the bulky phosphate moiety and completely restoring normal acetylcholinesterase activity.

2) Direct reaction and detoxification and unbound the OP molecules.

3) Endogenous anticholinergic effect in normal doses.

Dose- 1gm every 8-12 hrs IV in adults and 25-50mg/kg in children.

Maintenance and duration of treatment:

Average duration of treatment 5 to7days. [8]

The therapeutic concentration of the oximes should be maintained to regenerate as much active enzyme activity as possible until the OP compound has been eliminated. [20]

OP residues that are present may bind the circulatory free PAM and lower its serum concentrations. Therefore PAM should be continued as long as nicotinic symptoms persist, [28] those who develop the IMS are given the drug for longer periods until they are weaned from ventilatory care. [8]

Delayed clinical manifestations occur with fat soluble organophosphates like fenthion, chlorfenthion and parathion. Cardiac and respiratory arrest have known to occur. [30,41]

Cardiac monitoring and blood pressure monitoring are advised during and for several hours after the infusion of oximes. Rapid infusion can cause tachycardia, laryngospasm, muscle rigidity and weakness. [49,52]

D. *Benzodiazepines:*

They are used when the patients are agitated and who develop seizures. Diazepam appears to counteract some aspects of CNS-derived symptoms, which are not affected by atropine. [20]

2. INTENSIVE CARE MANAGEMENT

Recognition of OPP and correct initial treatment in hospitals and by general practitioners, with early referral of serious cases can be of vital importance in determining prognosis. Treatment of seriously ill patients in an ICU is important for many reasons, including good observation to assess the need for ventilator support and intensive nursing care. [53]

Patients with moderate to severe organophosphorus pesticide poisoning usually require management in an intensive care unit. Mortality from severe poisoning is high (10%) compared with the overall mortality from pharmaceuticals (0.5%). Current evidence suggests that prompt and appropriate management optimises outcomes. [54]

Patients with moderate or severe organophosphorus poisoning should be admitted to an intensive care unit after resuscitation to allow careful titration of antidotes, intubation, ventilation, and inotropes or vasopressors if required. [55]

3. MANAGEMENT OF DELAYED POLYNEUROPATHY

.No specific drug therapy is useful.

Role of antioxidants in OP poisoning: The toxicity of OP compounds is mediated by generation of nitric oxide and other free radicals. These toxic molecules can be counteracted by antioxidants such as vitamins C and E, spin traps, melatonin and low molecular weight thiols. The latter compounds can also increase the synthesis of glutathione, which can both ameliorate the OP induced oxidative stress and enhance OP detoxification. [8,57]

Hence, it is suggested to include antioxidants in the prescription of the patients with OP poisoning.

MORTALITY:

The commonest cause of death in acute organophosphorus poisoning was respiratory failure. Singh et al reported cardiac arrest as

cause of death in 10% of cases. Namba reported that death in untreated cases occurred within 24 hours and was delayed up to 10 days in treated cases. Complete recovery usually occurred in 10 days. Mortality rate varied depending on poison used, duration after exposure, and atropinisation of all the toxins. In Indian studies mortality rate ranged between 4 to 38%. This mortality was similar to other developing countries like Srilanka, and unlike the west where it was < 1%. [30,56]

Prevention of OP Poisoning [42]

Due to the toxicity of pesticides and the risk involved in treatments, there was general agreement that emphasis should be on preventing pesticide illness rather than relying on treatment.

- Ensure that there was always adequate ventilation when using or applying pesticides in the home or on pets, i.e. keep the doors and windows open at all times.
- Do not use pesticides indoors if they were only designed to be used outdoors.
- Always read and follow the pesticides label's instructions and safety warnings at all times.
- Use ready-to-use products (i.e., no mixing needed) whenever possible.
- Remove all foodstuffs and water supplies in the home from the vicinity of pesticide application or alternatively keep them sufficiently covered.
- Ensure that old pesticide or poison containers are safely discarded, instead of reusing them for storing or transporting drinking water. No matter how well you wash the container, it could still contain remnants of the pesticide.
- Do not transfer pesticides to other containers that children may mistake for cold drink or sweets container.
- Never pour pesticides or household chemicals down the drain, into the toilet or storm water drains, rivers or dams.

CONCLUSION

Acute organophosphorus poisoning may induce multisystem toxicity leading to severe toxicity and death .Poisoning is diagnosed on the basis of history and clinical examination; biochemical investigations can have a role for confirming the diagnosis.Management consists of prompt resuscitation, antidotes as required (particularly atropine, oximes, benzodiazepines), and selective decontamination .Ongoing monitoring and high quality supportive care are essential Healthcare staff treating exposed patients should exercise standard precautions.

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