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Study of Various Poisoning: A Review

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ABSTRACT: Organophosphate pesticides poisoning is a leading cause of morbidity and premature loss of life. Now those days it is very important factor in our life. Organophosphorus compound poisoning is a common cause of acute poisoning in India with high mortality, out of cause of death, an important are is respiratory failure. OPs cause toxicity after their absorption from skin, mucous membrane and respiratory tract following accidental exposures, or from gastrointestinal tract following suicidal ingestion. Organophosphorus compound are the chemical compound containing carbon-phosphorus bond. Poisoning with organophophorus compound may be i) Occupational ii) Accidental iii) Suicidal. The organophosphorus anti – chE agent are hydrolysed by two families of enzyme, carboxylesterases and paraoxonases, which are not inhibited by OP compounds. Discuss about the Pharmacokinetics, clinical feature of op compound poisoning The most widely used diagnostic tests for OP exposure are the estimation of plasma (PchE) cholinesterase and red blood cells AchE activity. For treatment used Atropine as anti-cholinergic agent. activated charcoal can proven to be effective then it should be an extremely valuable theropy since if is widely available in the developing world.

KEYWORDS: Organophosphate Pesticide; Poisoning; Pharmacokinetics; Antidote.

INTRODUCTION

Organophosphate pesticides poisoning is a leading cause of morbidity and premature loss of life in many developing countries of the Asia. The efficacy of current antidotes in largely unproved, and many other potential antidotes have been developed but are yet to be tested in humans. Mean while, preparation for the terrorist use of organophosphate were agent in loading to stock pilling of large amount of this unproved antidotes to treat mass poisoning [1].

Now organophosphorus compound poisoning is a common cause of acute poisoning in India with high mortality, out of cause of death, an important are is respiratory failure. The number of intoxication with OPs is estimated at some 3,000,000 per year, Fatality rates of 20% are common and the world health organization (WHO) has estimated that 2,00,000 people die each year from pesticide poisoning althrough the accuracy of these figure is keenly debated unfortunality the widespred use of OPs pesticides in the developing world's agricultural communities will make the reduction of death by primary prevention of a difficult task[3]. In addition

to numerous case of accidental intoxication from the use and manufacture of organophosphorus compound as agricultural insecticides these agent have been used frequently for homicidal and suicidal purpose, largely because of their accessibility.

OPs cause toxicity after their absorption from skin, mucous membrance and respiratory tract following accidental exposures, or from gastrointestinal tract following suicidal ingestion. They are metabolically subjected to hydrolysis by esterases although they bind to and interact with a number of enzymes acetyl cholinesterase (AchE) that is of clinical importance.[2]

These compound bind to the esteratic site on the acetyl cholinesterase molecule phospohorylating the enzyme, leading to inhibition of its normal action. The bond between esteric site on the enzyme and the phosphorus atom is stable and takes hours or weeks to break off, depending on the compounding involved. Studies have shown that a phenomenon of enzyme ageing occurs with involves cleavage of a radicle from the inhibited enzyme making it resistant to rephosphorylation. The net result is the accumulation of excess acteylcholine (Ach) at the cholinergic nerve endings all over the body resulting in the characteristic clinical manifestation, following inhibition, recovery of this enzyme occurs of a rate of about 1% per day. Restoration of AchE occurs by spontaneous rephosphorylation of the enzyme and by new enzyme synthesis. The toxicity of some nerve gases like soman is directly related to relatively quicker agening which occurs with OP compounds.

The case fatality for intentional self poisoning in rural Asia is 10-30 times higher than in the west, mostly due to use of highly toxic poisons [4].

ORGANOPHOSPRHORUS COMPOUNDS

Organophosphorus compound are the chemical compound containing carbon-phosphorus bond.

a) The common organophosphorus compound

Name	**Chemical name**
DFP	Diisopropyl flurophosphate
Tabus	Ethyl-N-diethylphosphoramido cyanidate
Sarin	Isopropyl methylphosphonofluoridate
Paraoxon	O, O-Diethyl O-(4-nitrophenyl)phosphate
Malaoxon	O,O-dimethylS-(1,2-dicarboxyethyl)-phosporothioate
Parathion	O,O-Diethyl-O(4-nitrophenyl) phosphorothioate
Diazinon	O,O-diethyl O(2-isopropyl-6- methyl -4 pyrimidyl) phosphorothioate
Malathion	O, O- Dimethyl S – (1,2- dicarbethoxy ethyl) phosphorodithioate)
Soman	Pinacolyly methylphosphonofiluo ridate

b) Types of – organophosphorus compound poisoning

Poisoning with organophophorus compound may be

i) Occupational

Its may me happened when a person engaged in spraying insecticides.

ii) Accidental

Its may be happened by consumpsion of the agricultural product sprayed with these insecticide.

iii) Suicidal

Its due to intentional ingestion of any of these compound.

PATHOPHYSIOLOGY OF OP POISONING

Acetylcholine is the neurotransmitter released by the terminal nerve endings of all postganglionic parasympathetic nerves and in both sympathetic and parasympathetic ganglia. It is also released at the skeletal myoneural junctions are serves as a neurotransmitter in the central nervous system. Actylcholinesterase in present in two forms-true cholinesterase which in found primarly in the nervous tissue and erythrocytes and pseudocholinesterase which is found in the serum and liver. OP bind to the active serin residue of acetyl cholinesterase irreversibly and convert the enzyme in to an inactive protein complex, resulting in the accumulation of acetylcholine at the receptors, leading to over stimulation and subsequent disruption of nerve impules transmission in both the peripheral and central nervous system.

PHARMACOKINETICS

The organophosphorus anti – chE agent are hydrolysed by two families of enzyme. The carboxylesterases and the paraoxonases. Which are not inhibited by OP compounds. These enzyme are found in the plasma and liverand scavenge or hydrolyse a large number organophosphorus compound by cleaving the phosphoester and split the anhydride, P-F,P-CN, ester bond. The paraoxonases are low molecular lipoprotein, and in adition to their capacity to hydrolyse organophosphate. The metabolic products are then excreted in urine.

Young animal are deficient in carboxylesterase and paraoxonases which may account for age related toxicities seen in new born animal. Plasma and hepatic carboxylesterases and plasma butyrulcholinesterase and inhibited irreversibly by organophosphate compound, their scavenging capacity for OPs can effort partial protection against inhibition of AchE in the nerveous system.

The carboxylesterase also catalyse hydrolysis of malathion and other OPs agent. That contain carboxyl ester linkage rendering them less active or inactive. Since carboxylesterase are inhibited by OPs toxicity from exposure to two OPs in insecticides can be synergistic [5]

CLINICAL FEATURE OF OP COMPOUND POISONING

There may be acute , intermediate and delayed sequelae in patients who have anticholinesterase poisoning,[5] organophosphate may cause life threatening conditions such as an initial acute cholinergic crisis and intermediate syndromes [19].

Organ of system	**Muscarinic effects**	**Clinical effects**
Occular	miosis ncreased lacrimal secretion	Blurred vision
Cardiovascular	Bradycardia Junctional rhytham Peripheral vasodilation	Hypotension warm skin
Respiratory	Brochoconstriction Bronchorrhoea Pulmonary oedema	Dyspnoea cough, cyanosis crackles wheezes
Gastrointestinal	Increased tone and motility Decreased tone of sphincters And increased secretion	Salivation, vomiting diarrhoea Abdominal cramps

Genito urinary	Contraction of detrusor relaxation of trigone and spinster.	Urinary incontinence.
Skin	Increased sweat production	Diaphoresis

Table 1 CLINICAL FEATURES OF ORGANOPHOSPHORUS COMPOUND POISONING TOXICITY IN RECEPTOR BASIS- MUSARINIC

Organ or system	**Nicotinic effect**	**Clinical effect**
Musco skeletal	Skeletal muscle, intial stimulation followed by paralysis	Fasciculation, (eyelide, tongue) followed by weakness and paralysis
Cardiovascular	Sympathetic gangila intial stimulation followed by paralysis	Tachycardia hypertension
Central nerovous	Muscarinic and nicotinic effect	Brady cardia, hyprotension, tremor, anxiety ,confusion, scizuras, coma

Table 2 CLINICAL FEATURES OF ORGANOPHOSPHORUS COMPOUND POISONING TOXICITY IN RECEPTOR BASIS- NICOTINIC

a) Acute cholinergic syndrome

Acute anticholiesterase poisoning may occure from inhalation, skin absorption, or ingestion with symptoms characteristically beginning after 30-60 min and reaching a maximum after 2-8 hours. In some cases symptomatology may be delayed for upto 12 hours. And with dichlofernthion and fenthion the onset of symptoms may be delayed by up to 2 and 5 days respectively. With fenthion the symptoms may recure after 24 days. The organophosphate poisoned patients often emits a characteristic odour. The acute clinical picture may be mild, moderate or severe depending upon the quantity of cholinesterase inhibitors ingested.

With severe poisoning, multiple organ failure (e.g – respiratory failure, renal failure, hypotension, complete heart block, ventricular, trachycardia and venticulat fibrillation) a rare syndrome of prolonged QTc interval and sudden death has also been reported in patients form 1-15 days after the exposure [8].

The clinical finding are thereby a mixture of muscarinic effects resulting from the exitation of postganglionic parasympathetic activity, nicotinic effects resulting from accumulation of Ach at neuromuscular junction and consequent depolarization and central nervous system effects causing initial excitation and subsequent inhibition of all CNS activity.

The muscrinic symptoms are diarrhoea, lacrimation, salivation, bronchorroea, brochospasm, bradycardia, urination and miosis. However depending upon the balance between the nicotinic and the muscarinic effects, patients may have hypertension and trachycardia occurring due to nicotinic action rather then hypertension and brady cardia.

The nicotic receptor activated during acute intoxication lead to muscle paralysis, fasciculation may be seen and are a reliable sign of poisoning. The mechanism of action of paralysis is depolarization and desensitization block induced by acetylcholine at the neuromuscular junction. In cholinergic phase paralysis usually passes of within 48-72 hours but complete clinical recovery from all the effects may take up to a week after expossure to these compounds [2].

Its incidence in different studies has been reported to be between 20-68%. This syndromes has been shown to be commonly associated with organophosphorus compound like diazinon, dimethoate, methylparathion, methamidaphos, monocrophos, fenthion and ethylparathion. It develops 12-96 hours after exposure and reflects prolonged action of acetylcholine on the nicotinic receptor and its characterized by muscular weakness in the ocular, neck, bulbar, proximal limb and respiratory muscle.

Prolonged suppression of the enzyme acctycholinesterase is seen during this stage and metabolites of the parent comound may be demonstrable in the urine. [2]

b) Intermediate syndrome

Intermediate syndrom in diagnosed by the onset of motor paralysis developing 1-4 days after organophosphate poisoning. It is characterized by an acute respiratory paralysis, weakness of proximal limb muscle and muscle supplied by cranial nerves, and depressed tendon reflex. Patients with the intermediate syndrome may required mechanical ventilation. Parathion in the causative agent in upto 75% of cases.

c) Delayed sequelae

In some cases (due to phosphorylation of a peripheral nervous tissue esterase) the acute cholinergic phase may be followed by a peripheral polyneuropathy involving the distal muscle of the extrimites. The rapid onset of a distal and symmetrical sensorimotor polyneuropathy (with weakness and ataxia) is diagonistic appearing 2-5 weeks after the exposure.[8]

Chronic neuropsychological functional impairment may also occure after an acute episode of organophophate poisoning and after long term occupational exposure.

d) Chronic organophosphate induced neuropsychiatric disorder (COPIND)

Follow-up studies of individuals who have been exposed to high level of organophophorous compound have shown that certain neurobehavioral change may develop in them, which have been termed together as COPIND.

These effect include drowsiness, confusion, lethargy, anxiety, emotional lability, depression fatigue, and irritability. Many of the studies of long term effect of high dose organophosphorus compound exposure, are limited by the non-specific nature of these symptoms and by the low sensitivity and specificity of the neurophychological scoring system.

Chronic neurophychiatric disorders like anxiety, depression, problem with memory and concentration have been described in workers expose to organophosphorus compound. In addition dystonic reaction, schizophrenia, cog-wheel rigidity, choreoathetosis and electroancephalo graphical change have been reported.

These extra pyramidal symptoms are thought to be due to the inhibition of the acetylcholinesterase in the human extrapyramidal area. Psychosis, delirium, aggression, hellucination and depression many also be seen during recovery from the cholinergic syndrome [2]

LABORATORY INVESTIGATION

The most widely used diagonistic tests for OP exposure are the estimation of plasma (PchE) cholinesterase and red blood cells AchE activity. The AchE of RBCs in the same as the are present at target synapses and can be assumed to mirror the effect of OPCs at target synapses. However, between the clinical state and PchE activity and even RBCs AchE activity, no-good correlation has been observed as the acute effects of anticholonesterase depend upon the inhibition of brain and neuromuscular junction AchE are large reserver of the exist at target organs. The usefulness of estimating the cholinesterase activity in OP poisoning is further limited by the variation in the enzyme activity which occurs in the individuals are there exists considerable inter individuals variation in the same population and can also be effected by disease states. Thus serial estimation of the enzyme may be more useful. More over

considerable variation exists between the method used for estimation and each method has its own range. The method includes electrometric, titrometric and calorimetric assays. Field and fast methods using papper strips are also available[2].

TREATMENT

a) Resuscitation:

Resuscitation is the essential for the oranophosphorus compound poisoning. Intravenous fluids, intubation ventilation and control of seizures by using benzodiazepines or barbiturates may be required, as well as gastric levage and oral activated charcoal [8]. The trial is given important information of the effectiveness of both sigle and multiple dose activated charcoal in the forms of poisoning commonly seen in rural asia [4]. Activated charcoal is available in some hospitals but is not routinely used in all, due to doubt about its effectiveness. Medical and nurshing personnel should wear protective clothing and gloves, when dealing with these patients to avoid contact with the pesticides [8].

Gastric levage with activated charcoal (50-100g) In 300 – 800 ml of water along with sorbitol (1-2g/kg) [11]. Animal are stimulated human overdoss studies have shown that a single dose of activated charcoal, if given soon after a poison is ingested, compound reduced the absorption of poison. The ability of charcoal to prevent absorption of poison falls of rapidly with one hour.

b) Anticholinergic agent (e.g atropine)

These agents reverse the muscarinic symptoms of bradycardia, and excessive gastro intestinal and respiratory secretion. While one study found that 7.5 mg of glycopoyrrolate in 200ml of 0.9% saline was just as effective as 15 mg of atropine in 100ml of 0.9 % saline (both of which were infused until the heart rate was > 60 and fasciculation were absent) in the management of organophosphate poisoning. [8].

Atropine is usually regarded as the drug of excessive secrection are controlled; the pulse rate is greater than 80 beats per minutes and the pupils are dilated up to 10-30 mg of atropine may be required initially, there after 1-5mg may be required every 30 minutes for manifestation [8].

Other dose suggest that atropine sulphate 0.4 – 2 mg i.v. or i.m in adults (0.05 mg/kg in children below 12 years) the mainstay of treatment. It is repeated every 15 min until full atropinization. The bible of pharmacology mentions “Atropine is virtually without effect against peripheral neuromascular compromise which can be reversed by PAM. [12]. Acute poisoning with organophosphorus (op) pesticide frequently cause ill health and death all over the world the treatment of OP poisoning is primarily aimed at reversing the effect of the compound by administration of atropine [13].

Cythioate a systemic organophosphorus compound has progressively increased the acetylcholine (Ach) content (16.54 to 118.04%) and decreased the cholinesterase (chE) activity (23.0 to 98.4%) of rat brain with 3 to 100 mg/kg. given by i.p. route. Atropine protected the rates from the toxic effects of cythioate by blocking the action of Ach at the receptor without affecting Ach content and chE activity. [14]. The study also recomended the muscarinic effects of excess acetycholine consequent to the inactivation of the acetylcholinesterase are countered by atropine therapy. [15]. Otherway in one trial mortality was shown only 9% (4/43) in the atropine treatment. [3].

Anticholinetgics are still the mainstay of treatment and should be started as soon as the airway has been secured. Atropin can be started initially as a 2-mg iv bolus and the at doses of 2-5 mg iv bolus every 5-15 min until atropinitation is achieved. The dose in children is 0.05 mg/kg iv with a maintenance dose ranging from 0.02 to 0.05 mg/kg. [20].

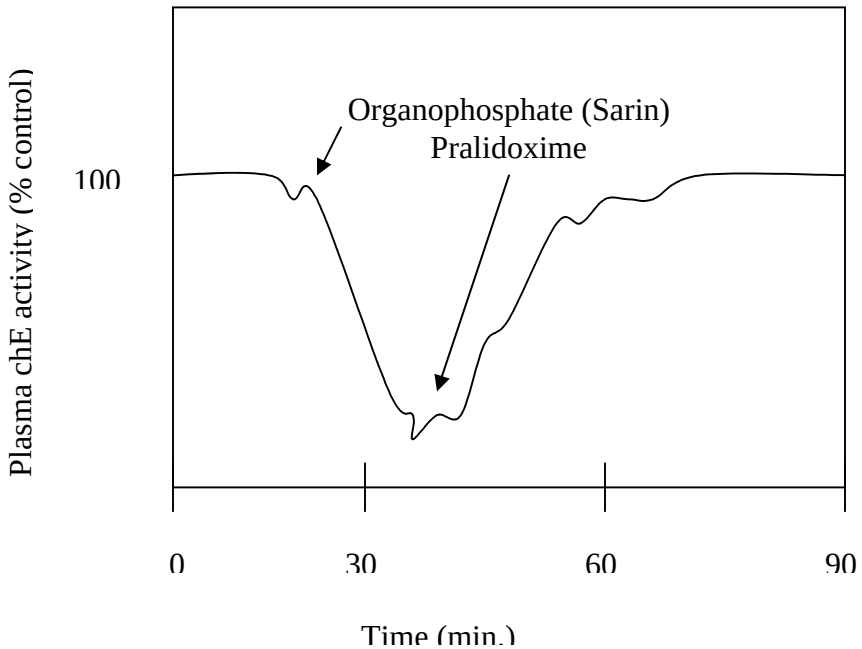
c) Chlonergic reactivator (oxime derivative)

Cholinergic reactivator or oxime derivatives have a high affinity oxime group for the phosphoryl group bond to the esteric site forming a soluble complex, thereby setting the esteric site free and reactivation of enzyme [11].

Several bis-quatenary oxime are even more potent as reactivators for insecticides and nerve gas poisoning. HI- 6 are use as antidote in Europe.[5]. The oxime are particularty effective in reversing the neuromuscular paralysis, due to OPS where the atropine is not effective[6].

Pralidoxm (Pyridine -2 aldoxime chloride, 2- PAM)

Pralidoxime is the oxime most often most often used world wide [3] pralidoxime reactivates the enzyme by bringing an oxime group into close proximity with the phosphorylated esteratic side. This group from the serin-OH of the enzyme. The effectiveness of pralidoxime in reactivating plasma cholinesterase activity in a poisoned syject in shown.



The main drawback to its use as an antidote to organophosphate poisoning is that within a few hours the phosphorylated enzyme undergoes a change that renders it no longer susceptible to reactivation. So pralidoxime must be given early in order to work. Pralidoxime does not cross the blood brain barrier (BBB) [16]

In another random trail shows no mortality in the group treated with 2 PAM in eight patient [3] . In other random trial the high dose regimen was associated with a significantly higher risk of death in 110 adult patient (29% v/s 5% or 7.1). the author concluded that 2-PAM has no role in the management of patients with organophosphorus poisoning and does more harm than good.[3]. Current WHO guidelines recommend giving a 30 mg/kg loading dose of pralidoxime over 10-20 minutes followed by a continuous infusion of 8-10 mg/kg in until clinical recovery or seven days have elapsed which ever is later[3].

One study is done in an hospital in chennai the effectiveness of high dose P_2 AM in OP poisoning .the poisoning are classified as based on serum cholinesterase(SchE) activity mild (20-50%), moderate(10-20%) and severe(<10%).all patients under went gastric levage high dose 2-PAM > 4,gm/day [17].

COMPARATIVE DATA OF SURVIVAL ON 2-PAM(HIGH DOSE VS LOW DOSE)

	Total	High dose 2-PAM >4gm/day	Low dose 2-PAM <=4gm/day
Patient (No)	58	43	15
Survived	44	36(83.7%)	8(53.3%)
Died	14	7(16.3%)	7(46.7%)
Ventilator Support	22	15	7
Survived	8	8(53%)	0
Dead	14	7	7

Some other studies suggest that pralidoxime is more effective in treating the nicotinic symptoms (muscular fasciculation and paralysis) of certain organophosphate poisoning such as – dimethoate , methyl diazinon .It is only effective if it is administered with 24 hours as the organophosphate cholinesterase bond becomes relatively permanent after 48-72 hours . To reach plasma concentration of 4 mg/L should be administered as a 1gm i.v bolus dose by an infusion of 0.5 gm/hr (12gm/day) and also higher dose have been used (e.g -30 mg/kg followed by 8 mg/kg /hr , in children 25-50 mg/kg continuous infusin of 10-20 mg/kg/hr).[8].

In another study , where effectiveness of oximes was studied in 58 patients of OP poisoning , the cases were classified under nimbus criteria into mild , moderate and severe and effectiveness of high dose of PAM(> 4 gm/day) was compared to with low dose (<4 gm/day), authors concluded that the high dose PAM has valuable role in severe OP poisoning and along with good ventilatory support and aggressive atropinization, mortality could be definitely reduced and recommended that high dose PAM should be administered without delay in patients with clinically moderate and severe OP poisoning .[12].

d) Other Drugs

Tenocyclidine –TCP and its adamantine derivative TAMORF

Tenocyclidine – TCP showing a broad spectrum of pharmacological activity as a antidotal effect in organophosphorus compounds poisoning . authors are investigated in vitro interactions of TCP and its adamantine derivative – TAMORF with human erythrocyte acetylcholinesterase (AchE). The tested compound were found to be weak inhibitors of AchE for TCP and for TAMORF without reactivating the protective effect on AchE inhibited by soman compound shown low cytotoxicity.[20].

HI-6

The in vitro dissolution of the new organo phosphorus antidote HI-6 has been investigated by using the rotating disctechnique. There the enthalpy of activation of the dissolution rate indicates that the ability of HI-6 to dissolve in very high.[18]

Benzodiazepines

However, no evidence exists that benzodiazepines are effective at reducing the mordibity or modality in humans .No good quality clinical research has been performed on these antidote in humans.[1]

Replacement of blood volume has been used successfully and plasmapheresis (with fresh frozen plasma replacement) may also be use. In the experimental model, adenosine receptor agonists (5'N-ethylcarboxamido – adenosine and N6 – cyclopentyle adenosine) if given within a minutes of organophosphorus poisoning, prevent or reduce salivation, seizures and respiratory distress and improve survival [8]. Magnesium sulphate has also been used to control tachycardia, ventricular arrythmias and muscle fasciculation. Pretreatment of mice with clonidine (0.1 – 1 mg/kg) resulted in protection against toxic manifestation.

DISCUSSION

If activated charcoal can proven to be effective then it should be an extremely valuable theropy since if is widely available in the developing world. Since the gretest benefits has been seen when charcoal is given within 15 mins of poisoning its be effective [4].

Human stimulated overdose studies indicate that around 30% of tablets can washed out if gastric lavage is initiated within 15 mins. of poisoning. However the yield from liquid poisons such as pesticides is likely to be even less since liquid pass out of the stomach into the small bowel quicker than the tablets on which most studies have been performed.

The clinical benefits of oximes in OP poisoning is not clear, being limited by the type of OP, poison load, time to start therapy and dose of oximes. There are four published RCTs of pralidoxime in 266 patients with acute OP poisoning. De. Silva et al. compared atropine for the treatment of OP poisoning v/s atropine and pralidoxime in a controlled trial.

No benefit from pralidoxime was found, however the dose of praliedoxime given was small considering the available data. Considering the available data, it seems that about 500 mg/hr. should be infused to maintain adequate therapeutic concentration of pralidoxime (about 4 mg/l) in a severely poisoned adult. A prospective study in compared atropine, obidoxime + adtropine and pralidoxime + atropine for OP pesticide poisoning;. There were no death in the pralidoxime group and doses of pralidoxime used were welll tolerated (8 mg/ kg followed, by 2 mg/kg/hr). a high rate of hepatotoxicity was observed in the obidoxime group [3].

The study tried to evaluvate lethality in OP poisoning and shows mean pseudocholin esterase level was significantly less in those who died compared to survivors. So there are controversies about the correlation between plasma cholinesterase activity and the severity of organophsphorus poisoning. Lethality is an important clinical variable for both medical and psychiatric evaluation and management. Period between ingestion of poison and initiation of specific treatment may help to decrease the chance of death in some [7].

The diagonosis of OP poisoning is based essential on a clinical assessment, followed by laboratory examination. As in case one identified initially as brainstem stroke. How ever neurological syndromes associated with a OPs are well known. However in another case did not have severe poisoning on admission but needed artificial ventilation [19].

Despite the use of traditional therapeutic regimen of adtropine and oxime, the morbidity and imortality associated with OP poisoning has not decreased despite major advance in critical care/ the need to develop more effective regimes has to be recognized and collaborative work between technologically advanced countried. Where the incidence of poisoning is low and developing countries where poisoning is very common [15].

GLOBAL FAILURE OF ANTIDOTE DEVELOPMENT

The organophosphate are of world wide interest. Their toxicity is well understood. Current treatment for organophosphate poisoning is – Atropine, oxime derivatives (pralidoxime, obidoxime), benzodiazepines, charcoal.

Newer more effective antidotes are needed. The currently recommended antidotes are the tip of a treatpentic iceberg that could be mobilized. Animal studies have shown many beneficial compounds yet no new treatment has reached the beside in the past 30 years and no new treatment is in clinical trials. Potential new treatment identified in animal models include organophosphate hydrolases, which breack down organophosphate and reactivation of acetyl cholinesterase, reversible anticholinesterase and which reduce re-inhibition of acetyl cholinesterase. Information on these potential treatment has been available for years, but neither the military nor the pharmaceutical industry has attempted to test them or develop new drug.

Much of the research on treatment for nerve gas poisoning was concentrated on prophylaxis. However, in all recent reported exposure treatment, and usually diagnosis of nerve gas poisoning has been delayed. Thus the situation is similar to the faced with pesticide poisoning. Ample opportunity exists for clinical trails because at least two million people are poison by organophosphate pesticides each year in the world. The problem are compound by the conditions in which most patient with pesticide poisoning are seen in hospitals without sufficient doctors, nurses, ventilators, or antidote to offer a good service.

CONCLUSION

Thus the use of atropine and oximes derivatives in OP poisoning remains conflicting and controversial. From the various randomized and controlled trails and also from hospital treatment documents shows they have no effect in moderate and severe poisoning and do more harm than good. Pralidoxime is more effective in organophosphorus poisoning. Atropine is effective in some cases but its also depended on the toxicity of the substance and the duration of toxicity.

The other new drug such as benzodizepines are effective only few times for some special condition. No new drug are found which is more effective in OP poisoning. Assessment of severity and lethality of the attempts were able to differentiate the attemptes from the committers in most cases. However restricting availability of OP compounds and banning more toxic ones to prevent suicidal death.

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