“Serum creatine phosphokinase a prognostic indicator in Organophosphorus compound poisoning”

By

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Dissertation submitted to

Tamil Nadu Dr M.G.R Medical University

in partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

Under the guidance of

Dr.R.Anbalagan M.D.,

H.O.D and Professor

DEPARTMENT OF MEDICINE

G.M.K.MEDICAL COLLEGE

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Serum creatine phosphokinase a prognostic indicator in Organophosphorus compound poisoning"** is a bonafide and genuine research work carried out by me under the guidance of Dr.R.Anbalagan M.D, Professor, G.M.K.Medical College, Salem, Tamil Nadu

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ENDORSEMENT BY THE HEAD OF DEPARTMENT AND DEAN OF THE INSTITUTION

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Date:

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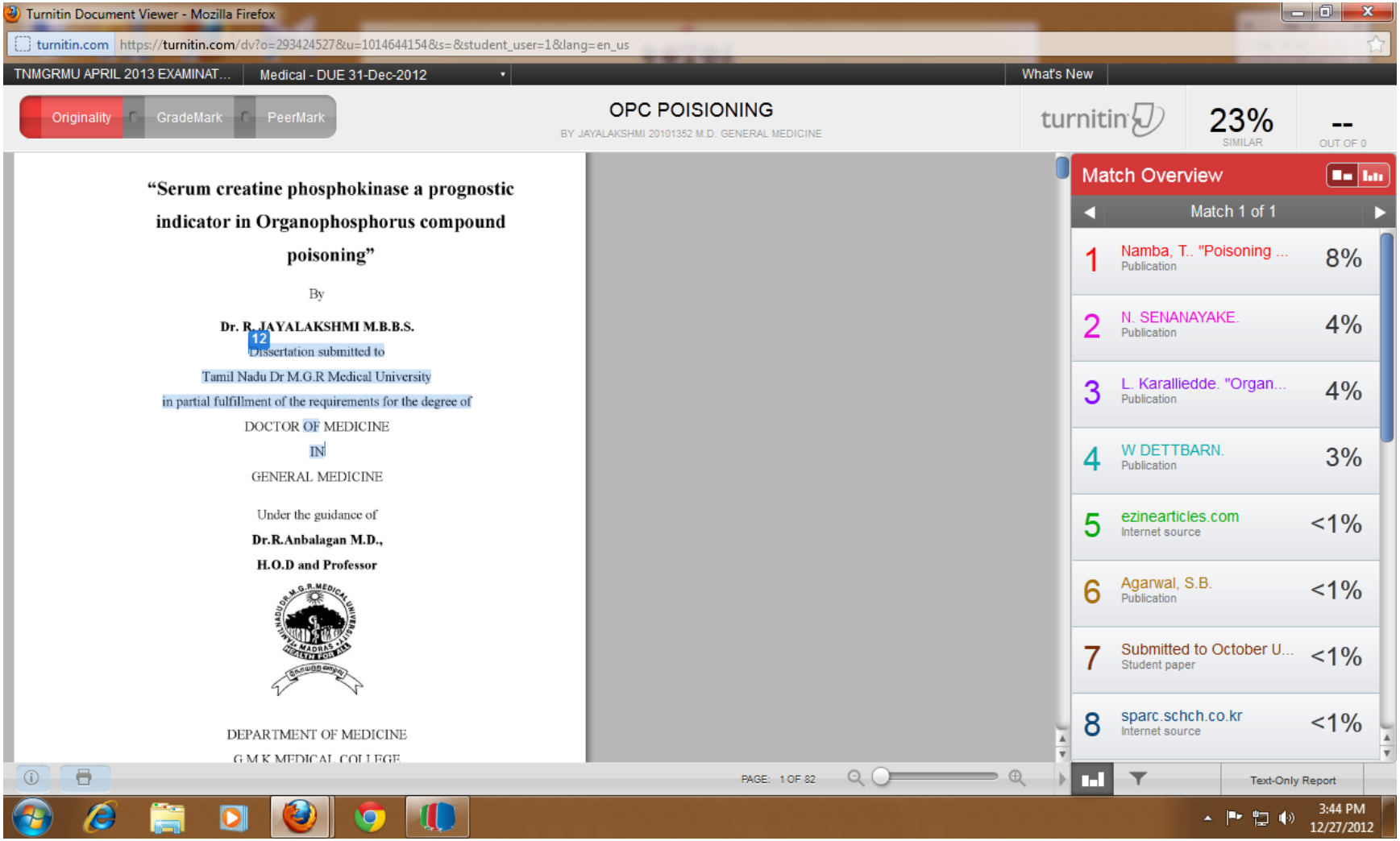
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LIST OF ABBREVITATION USED

AchE -- Acetyl cholinesterase

BchE -- Butryl cholinesterase

CNS -- Central nervous system

CPK -- Creatine Phosphokinase

DDT -- Dichloro diethyl tri chloro ethane.

EchE -- Erythrocyte Cholinesterase

IMS -- Intermediate syndrome

OPC -- Organophosphate compund

PAM -- Pralidoxime

PChe -- Psedocholinesterase

POP scale -- Peradeniya Organophosphorus poisoning scale

TOCP -- Triortho cresylphosphate

ABSTRACT

Background and Objectives: Organophosphorus compound poisoning is the commonest medico toxic emergency in India, because of its easy availability. Respiratory failure is the most common complication of OPC poisoning leading to death. Early recognition and prompt ventilatory support may improve survival. Hence this study was undertaken to assess the severity of organophosphorus compound poisoning both clinically by using Peradeniya scoring and by estimating serum creatine phosphokinase level.

Methods: A prospective study was conducted on 50 patients admitted at emergency ward of GMKMCH, Salem within 6hrs of OPC intoxication. Detailed history and clinical examination were done. Patients were evaluated for Peradeniya OPC poisoning scale and serum CPK was taken at the time of admission.

Results: Age group ranged from 17-67 years. Majority of the patients were in the age group of 21-30 years. 66% of patients were males and 34% were females. Most common poison encountered is monocrotophos. Common signs were miosis 88%, difficulty in breathing 76%.According to POP scale 52% were in mild grade, 40% were in moderate grade and 8% were in severe grade. Study revealed significant elevation of serum CPK in moderate to severe grade of POP scale.

Interpretation: Serum CPK more than 500 IU/L predicts high degree of suspicion of subsequent respiratory failure. Peradeniya scoring more than 5 provide high degree of suspicion of subsequent respiratory failure.

INTRODUCTON

Organophosphorus compounds are becoming one of the most common causes of poisoning.

OPC were first synthesized by Schrader during the Second world war. OPC were first used as an agricultural insecticide and later as potential chemical warfare agents. Organophosphorus compounds are used as pesticides, herbicides, and chemical warfare agents in the form of nerve gases.

WHO has estimated approximately 3 million pesticide poisoning occur every year and cause more than 220000 deaths. India is a predominantly an agrarian country with about 60 – 80 % of rural population. So, pesticide is an easy access for the suicidal purpose.

Organophosphorus compounds act by irreversibly inhibiting the enzyme cholinesterase, resulting in accumulation of acetylcholine at synapse and myoneural junction leading to cholinergic over activity.

Respiratory failure is the most common complication leading to death.Early recognition and prompt ventilatory support may improve survival.

Peradeniya OP poisoning scale has not been studied much in Indian scenario. It is a simple effective scale to determine the need for ventilatory support early on the course. Serum cpk is found elevated in op poisoning .it can be used as a biomarker in predicting the prognosis. Hence this study was undertaken to assess the severity OP poisoning using both Peradeniya scoring and by estimating serum CPK levels.

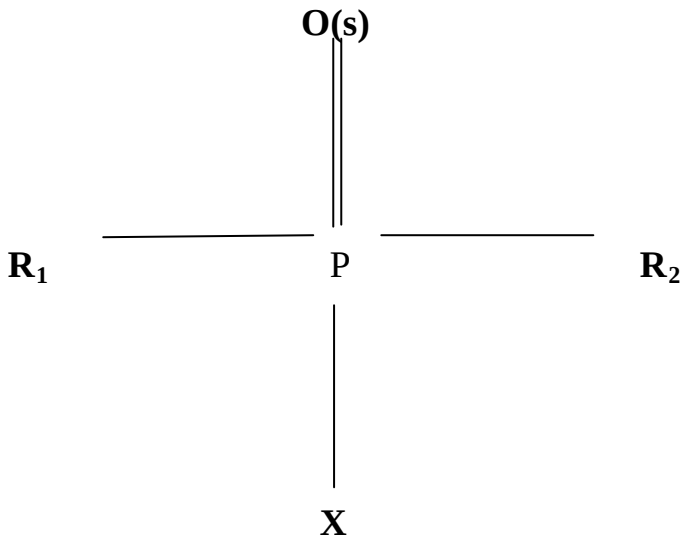
AIMS OF STUDY

To correlate serum CPK levels and clinical parameters (Peradeniya op poisoning scale) to preditct the need for ventilatory support.

Review of literature

The synthesis of a highly potent compound tetraethyl pyrophosphate(TEPP) by phillipe de clerment in 1854 gave him the honour of conceiving the idea of organophosphorous compound[5].In 1932 Lange and kreuger, discovered the biological activity of OP esters producing a strong cholinergic effect in human beings. In 1936-1937, Gerhard Schrader[5], German scientist also noticed similar effects. This made Schrader to synthesis around 2000 compounds like parathion, tabun, sarin etc. The word “cholinesterase” was introduced by Stedman and his co-workers in 1932. Extensive research lead to find that there are two main type of cholinesterase. One is called acetyl cholinesterase or true cholinesterase. The other one is called non specific cholinesterase or pseudo cholinesterase.

The structure of OP compound is



The central compound is phosphorous atom with a double bond to either oxygen (P=O) or sulfur (P=S) and three side chains, one x group,R1 and R2 may be alkyl, alkoxy, amido mercapten or other groups. The effectiveness as insecticides and the lack of persistence in the environment made the organophosphorous compound a great popularity.

Due to their unstable structure these compounds disintegrate into harmless radicals within days of application. The OP compounds are used as insecticides in agriculture; some formulations are used in veterinary and human medicine. Some compounds are used as lubricants, plasticizers and flame retardens. Usage of some of these compounds as very potent agents of warfare is of global significance.

Anatomy and Physiology of Autonomic Nervous System.

The autonomic nervous system controls the visceral function of the body. Autonomic nervous system centers are located in the hypothalamus, brainstem and spinalcord. Anatomicaly this system is divided into sympathetic and parasympathetic system. Under sympathetic nervous system preganglionic fibers exits from spinalcord between first thoracic and second lumbar segments. A parasympathetic fiber leaves CNS through cranial nerves III, VII, IX, X and second to fourth sacral spinal nerves. Acetylcholine is a neurotransmitter found throughout the central nervous system, the sympathetic and Parasympathetic autonomic ganglia, postganglionic parasympathetic nervous system, most sympathetic glands and at the skeletal muscle motor endplate.

Acetylcholine (Ach) is first synthesized by BAYER in 1867. The Ach is synthesized in the motor nerve terminal from choline and co-enzyme A (CoA) by a process facilitated by the enzyme choline acetyl transferase.

Choline+Acetyl-CoA ⟶ Acetycholine

(Choline Acetyl Transferase)

Acetylcholine: 20% of Ach is Present as free Ach in axoplasm and 80% is contained within the vesicles.

When a nerve impulse arrives at the nerve terminal causing release of acetylcholine into the synaptic space. Ach binds to and activates muscarinic and nicotinic receptors. Duration of Ach is curtailed as it is hydrolysed by the enzyme acetylcholinesterase.

Acetyl choline ⟶ Acetate ion + choline

(AChE)

The choline is reabsorbed actively into the neural terminal and reused in forming new acetylcholine. These events takes less than 5-10 milliseconds and within about 20 seconds new vesicles will be formed and within another few seconds acetylcholine is transported into the interior of these vesicles and they are ready for a new cycle of acetylcholinesterase. The actions of acetylcholine in the body depend on the receptors involved and the site.

Activation of the muscarinic receptors stimulates or inhibits cellular function through G protein at visceral smooth muscle, cardiac

muscle and secretory glands. Nicotinic receptors are Na channels at post synaptic membrane in autonomic ganglia and at skeletal muscle motor endplates. The enzyme acetyl cholinesterase (AchE) regulates the activity of acetylcholine within the synaptic cleft. There are two types of cholinesterase in human body. One is psedocholinesterase and other is true cholinesterase.

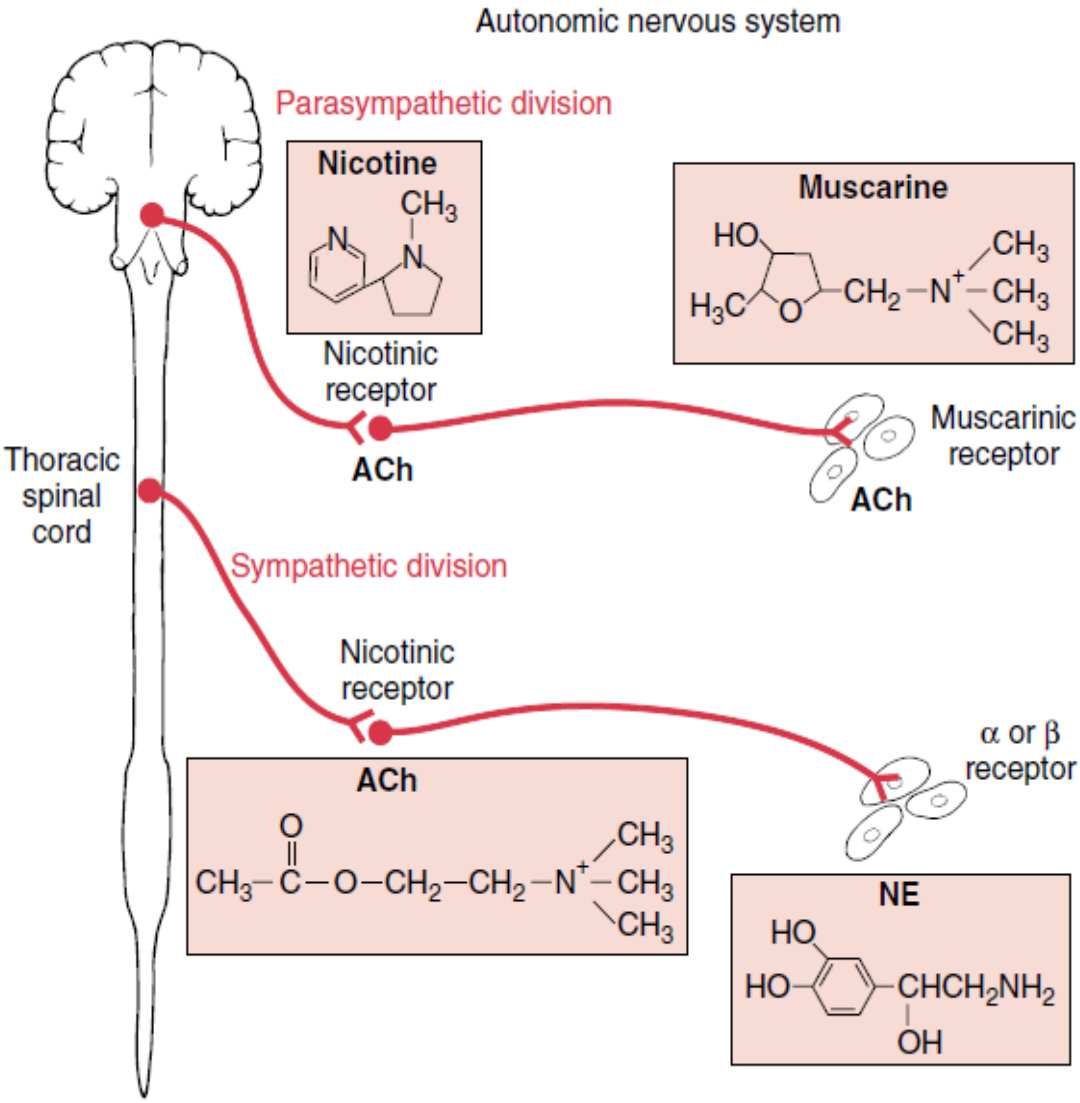
True Cholinesterase- (RBC Cholinesterase)

It is found in nervous tissue, erythrocytes, lung, spleen and greymatter. It is decreased in pernicious anemia and after antimalarial therapy. Ach is inactivated by combination with two sites on the enzyme RBC cholinesterase anionic site and esteratic site.

Plasma cholinesterase (pseudocholinesterase)

It is found in plasma, pancreas, liver and intestinal mucosa.

NEUROCHEMISTRY OF AUTONOMIC PATH



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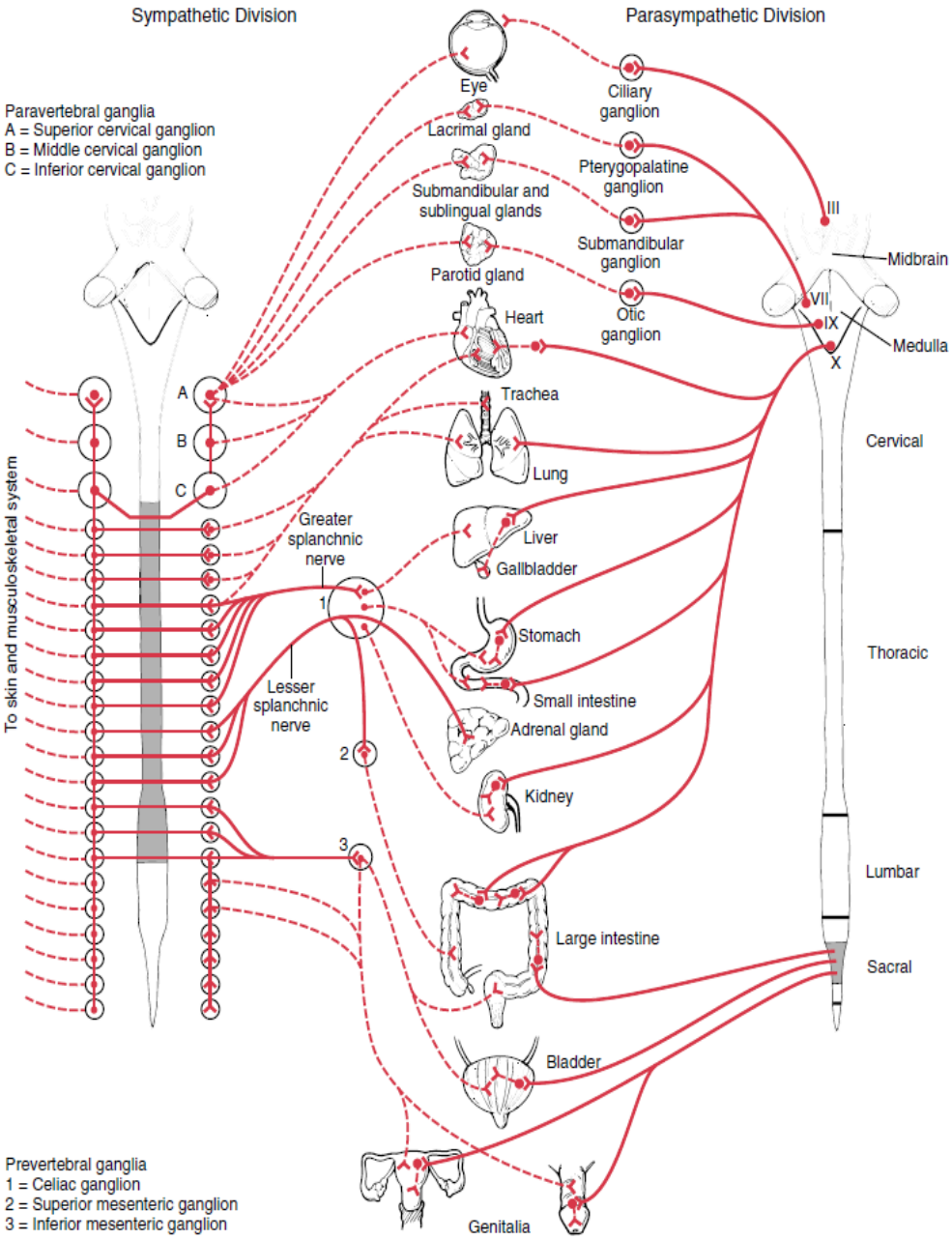


Plasma cholinesterase deficiency could be due to physiological variation , disease, iatrogenic causes and genetic defects.

1) Physiological variations:-

a. Age:

- A newborn has about 50% of normal PchE activity.
- PchE activity reaches normal level at puberty.
- In old age (75-80years) the activity is 75% of normal.

b. During pregnancy PchE activity decreases 20 -30%.

2. Diseases

a. Liver disease:

- PchE activity decreases upto 50% in acute hepatitis, cirrhosis and liver metastasis.

b. Renal disease:

- PchE activity decreases to 30% normal in renal disease (uremia).

3. Drugs

- Organophosphorous and organocarbamate compounds.
- Anticancer drugs.
- Ecothiopate eye drops.
- Bombuteral .

4. Genetic.

Patients with atypical PchE have low PchE activity.

Classification of Organophosphorous Compounds

Organophosphorus Compounds are classified as

I. By chemical structure:

A) Alkyl phosphates:

1. HETP (Hexaethyl tetra phosphate)
2. TEPP (tetraethyl pyrophosphate) tetron,fosvex
3. OMPA (octamethyl pyrophoramide) schardan

4. Dimefox (bis[dimethyl amino] flurophosphine oxide)
5. Isopestox (bis[isopropylamino] flurophosphine oxide)pestox
6. Malathion(5,[1,2dicarbethoxyethyl]0,o dimethyl dithiophosphate)
7. Sulfoteppa(tetra ethyl 0,dithiopyrophosphate)-dithione Asp-47
8. Systox,demeton(0,0 diethyl 10-2 ethylmercapto ethyl thionophosphate)
9. Dipterex(0,0 dimethyl 2-2-2 trichloro hydroxyl ethyl phosphate-tug orbait.

B) Aryl phosphate

1) Paroxon
2) Parathion
3) EPN-o, ethyl-o-p nitropheyyl benzene thionophosphate,EPN 300
4) Methylparathiono, o-dimethyl o-p nitrophenyl thiophosphate

II) By Toxicity:

Highly toxic(<D_{50}<50 mg/kg)

1. Azinophos-methyl
2. Bomyl
3. Carbophenthion
4. Chlorfenvinphos
5. Chlormephos
6. Coumaphos
7. Cyanofenphos
8. Demeton
9. Dialifor
10. Dicrotophos
11. Disulfoton
12. EPN
13. Famphur

14. Phenamiphos

15. Fenophos phan

16. Isophenfos

17. Isofluorphate

18. Mephosfolan

19. Methmidophos

20. Methidathion

21. Mevinphos

22. Monocrotophos

23. Parathion-ethyl

24. Parathion methyl

25. Phovate

26. Phostolan

27. Phosphomidan

28. Prothoate

29. Sulfotep

30. Tetraethylpyrophosphate(TEPP)

Moderate Toxicity (D_{50}=50-1000mg/kg)

1) Acephate

2) Bensulide

3) Chloropyrofos

4) Crotoxyphos

5) Cythioate

6) DEF

7) Deneton-s-methyl

8) Diazinon

9) Dichlorvos

10) Dimethoate

11) Edifenphos

12) Ethion

13) Ethoprop

14) Fenitrothion

15) Fenthion

16) IPB

17) Leptophos

18) Merphos

19) Naled

20) Phosalone

21) Phosmet

22) Pirimiphos-ethyl

23) Profenofos

24) Propetaamphos

25) Pyrazophos

26) Quinalphos

27) Sulprofos

28) Thiometon

29) Triazophos

30) Tribufos

31) Trichlorfon

Low Toxicity(D_{50}=>1000mg/kg)

1) Bromophos

2) Etrimfos

3) Iodofenphos

4) Malathion

5) Phoxim

6) Prophylthiopyrophosphate

7) Temephos

8) Tetrachlorrinphos.

PHARMACOKINETICS

Most of the OP insecticides are rapidly absorbed by all routes dermal, respiratory, gastrointestinal and conjunctival. Plasma half life after single administration ranges from a few minutes to a few hours depending on the compound and the route of administration. Most of the op compounds are excreted almost entirely as hydrolysed products in the urine. 80-90% occurs within 48 hrs. A small proportion and their active forms are eliminated unchanged in the urine. Compounds like fenthion , fenithrotion are known to persist in the body for longer periods.

Mechanism of Action

OP compounds inhibit enzyme acetyl cholinesterase. The mechanism of inhibition of the enzyme is by reacting with the esteratic site on the acetyl cholinesterase molecule. The bond formed between phosphorus atom and the esteratic site of enzyme is stable and requires hours to weeks to reverse depending on the type of OP compounds. Phosphorylated enzyme is inhibited because of occupation of its active site. It is incapable of carrying out its normal function of hydrolyzing acetylcholine. The effect of the OP poisoning is therefore the result of continuing increased production of acetylcholine at the neuromuscular junction, resulting in depolorisation block.

This phosphorylated enzyme can undergo spontaneous hydrolysis or dealkylation. Due to spontaneous hydrolysis active enzyme cholinesterase is released and this is called reactivation. The phosphorylated enzyme can also undergo dealkylation. Once this occurs, reactivation is impossible. This process is called ageing[1]. Once ageing occurs recovery of cholinesterase activity depends on synthesis of new enzyme by liver which may take days or weeks.

Hence the three independent reactions determine the speed of onset and severity of poisoning i.e

1. Phosphorylation of cholinesterase by organophosphorus compounds.
2. Reactivation.
3. Ageing.

Alkylphosphates (direct inhibitors) like malathion ,and arylphosphates(in direct inhibitors) like parathion. Poisoning by direct inhibitors of acetyl cholinesterase presents as an acute cholinergic crisis, they do not develop late type muscular weakness. Response to atropine is rapid. Indirect inhibitors do not develop signs of cholinergic crisis but show persistent fasciculations along with sudden increase in atropine

requirement. The incidence of development of late type of muscle weakness is high.

In acute poisoning clinical manifestations occur after more than 50% of serum cholinesterase is inhibited and severity of manifestations correlates with the degree of inhibition of serum cholinesterase activity.

- Mild poisoning - cholinesterase level reduces to 20-50%
- Moderate poisoning - cholinesterase level reduces to 10-20%
- Severe poisoning - cholinesterase level reduces to lessthan10%.

The correlation between the degree of enzyme inhibition and the severity of manifestations is pertinent only in the initial stage of acute poisoning ; inhibition is greater in repeated exposures[2]. Inhibition remains even after recovery from symptoms.

CLINICAL MANIFESTATIONS[16, 19, 20, 21, 24]

The clinical manifestations 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[16].

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[16].

LOCAL EFFECTS:

GI symptoms appear first before the onset of systemic symptoms. In inhalation typically exhibit 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.[18, 19, 20, 21, 22, 23, 24]

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

1) Muscurinic(all postganglionic nerve endings)

2) Nicotinic (Autonomic ganglia and skeletal muscle end plate)

3)CNS manifestations(synapses in CNS)

Each is summarized as follows.

1) Muscuranic manifestation:

Bronchial tree	Tightness in chest, wheezing, dyspnoea, increased bronchial secretions,cough,pulmonary edema, cyanosis.
Gastro intestinal system	Nausea, vomiting, abdominal tightness, cramps, diarrhea, tenesmus, fecal incontinence.
Sweat glands	Increased sweating
Salivary glands	Increased salivation
Lacrimal glands	Increased secretions
Cardiovascular system	Bradycardia, hypotension.
Pupils	Miosis
Ciliary body	Blurring of vision
Bladder	Frequency,urinary incontinence.

2)Nicotinic manifestations:

Striated muscle	Muscle twitching, cramps, fasciculation,respiratory muscle weakness.
Sympathetic ganglia	Pallor, tachycardia,hypertension.

3) Central nervous system manifestations:

Anxiety,restlessness, giddiness, emotional liability,slurred speech, ataxia,seizure, 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.

1.The combination of symptoms may vary[13, 14, 18, 19, 21, 22, 23]

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

2. The intermediate syndrome (IMS)[12, 24]

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 11 paralysis first described by Wadia et al. In 1974 and later christened as “Intermediate syndrome(IMS)” by Senanayake,Karalliedde L. The syndrome is of Acute onset, seen within 24-96 hrs(1-4days) after poisoing,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.The muscles innervated by motor cranial nerves III,VII and X are affected in different combinations. These patients were conscious and showed marked anxiety,sweating and restlessness caused by progressive hypoxia. These patients try to situp in bed,having bathed in sweat, with accessory muscles of respiration in action. The neck muscle weakness was a constant feature. Patients were unable to raise head above the pillows. Weakness of shoulder abduction and hip flexion was also noted.

However normal strength in the distal muscle gives a false impression that the limbs are spared. Tendon reflexes are diminished or in most patients. There is no sensory impairment.

Complete recovery occurs within 4-18 days if adequate ventilator support is given. But altered function at neuromuscular junction may persist upto 2 yrs after its occurrence.

The syndrome carries great mortality if not recognized in time and treated. The agents commonly responsible are fenthion, monochrotophos and Dimethoate. Respiratory insufficiency develops over 6 hrs approximately. Initially patient uses accessory muscles of ventilation. There is increase in ventilator rate, sweating, restlessness and later cyanosis if not recognized patient soon becomes unconscious and death follows. A consensus from literature search appears that IMS may result from inadequate therapy with oximes.

IMS is likely to result from post synaptic neuromuscular dysfunction.

The symptom complex begins at a time when the cholinesterase function is very low and the OP compounds is still detectable in the body.

As blood levels of OPC's fall and OPC's tissue redistribution occurs the motor end plates may be rechallenged by the cholinesterase inhibitor in the presence of inadequate circulatory oximes.

3. Delayed polyneuropathy.[13, 19, 21]

Though uncommon in India the neuropathy develops following a latent period of 2-4 weeks after the cholinergic crisis. The main clinical features are weaknessof distal muscles of feet and hand. The weakness is preceded by pain and parasthesia of limbs. Wasting of distal muscles of particularly small muscle of the hand and those of anterior and peroneal compartments of the leg is a 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. Several out breaks of OP induced delayed polyneuropathy have occurred in various countries where the poison was traced in most instances to be accidental contamination or adultration of cooking oils with mineral oils. In 1930’s more than 50000 US citizens became paralysed after drinking Jamica ginger contaminated with TOCP.

OTHER EFFECTS OF OP POISOING:

Cardiovascular system[32,33,34,35]

Tachycardia and increased blood pressure occurs in initial stage and Bradycardia and low blood pressure in the later stage. Commonest effect observed was tachycardia. Late onset bradycardia is attributed to direct action on myocardium by organophosphorus compound. Hypertension occurs due to the combined effect of vasoconstriction from cholinergic stimulation of sympathetic ganglia and noradrenaline release from adrenal medulla. Hypotension may also occur due to muscarinic action or blocking of ganglia by hyperpolarisation. Cardiac manifestations including atrial fibrillation, conduction block and ventricular fibrillation and further usually occur in terminal stages.

The cardiovascular actions of anticholinesterase are extremely complex, as they reflect at any moment the algebraic sum of the excitatory and inhibitory actions of the accumulated endogenous acetyl choline at several levels of the innervations of the heart and blood vessels. ECG changes seen were sinus bradicardia, right axis deviation,AV Block, ST segment depression in all leads and T wave inversion. A combination of metabolic and electrolyte derangements cause myocardial injury, autonomic dysfunction and asyncronus

repolarisation producing variable QRS morphology and varying RR interval.

Sinus tachycardia could be due to effect of cholinesterase inhibition, acting either directly on the myocardium and conducting tissues or through neurogenic mechanisms. Right axis deviation could be related to pulmonary oedema. ST segment and T wave inversion has been suggested to be due to potassium shift or disturbance of other ions transport across membrane.

2. Respiratory system[37, 38]

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, Bronchoconstiction leading to pulmonary oedema and chest tightness. On other hand nicotinic action produce intercostals muscle paralysis and respiratory muscle weakness leading to respiratory paralysis.

Direct action on respiratory center reduces respiratory rate. Combined effects of all these factors results in respiratory failure.

During clinical course it was observed by M.L.Chhabra et al,

That some cases apparently recover in respect of level of consciousness and pulmonary oedema, to fall back into a second and often a terminal phase of acute pulmonary oedema . Inspite of the fact that atropine is continued in optimum doses. Limaye et al suggested that diazinon exerts a toxic action on myocardium leading to toxic myocarditis and explained this as the genesis of the rebound or second phase of pulmonary oedema .

3. Altered immunity to infection:

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

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

5. Effects on reproduction:

Following organophosphorus poisoning in females abortions were being reported.

6.Effects on temperature regulation:

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 :

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

8. Effects on other systems:

Eyes: myopia and pigmentary degeneration of retina.

Joints:arthritis, cerebellar ataxia.

Interference with mitochondrial oxidative metabolism.

9. Changes in metabolism and endocrine activity :

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

excessive blood glucose. Changes in diurnal pattern of plasma adrenocorticotrophic hormone have been reported. Nicotinic receptors also function in brain pathways that increase the release of several pituitary hormones,including vasopressin, adrenocorticotrophic hormone and prolactin. Significant decreases in serum concentration of thyroxin and tri-iodothyroxine and an increased secretion of thyroid stimulating hormone were observed after OP poisoning. Hyper amylasaemia and acute pancreatitis have been reported.

Grading of severity of organophosphorus poisoning:

There are several system of grading of severity in acute organophosphorus poisoning. Recently Senanayake N.(1993) proposed Paradeniaya Organophosphorus Poisoning (POP) scale for grading the severity,which is based on five cardinal manifestations of organophosphorus poisoning as given below in the table

S.NO	PARAMETER	SCORE
1.	Miosis - Pupil size >2mm -Pupil size ≤2mm -Pupils pin point	 0 1 2
2.	Fasciculations -None -Present but not generalized or continous -Generalized and continous with central cyanosis	 0 1 2
3.	Respiration -Respiratory rate ≤20/min -Respiratory rate >20/min -Respiratory rate >20/min with central cyanosis	 0 1 2
4.	Bradycardia -Pulse rate >60/min -Pulse rate 41-60/min -Pulse rate ≤ 40/min	0 1 2
5.	Level of consciousness -Conscious and rational -Impaired, responds to verbal commands -Impaired, no responds to verbal commands(if convulsion present add 1)	0 1 2
	TOTAL	11

POP scale uses only cardinal clinical manifestations where each sign is given a score according to the severity and all are added up to assess the severity on a 1-11 scale.

Peradeniya organophosphorus poisoning (POP) scale grading.

Score	Grade
<4	Mild
4-7	Moderate
>7	Severe.

The revised grading for organophosphorus poisoning by Bardin et al (1990) to assess the severity was proposed. This grading includes the history of intake exposure to organophosphorus, attempted suicide, clinical signs and makes use of investigations(decreased PaO2 and abnormal chest roentgenogram) in early assessment of respiratory failure.

Revised grading for organophosphorus poisoning :

Grade	Criteria
Mild poisoning	History of intake/exposure
	Mild signs:
	③Normal consciousness
	③Secretions 1+
	③ Fasciculations 1+
Severe poisoning	Severe signs:
	③Altered consciousness
	③Secretions 3+
	③Fasciculations 3+
Life threatening poisoning	Suicide attempt
	Stupor
	PaO2<75mm Hg(<10mm Hg)
	Abnormal chest roentgenogram.

DIAGNOSIS

1. History or evidence of exposure to organophosphate.
2. Signs and symptoms of poisonoing.
3. Improvement of these signs and symptoms after the administration of Pralidoxime and atropine.
4. Inhibition of cholinesterase activity of blood.

In most patients a history of exposure to organophosphate insecticide can be obtained. After suicidal attempt a container is often found. Most organophosphates used as insecticides have characteristic garlic like odour and patients who have ingested or absorbed these compounds usually retain such an odour for several days. The organophosphate compound can frequently be identified in gastric aspirate, skin, urine, or clothing by means of gas or thin layer chromatograph, or by demonstration of anticholinesterase activity in vitro. Metabolites of organophosphate may also be detected in gastric aspirate, blood or urine. P-nitrophenol is a metabolite of parathion, methyl-parathion chlorothion, dicapthon and EPN, and its detection in urine indicates prior exposure to one of these or related compounds. However a history of exposure and detection of organophosphate or its

metabolites does not always indicate that signs and symptoms are due to organophosphate poisoning since the patients may have other diseases. Signs and symptoms do not occur unless the amount of absorbed organophosphate is so great acetylcholinesterase of synapses is inhibited over the critical level.

For example tests for urinary p-nitrophenol were positive in 75 out 90(83%) farm workers after spraying parathion in the field in one study and yet they did not have any symptoms and p-nitrophenol bore no relationship to the degree of inhibition of concentration of serum cholinesterase activity.[2]

The signs of organophosphate poisoning that are most helpful diagnosis are miosis and muscular fasciculations which are almost always present in moderately severe or severe poisoning

Other signs that are helpful in diagnosis include excessive sweating, salivation, lacrimation and bronchial secretions. The occurrence of frothy sputum and basal pulmonary rales may lead to an erroneous diagnosis of pulmonary oedema. Careful observation of the effect of pralidoxime and atropine is valuable for differential diagnosis. Intravenous injection of 1 gm pralidoxime generally causes some recovery from signs and symptoms particularly in parathion poisoning.

Patient with organophosphate poisoning are resistant to the action of atropine and therefore failure of 1 to 2mg of atropine administered parenterally to produce signs of atropinization (flushing, mydriasis, tachycardia or dryness of the mouth and nose) indicates organophosphate poisoning whereas occurrence of these signs casts doubt in the diagnosis or indicated that poisoning is of mild degree.[2]

Inhibition of cholinesterase activity of the blood is the most specific test for systemic absorption of an organophosphate anticholinesterase compound. Normal cholinesterase activity of the blood excludes systems poisoning by these compounds. Most of the organophosphate used as insecticides inhibit both psedocholinesterase and acetylcholinesterase. Estimation of erythrocyte cholinesterase (acetylcholinesterase) is theoretically preferred since it would reflect the degree of inhibition of synaptic cholinesterase . Estimation of plasma cholinesterase (psedo cholinesterase) has an advantage because the measurement is simpler and more accurate than estimation of erythrocyte cholinesterase following pralidoxime administration.

Erythrocyte cholinesterase indicates the effectiveness of pralidoxime and plasma cholinesterase indicates the prior presence of cholinesterase inhibition even after recovery of erythrocyte cholinesterase

activity by pralidoxime. In acute poisoning manifestation generally occur only after more than 50% of plasma cholinesterase is inhibited and the severity of manifestations parallel the degree of inhibition of serum cholinesterase activity 20 to 50 % of normal in mild poisoning, 10 to 20% of normal in moderately severe poisoning and less than 10 % in severe poisoning. The correlation between the degree of plasma cholinesterase inhibition and the severity of manifestations is pertinent only in the initial stage of acute poisoning and inhibition is greater in repeated exposures, inhibition remains even after recovery from symptoms.[2]

In severe poisoning return to normal level requires about 3-4 weeks for plasma cholinesterase and about 5 weeks or more for erythrocyte cholinesterase when pralidoxime is not administered.

Therefore plasma cholinesterase seems to recover far more rapidly than RBC cholinesterase.

- Blood/serum chemistry :
    - ✧ Serum electrolytes, Random blood glucose, Serum creatinine
    - ✧ Hematology (including white cells count as leukocytosis is common)

- ✧ Plasma cholinesterase

Sequential rise of plasma cholinesterase activity every few days for 14 to 28 days may confirmation of organophosphate exposure in the absence of pre exposure baseline values.[3]

- ✧ Serum amylase
- ✧ Lipase
- ✧ Serum levels of organophosphorus compounds and their metabolites.

- ➢ Aretrial Blood Gas :
  - ✧ Aretrial blood gas analysis in patients with CNS or respiratory depression.
- ➢ Urine analysis :
  - ✧ Estimation of excretory products of organophosphorus agents.
- ➢ Chest radiograph :
- ➢ Electrophysiological studies :
  - ✧ Electromyography

- ✧ Train of four
- ✧ Single fibre electromyography

➢ Indirect laryngoscopy :

- ✧ To evaluate vocal cord functions

➢ Ultra sound/CT scan :

- ✧ To evaluate pancreatic status

➢ Positron emission tomography :

- ✧ To estimate cortical visual loss following respiratory failure.

MANAGEMENT:

I. ACUTE CHOLINERGIC CRISIS [30]

All patients should be managed as emergencies in hospital.

A. First aid

B. Prevent further absorption of insecticide

C. Specific antidote therapy

1. Anticholinergic medication

2. Reactivation of Aectylcholine-oximes

D. Benzodiazepines

E. Other medications

Mild poisoning: warrants admission to hospital for atleast 72 hrs for observation and treatment.

Mooderate poisoning: admission in ICU.

Severe poisoning: merit immediate transfer and admission to ICU.

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) Resusciate if necessary

f) Support vital function if necessary

- O2 inhalation
- Lung ventilation
- Ionotropes

g) Control of convulsion

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

B. Prevent further absorption of insecticide:

a) Gastric lavage: performed using largest possible oro-gastric tubes with 50-100ml of fluid/lavage,preferably within 1 hr of ingestion protect airway in patients with impaired consciousness.

b) Administer activated charcoal: dose initial 60-100 gms, followed by 0.25 gms to 0.5gms/kg every 1-4 hrs.

C. Specific antidotal therapy:

Treatment aims:

a) Reversal of synaptic biochemical abnormalities.

b) Reversal of cholinesterase blockade.

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

i) Anticholinergic medication- atropine or glycopyrrolate.

ii) Reactivation of AchE-oximes.

i) Anticholinergic medication:

Atropine:[11, 32, 33]

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 muscarinic symptoms are relieved.[20]

The action of 2 mg atropine sulphate begins 1 to 8 minutes after IV,IM administration respectively and it is maximal at 6-15 min.[26]

Half life elimination 2-5 hrs.

Alternatively atropine can also be given by continuous infusion Atropine 30 mg in 200ml of NS at the rate of 0.02-0.08mg/kg/hr 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.[30]

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.[30]

Atropine should be restricted at first sign of recurrences of cholinergic symptoms.

The patient should be oxygenated prior to atropine administration in order to prevent ventricular dysarrhymias 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 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.

Side effect –atropine crosses the blood brain barrier and may cause

severe toxic effects such as confusion, psychosis, coma, seizure, delirium, hallucinations, fever, tachycardia and ileus.

Monitor with continuous pulse oxymetry, cardiac monitoring during atropine administration-to observe cardiac dysarrhythmias early and late.

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: [33]

It is 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 they are

- ✧ Better control of secretions.
- ✧ Lesser tachycardia.

- ✧ Fewer CNS side effects, because unlike atropine glycopyrrolate does not cross the blood brain barrier.

Fewer respiratory infections-this may be consequence of better control of endobronchial secretions,decreased mucous impaction in the smaller airways, followed by decreased obstruction and infection.

Dose 0.05mg/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/day.

ii) Reactivation of AchE-oximes

Derivatives of hydroxamic acid and a number of other oximes were shown to reactivate cholinesterase inhibited by organophosphorus compounds.

Mode of action:

1. Functions by nucleophilic and detoxification 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:

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

Therapeutic response observes is

- Recovery of consciousness
- Disappearance of manifestation, especially, weakness and fasciculations occurs within 10-40 minutes.

The second and third doses may be administered at interval of 1 hr if indicated by the persistence of muscle weakness.[30]

Disadvantages:

In view of the short elimination half life of 1-2 hr following IV bolus (intermitent) injection (1 gm 8 hrly) it would maintain the desired target concentration for <5 hrs in 24 hr period.

Therefore recommended regimen is

- Loading dose of20-50mg/kg based on symptoms severity(dissolved in 0.9%NS infused over 30 minutes)
- Followed by a continuous infusion of 10-20mg/kg/hr.[13]
- The maximum recommended dose in adults is 12gm in 24 hours.[13]

PAM should be administered soon after diagnosis is made. Once the phosphorylated enzyme has aged the phosphate group becomes irreversibly bound to the enzyme and oxime therapy is no longer effective. Probably more effective if given within 6 hrs of poisoning.

Maintenance and duration of treatment:

Average duration of treatment 5 to 7 days. 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.

OP residues that are present may bind the circulatory free PAM and lower its serum concentration. Therefore PAM should be continued as long as nicotinic symptomspersist those who develop the IMS are given the drug for longer periods until they are weaned from ventilator care.

Delayed clinical manifestations occur with fat soluble organophosphates like fenthion, chlorfenthion and parathion.

Cardiac and respiratory arrest have known to occur. Cardiac monitoring and blood pressure monitoring are adviced during and for several hours after the infusion of oximes.

Rapid infusion can cause tachycardia, laryngospasm,muscle rigidity and weakness.

Drug interactions:

Drugs which should be avoided when PAM is given are Morphine,aminophylline,succinylcholine.theophylline,resrpine and phenothiazines like tranquillizers.

The other commonly used oxime is obidoxime

Is effective in smaller doses i.e. 250mg IV/IM as a slow bolus or infusion.

Is more potent cholinesterase reactivating agent than pralidoxime but its toxicity is slightly greater.

The drug combination of pralidoxime and atropine is complementary and superior to used alone.

D. Benzodiazepins:[13]

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.[13]

E. Other medications:

a. Magnesium;

It was thought to be counteracting the direct toxi inhibitory effect of OPC'c on N.K.Atase.Singh et al administered magnesium sulphate 4mg IV to patients intoxicated with OP and observed that the neuroeletrophysiological effects that had been observed earlier were reversed.

b.Clonidine:

- Protective effects of clonidine or likely to involve multiple effects including
- Blockade of acetylcholine release and post synaptic muscarinic receptors.
- Transient inhibition of acetylcholinesterase
- Inhibits the release of acetylcholine from central and peripheral cholinergic neurons.[13]

MANAGEMENT OF INTEDRMEDIATE SYNDROME:[14]

PAM should be continued and provide adequate ventilator support.

Patient should be kept in hospital upto 5 days because patient may develop respiratory difficulty during the recovery phase of cholinergic crisis.

During the intermediate syndrome patient may develop profuse diarrhea. They should be managed with fluids and electrolytes.

MANAGEMENT OF DELAYED POLYNEUROPATHY:

There is no specific drugs.

Physiotherapy and regular exercise may improve the muscle weakness.

MORTALITY:

Mortality rate in India and other developing countries ranges from 4-38%.

Mortality depends upon the poison used, quantity ,duration after exposure and atropinisation of all the toxins.

Malathion has the lowest toxicity because of rapid hydrolization of

carboxy ester group to products with little or no anticholinesterase activity. Fenthion has the maximum mortality.

Early death is due to

1) CNS depression

2) Seizures

3) Ventricular arrhythmias

4) Respiratory failure due to

- ✧ Excessive bronchial secretions
- ✧ Bronchospasms
- ✧ Pulmonary oedema
- ✧ Paralysis of respiratory muscles
- ✧ Apnea due to depression of medullary respiratory center.

Late death is due to

1. Respiratory failure associated with

Infection
Pneumonia
Septicaemia

2. Complication due to mechanical ventilation

3. Ventricular arrythymias ,sudden collapse.

PATHOPHYSIOLOGY OF SERUM CREATINE PHOSPHOKINASE

Experimental study done in rats with soman an OP showed decrease in tissues ChE activity accompanied by increase in serum CPK activity. The CPK activity was significantly elevated in poisoning cases and more significant changes in the patients who died due to poisoning.

Significant increase in serum creatine phosphokinase coincides with the appearance of myonecrosis , destruction of muscle membrane.

Subjunctional changes in the muscle fibers, such as supercontraction of subjunctional sarcomeres as well as disruption of cytiarchitectural organaizations, are always present. The initial changes are in the mitochondria, which swell and then show lysis of the central cristae.

Myelin figures beneath the end plate are frequently observed , here as the region more distal to the end plate is less affected .the nucleoli of the muscle cell nuclei are enlarged and move to the periphery of the nucleus. This Myopathy can be induced with several OP or CM AChE inhibitors, such as paraoxon, diisopropylphosphofluoridate (DPP),

pyridostigmine, aldicarb and carbofuran and the OP nerve agents soman, sarin, tabun and VX.Despite the diversity in structures of these AChEIs, the induced myopathic changes are the same, suggesting a common mechanism. This mechanism is an excess of Ach and its prolonged interactions with nAChRs and not a direct action of these inhibitors on the muscle. The common denominator is muscle hyperactivity, such as fasciculations.

Carbofuran in concentrations that cause fasciculations and Myopathy produced a significant and maximal increase in serum total CK activity that was seen as early as 0.5hrs after carbofuran injection and remained elevated for 3hrs. Under the influence of acute carbofuran intoxication, examination of thr serum and diaphragm revealed several characteristic changesin CK isoenzymes. The activity of the CK-MM isoenzyme was elevated more than two fold in the diaphragm within 0.5hr and remained significantly higher than control at 24hr. Such an increase in CK-MM activity was also seen in the serum at the time when fasciculations were evident(1-3hr), indicating damage to the muscle fiber integrity. The increased leakage of CK subsided following restoration of normal muscle activity.

Normal CPK in Male – 51-294 I.06U/L

Female – 39-238 IU/L

POP Score	Serum CPK
Mild 0-3	273.53
Moderate 4-7	456
Severe 8-11	1032.57

Ref: Toxicology of Organophosphate & Carbamate Compounds. Author Ramesh Gupta

Toxicology International Jul-Dec-2011/vol-18/ issue-2.

MATERIALS AND METHODS

This study was conducted at Government Mohan Kumaramangalam Medical College Hospital over the period of two and half years from June 2010 to December 2012.

50 patients who fulfilled the criterias were chosen as study subjects.

Study design:

Prospective and observational study.

Inclusion criteria:

Patient exposure to OPC poison within six hours, without any prior treatment.

Exclusion criteria:

Patients with history of illness like Myopathy,chronic renal disease,epilepsy, myocardial infarction, sepsis and trauma.

Patients on medication like statins,,fibrates,aspirin,anticoagulants, dexamethasone.

Patients receiving intramuscular injections.

Method of collection of data:

After obtaining the informed consent details of history and clinical examination were recorded.

Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe.

In all study subjects blood was collected on admission for estimation of serum creatine phosphokinase.

Other routine investigations were done.

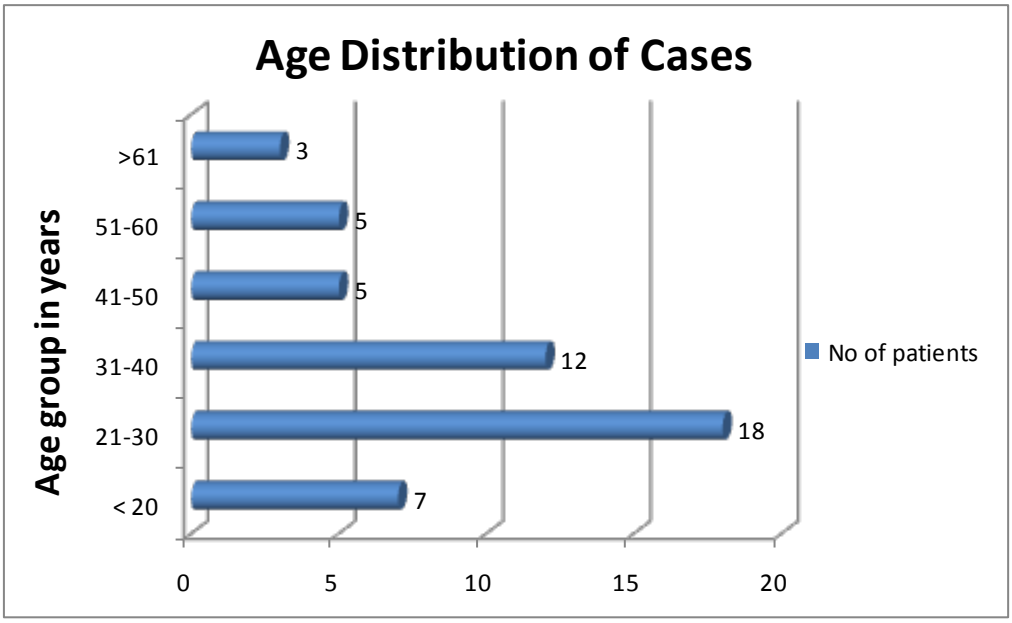
RESULTS

The following observations were made after studying 50 cases of suspected OPC poisoning.

TABLE – 1: Age Distribution

Age group (in years)	Total	Percentage (%)
<20	7	14
21-30	18	36
31-40	12	24
41-50	5	10
51-60	5	10
>61	3	6
TOTAL	50	100

Figure 1 Graph showing age distribution

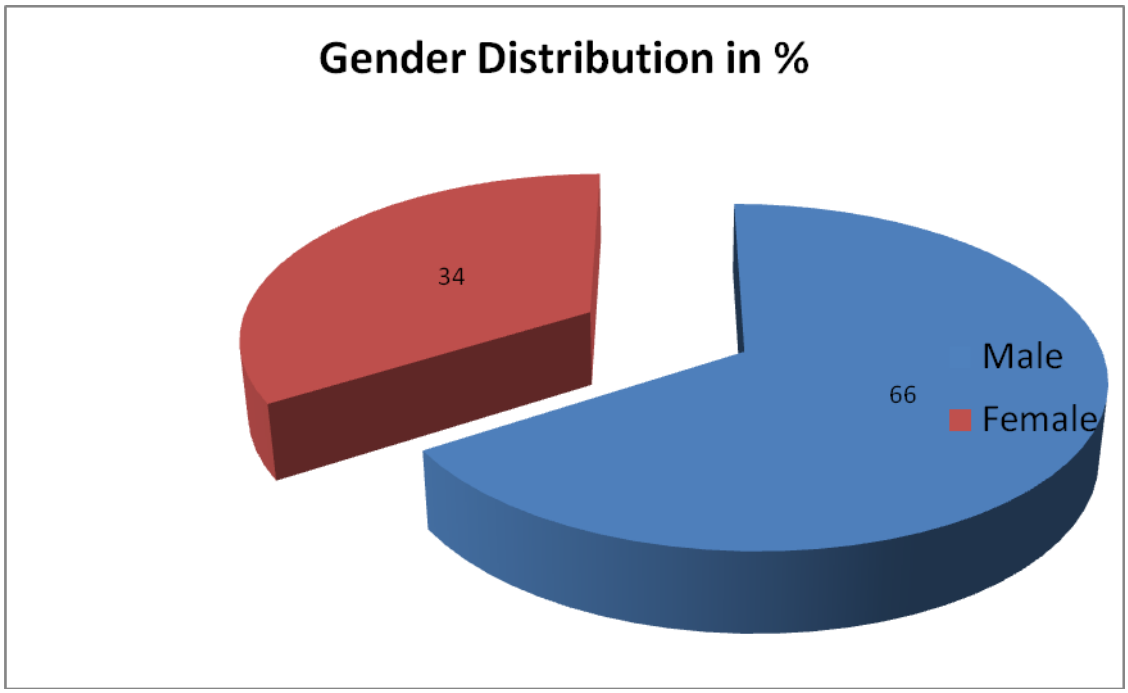


Age group ranged from 17 years – 66 years. Majority of the patients were in the age group of 21-30 years which comprised 36% of the study patients.

TABLE – 2 Sex wise Distribution

Gender	No. of cases	Percentage(%)
Male	33	66
Female	17	34

Figure 2: Graph showing sex distribution

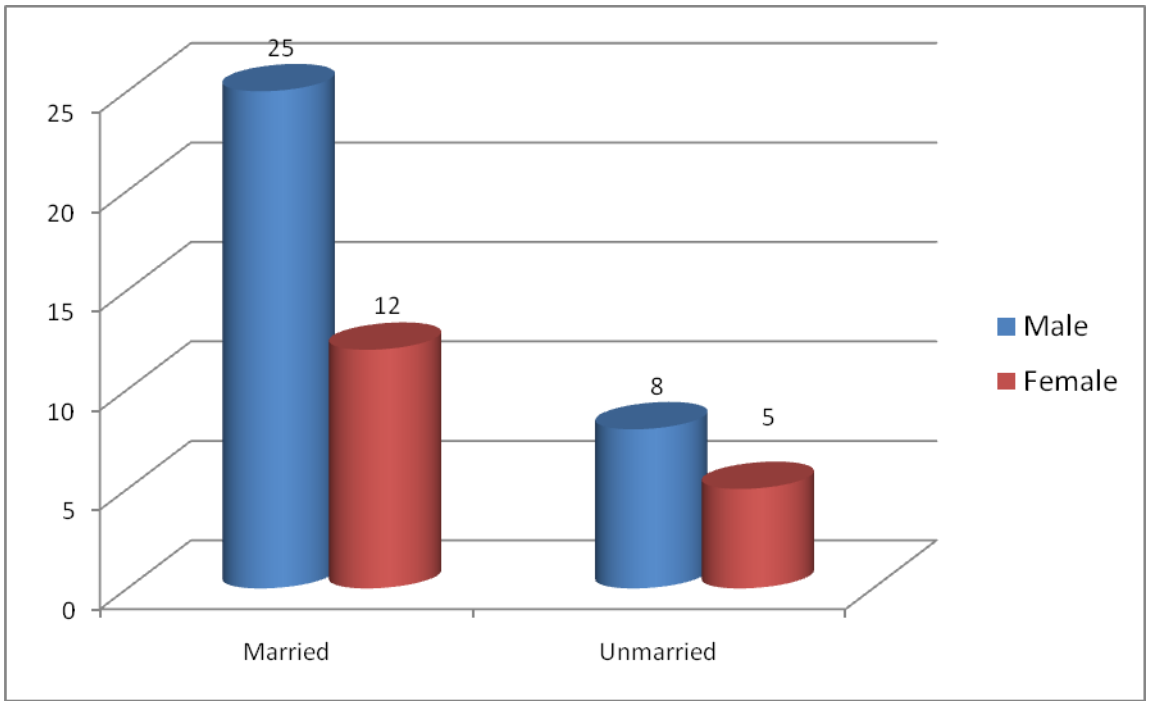


In this study 66% of patients were male and 34% were females. Males were more than females

TABLE - 3 Showing Marital status

Marital status	No. of patients	Percentage
Married	37	74
Unmarried	13	26
TOTAL	50	100

Figure 3: Graph showing Martial status

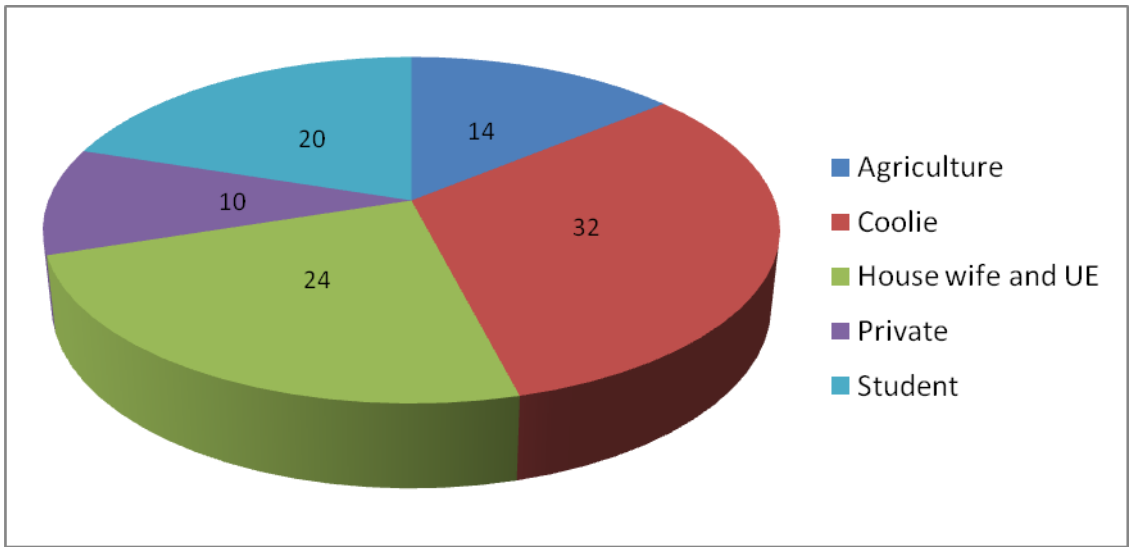


In our study 74% of patients were married, 26% patients were unmarried.

TABLE - 4 Occupation of patients

Occupation	No. of patients	Percentage
Agriculture	7	14
Coolie	16	32
House wife and unemployed	12	24
Private	5	10
Student	10	20
TOTAL	50	100

Figure 4: Occupation of patients in %

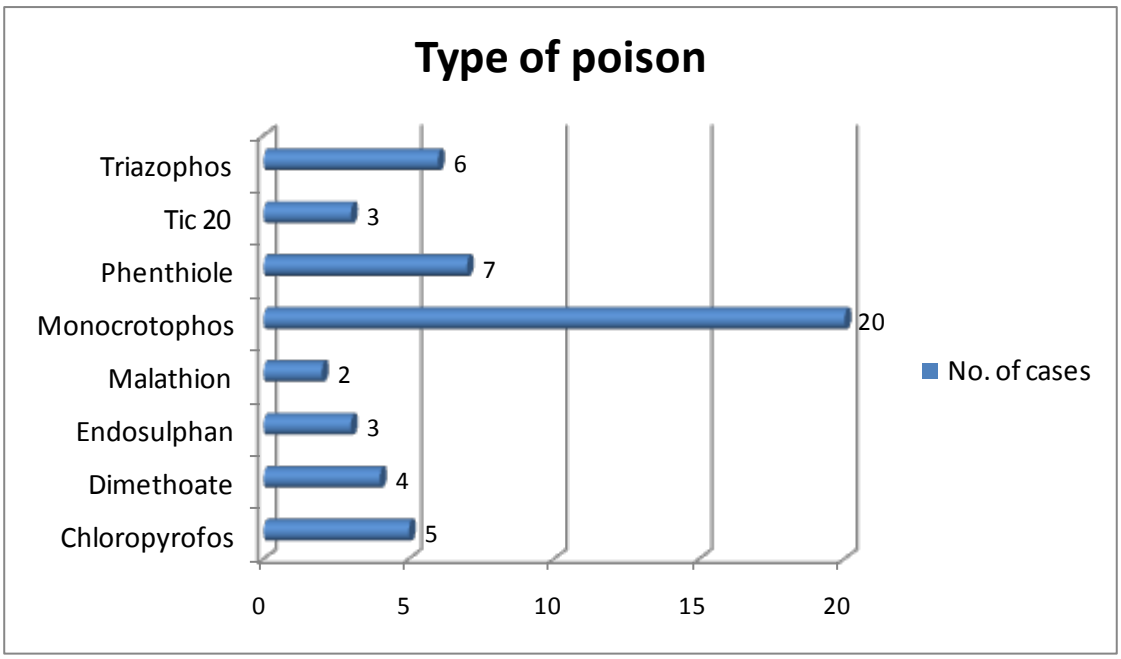


32% in our study were coolies. Next major group was constituted by housewives.

TABLE-5 Showing type of poison

Type of poison	No of cases	Percentage
Chloropyrofos	5	10
Dimethoate	4	8
Endosulphan	3	6
Malathion	2	4
Monocrotophos	20	40
Phenthiole 50% with epichlorhydrin	7	14
Tic 20	3	6
Triazophos	6	12
TOTAL	50	100

Figure 5: Type of poison

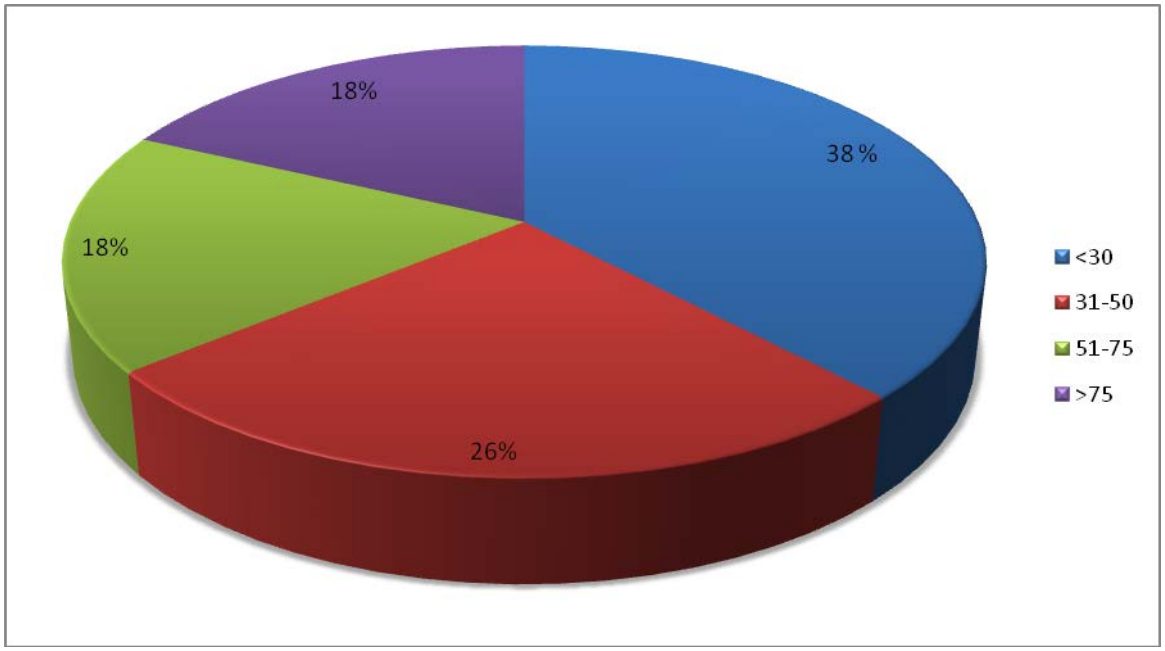


Most common poison encountered is Monocrotophos followed by Phenthiole 50% with epichlorhydrin.

TABLE 6: Showing quantity of poison consumed:

Amount of poison consumed in ml	No of patients	Percentage
<30	19	38
31-50	13	26
51-75	9	18
>75	9	18

Figure 6: Graph showing the amount of poison consumed



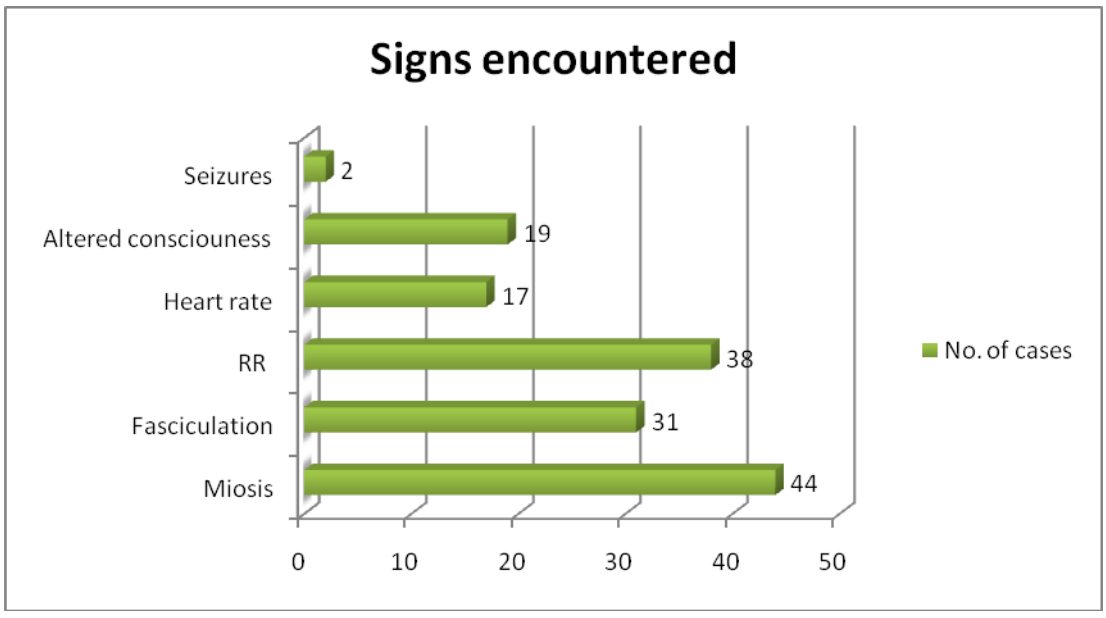
38% of the patient has consumed <30 ml.

18% of the patient has consumed >75 ml.

TABLE – 7 Clinical Signs

Sign	No. of cases	Percentage (%)
Miosis	44	88
Fasciculation	31	62
Respiratory rate >20	38	76
Heart rate	17	34
Altered consciousness	19	38
Seizures	2	4

Figure 7 Graph showing Clinical Signs



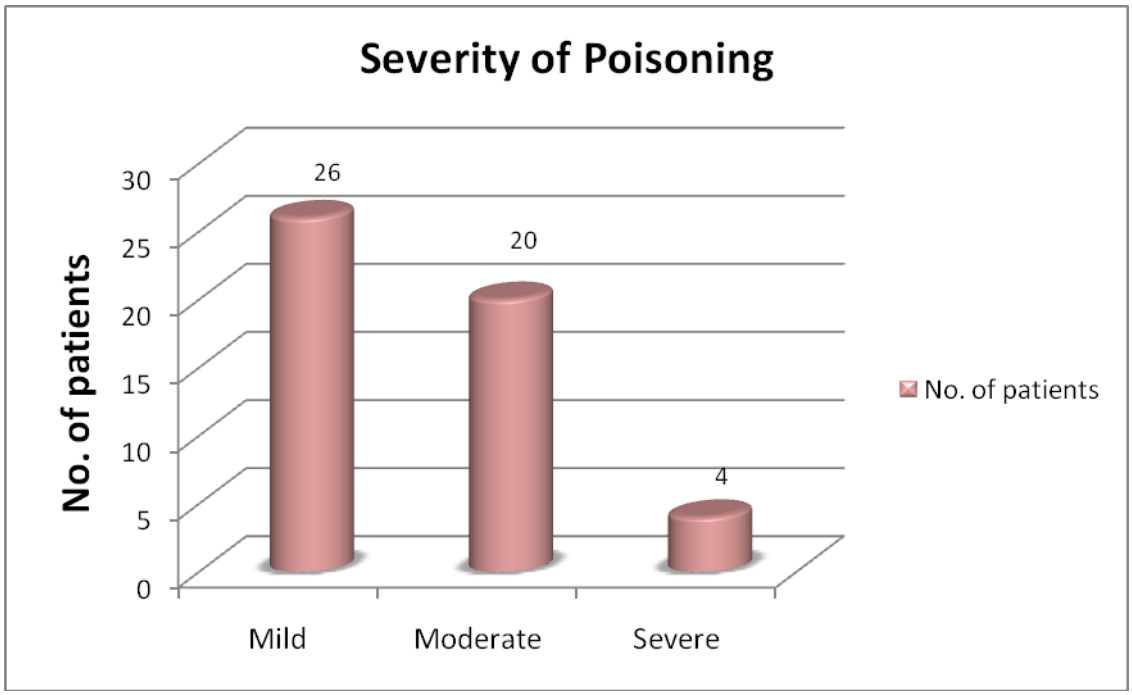
In this study most common clinical sign is Miosis followed by Tachypnoea

TABLE-8 Showing severity according to Peradeniya

OP poisoning scale

Severity	No of patients	Percentage
Mild	26	52
Moderate	20	40
Severe	4	8
TOTAL	50	100

Figure 8: Graph showing severity of poisoning to POP scale



More than 50% of patients in our study belong to mild grade of poisoning with a POP score1-3.

TABLE-9. SERUM CPK LEVEL

CPK Range IU/L	No of patients	Percentage
<350	25	50
351-500	9	18
501-750	4	8
751-1000	11	22
>1000	1	2

Figure 9: Graph showing Serum CPK Level

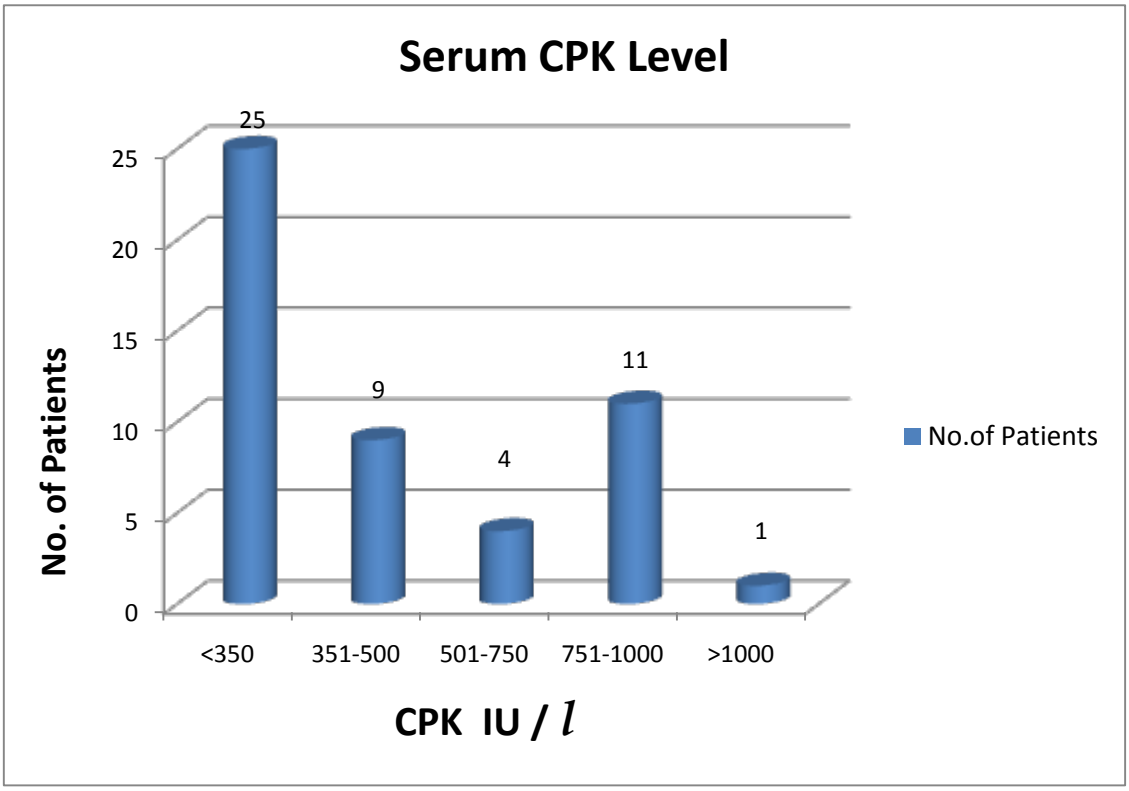
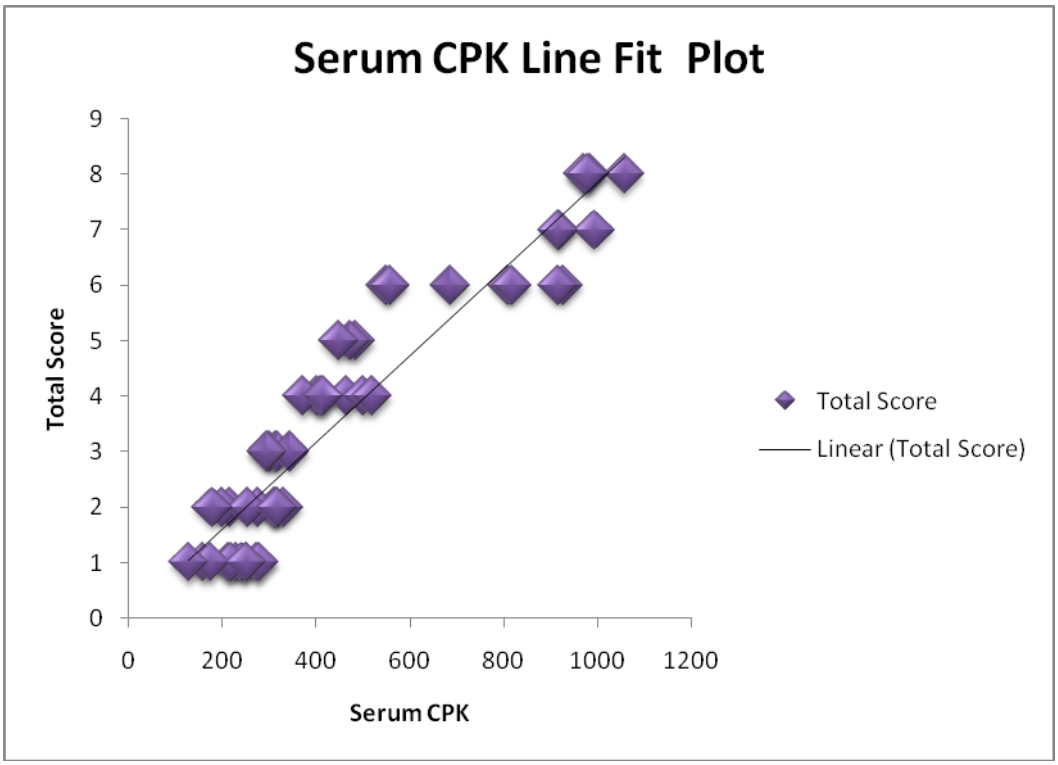


TABLE-10 Showing correlation between serum CPK level and POP score

CPK range	POP score	No of patient	Percentage
<350	0-3	25	50
351-500	4-5	9	18
501-750	6	4	8
751-1000	7-8	11	22
>1001	8	1	2



Serum CPK Level was directly related to the severity of the Peradeniya OP Poisoning Scale. (Pearson correlation P =0.000)

TABLE-11 Showing correlation between serum CPK level and ventilatory support

Serum CPK IU/L	Ventilatory Support		Total
	YES	NO	
<350	0	25	25
351-500	3	6	9
501-750	4	0	4
751-1000	10	1	11
>1001	1	0	1

Figure 11: Graph showing correlation between serum CPK level and ventilator support

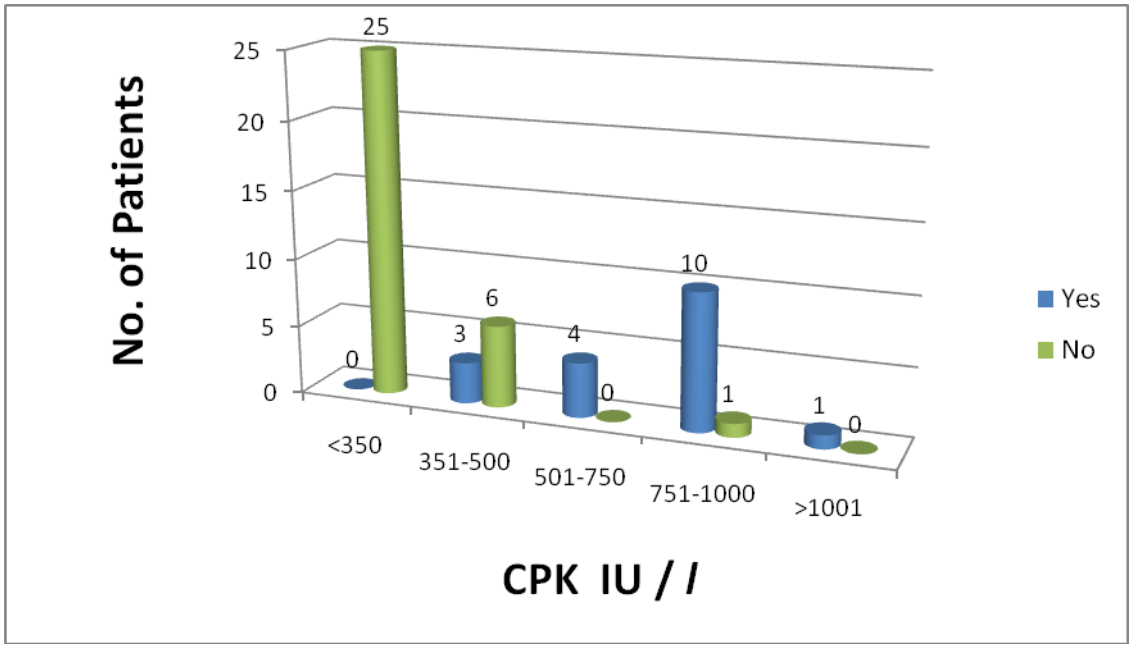


TABLE - 12 showing correlation between POP scale and ventilatory support

POP scale	Ventilatory support		TOTAL
	YES	NO	
Mild	0	26	26
Moderate	14	6	20
Severe	4	0	4
TOTAL	18	32	50

Figure: 12 showing correlation between POP scale and ventilatory support

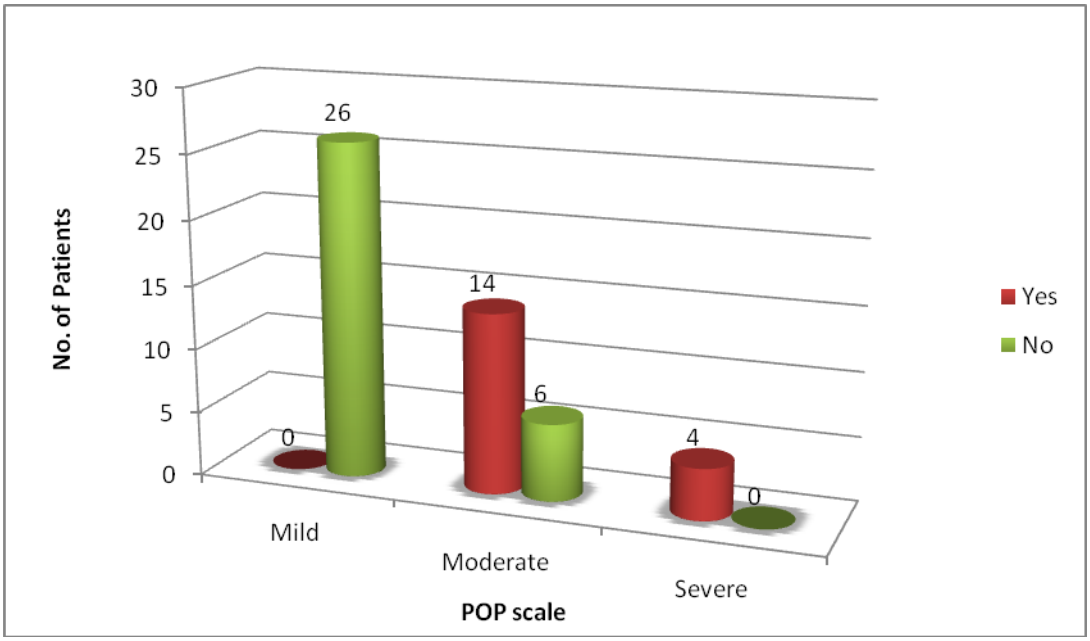
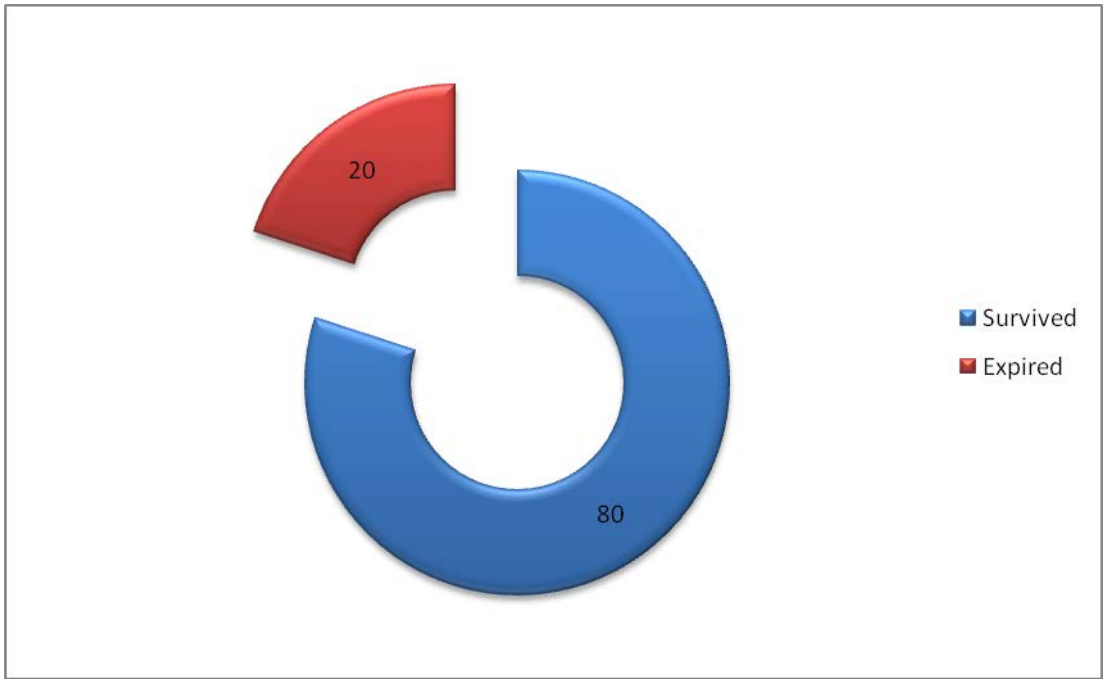


TABLE 13 Outcome of the patients

Outcome	No of patients	Percentage
Survived	40	80
Expired	10	20
TOTAL	50	100

Figure 13: Graph showing outcome of patients.



DISCUSSION

Organophosphorus compound poisoning is a major public health problem in the developing world. Since a high proportion of Indian population is involved in agriculture, the incidence of suicidal OPC poisoning is increasing as a result of easy access to highly toxic pesticide in the situation of stress.

The present study was conducted in Govt Mohan Kumaramagalam Medical college from June 2010 to December 2012. The clinical and diagnostic findings of this study is compared with studies in literature.

Age of the patient:

In our study majority of the patients were in the age group of 21-30 yrs. (36%).

COMPARING THE AGE GROUP WITH MAXIMUM INCIDENCE

Age group	Present Study(%)	P.S.Shankaretal(%)	Goeletal(%)	Saadehetal(%)
<20	14	25	-	46
21-30	36	59.4	86.4	-
31-40	24	9.4	-	-
41-50	10	6.2	-	-
51-60	10	-	-	-
>61	6	-	-	-

In this study maximum incidence of poisoning was among less than 30yrs of age, which was comparable to studies done by P.S.Shankar et al and Goel et al.

SHOWING SEX RATIO

Age group	Present study	P.S. Shankar et al	Goel et al	Thomas et al	Shoba TR et al
Male	66	71.85	72	56	56.5
Female	34	28.15	28	44	33.4
M:F	-	2.5:1	1.27:1	1.27:1	1.3:1

In this study incidence was more common in males with M: F of 1.9:1. This is consistent with studies of Goel et al,Thomas et al,Shoba et al reports.

COMPARING COMMONLY ENCOUNTERED OP COMPOUNDS.

OPC	Present study(%)	Goel et al	Avasthi et al
Chlorpryphos	10	-	-
Dimethoate	8	8.74	24.1
Endosulphan	6	-	-
Monocrotophos	40	26.21	41.3
Phenthiole	14	-	-
Malathion	4	15.3	-
Tic 20	6	-	-
Triazophos	12	-	-

Monocrotophos was the commonest used OPC in this study which was comparable to Avasthi et al studies.

COMPARISON OF CLINICAL SIGNS

Signs	Present study	Reihman et al	Goel et al	APN Kumar
Miosis	88%	60%	95%	62%
Fasciculation	62%	8%	55%	38.6
RR>20	76%	34%	42.5%	81.3%
Heart rate	34%	52%	39%	-
Alt conscious	38%	30%	75%	-
Seizures	4%	-	-	-

Common signs were Miosis, Fasciculation and Tachypnoea comparable to the studies of Goel et al.

Comparison of Peradeniya OP Poisoning score and serum CPK level.

POP score	SERUM CPK Mean $\pm$ SD	
	Present study	Bhattacharyya et al
0-3	257.23	273.53
4-7	634.05	456.06
8-11	997.75	1032.57

Elevationof serum CPK correlates with severity of POP score.

Our study was consistant with Bhattacharyya et al study.

COMPARISON OF MORTALITY

STUDY	Expired (%)
Present study	20
Kamath et al	8
Manimala et al	13.79
Johnsen Samuel et al	18.1
Sundaram et al	23.5

Mortality in the present study was comparable of the study of Sundaram et al

Peradeniya OP Poisoning scale

POP scale was calculated for all patients on admission. 52% of patients had mild grade of poisoning, 40% had moderate grade of poisoning 8% had severe grade of poisoning. Out of the 20 patients of moderate grading 14 patients required ventilatory support. Out of this 14 patients 7 patients were expired. All 4 of the severe grade of poisoning required ventrilatory support. Out of this 4 patients 3 patients expired.

Serum CPK level:

Serum CPK level was assessed in all patients. CPK level range

from 128IU/L to 1057 IU/L. Patients with mild POP scoring had range from 128IU/L to 344IU/L. Patients with moderate POP scoring had ranges from 372IU/L to 994IU/L. POP scoring of severe grade had ranges from 978IU/L to 1057 IU/L.

From this study we have found that there is a high degree of correlation between the POP score and the initial serum creatine phosphokinase level. A study conducted by Sharma et al has shown that CPK was elevated in a fraction of their cases who had severe poisoning. It has been shown that there is rhabdomyolysis in IMS and consequently there is raised CPK level.

But our study shown that serum CPK level is increased even in absence of IMS.

CONCLUSIONS

OPC poisoning is one of the most common modes of suicidal death in our country. In our study age group between 20 to 40 yrs are more commonly encountered in poisoning. There is male preponderance in our study. Most of the patients consumed poison with a suicidal intension. All patients had consumed the poison orally.More than 50% of the patients had consumed less than 50ml of poison. Quantity of the poison consumed correlate with the severity of poisoning. The most common poisonous agent is monocrotophos. There was a good correlation between the severity of the POP scale and the elevation of CPK and the need for ventilatory support.Peradeniya OP poisoning score more than 5 correlated in predicting the need for ventilatory support and mortality. Serum CPK level more than 500IU/L correlated in predicting the need for ventilatory support and mortality In this study requirement of ventilatory support was seen in 36% of patients. Mortality in our study was 20%.We found a high degree of correlation between initial CPK and POP score.The correlation was found to be highly significant ($P<0.000$).

SUMMARY

A prospective clinical study was undertaken in 50 patients with a history of organophosphate poison ingestion admitted at GMK Medical college from June2010 to December 2012.

The objectives of the study were to evaluate the prognostic value and correlation of serum CPK with Peradeniya OP poison scale. All patients aged between 15 to 65 years without any comormid conditions were eligible for this study.

A thorough clinical examination was carried out with particular reference to vital parameters. Pupil size, assessment of CNS system ,respiratory system, cardiovascular system as per prescribed proforma. This examnination took place during initial resuscitation of the patients.

Peradeniya OP poisoning scale was applied to all study subjects and the severity of OP poisoning was graded as mild, moderate, severe.

All patients were manged with decontamination procedure including gasric lavage. IV atropine 2-4 mg bolus and repeated every 5-15 minutes initially until atropinization. The end point of treatment was taken as the drying up of secretions. The atropinization was maintained for 24-48 hrs with intermittent doses. Pralidoxime chloride was given to

all patients as 2g IV bolus over 10-15 minutes immediately after admission and 0.5-1g IV 6^{TH} hourly for 48 hrs. Patients were kept under observation during their stay in hospital. Assessment of patients airway and need for endotracheal intubation was assessed, if nessassory ventilatory support given.

Psychiatric counseling was done for the patients who survived.The study revealed all the patients with OP poison ingestion had elevation of serum creatine phosphokinase levels correlated with the gradings of the Peradeniya OP poisoning scale, and ventilatory requirement. POP scale more than 5 and serum CPK level more than 500IU/L were more likely to be associated with the development of respiratory failure and subsequent requirement of ventilatory support.

PROFORMA OF THE STUDY

1. Name:

2. Age (yrs)

3. Sex: M/F

4. Address:

5. Occupation:

6. Marital status:

7. History:

   a) Nature of OP compound consumed

   b) Route of consumption

   c) Quantity consumed

   d)Time interval from ingestion to hospitalaization

   e) Homicidal/Suicidal/Accidental

8. Clinical signs:

    Miosis

    Fasciculation

    Respiration

    Heart rate

    Level of consciousness

9. POP score:

10. Serum CPK:

11. Requirement of ventilatory support:

12. Outcome:

ANNEXURE 2: POP scale

S.NO	PARAMETERS		SCORE	PATIENTS SCORE
1.	Miosis	Pupil size >2mm	0	
		Pupil size <2mm	1	
		Pin Point	2	
2.	Fasciculation	None	0	
		Present	1	
		Generalized/cyanosis	2	
3.	Respiration	≤20/min	0	
		>20/min	1	
		>20/min & cyanosis	2	
4.	Heart rate	>60/min	0	
		41-60/min	1	
		≤40/min	2	
5.	Level of consciousness	Conscious / alert	0	
		Impaired, responds to verbal commands	1	
		No responds	2	
		Convulsions	+1	
	TOTAL		11	

No	Name	Age	Sex	Marital stat	Occupation	Route	Quantity	Intention	Type of Poison	Time inter	Miosis	Fasciculation	Respiration	Heart rate	consciousness	Seizures	Total Score	Serum CPK	Ventilatory	Outcome
26	Latchumi	35	F	M	C	O	100	S	Monocroto	4	2	1	1	1	1	0	6	928	Y	E
27	Madhu	65	M	M	Nw	O	30	S	Endosulph	3	1	0	0	0	0	0	1	241	N	I
28	Vadivel	66	M	M	Nw	O	75	S	Tic 20	4	2	1	1	1	2	0	7	994	Y	E
29	Lalitha	30	F	M	C	O	40	S	Endosulph	3	1	1	0	0	0	0	2	312	N	I
30	Selvam	43	M	M	C	O	50	S	C+C	2	1	1	1	0	0	0	3	319	N	I
31	Ishwarya	17	F	Um	St	O	25	S	Triazopho	3	1	0	0	0	0	0	1	217	N	I
32	Muthusa	35	M	M	C	O	50	S	Dimethoa	4	1	1	1	0	1	0	4	416	N	I
33	Revathy	22	F	M	Hw	O	30	S	Monocroto	2	1	1	0	0	0	0	2	316	N	I
34	Sathya	45	F	M	C	O	50	S	Triazoph	4	1	1	1	0	0	0	3	344	N	I
35	Madhesh	21	M	Um	St	O	25	S	Monocroto	3	1	1	0	0	0	0	2	274	N	I
36	Vijayan	35	M	M	F	O	125	S	Monocroto	3	2	1	1	1	1	1	7	916	Y	E
37	Ramasam	55	M	M	F	O	25	S	P+E	4	2	1	1	0	0	0	4	520	Y	I
38	Sarasu	28	F	M	C	O	30	S	C+C	2	1	0	1	0	0	0	2	198	N	I
39	Chinnaya	48	M	M	F	O	30	S	Malathion	2	0	0	1	0	0	0	1	174	N	I
40	Laxshmi	20	F	M	Hw	O	75	S	Tic 20	4	2	1	1	1	2	1	8	978	Y	E
41	Raja	24	M	Um	St	O	25	S	P+E	2	1	0	1	0	0	0	2	252	N	I
42	Jayamma	58	F	M	C	O	50	S	Monocroto	3	2	1	1	0	1	0	5	472	Y	I
43	Menaka	18	F	Um	Nw	O	45	S	Dimetho	3	1	1	1	0	0	0	3	294	N	I
44	Saraswat	38	F	M	Hw	O	25	S	P+E	2	1	0	0	0	0	0	1	250	N	I
45	Karupan	58	M	M	F	O	50	S	Monocroto	3	2	1	1	1	0	0	5	448	Y	I
46	Bhasha	28	M	M	P	O	30	S	Dimethoat	4	2	0	0	0	0	0	2	317	N	I
47	Kumar	34	M	M	P	O	50	S	Monocroto	6	2	1	1	1	1	0	6	818	Y	E
48	Kumaran	18	M	Um	St	O	75	S	Monocroto	5	2	1	2	0	1	0	6	915	Y	E
49	Manikam	54	M	M	C	O	40	S	Triazoph	3	1	1	0	0	0	0	2	178	N	I
50	Kalpana	18	F	Um	St	O	25	S	Monocroto	1	0	0	1	0	0	0	1	128	N	I

KEY TO MASTER CHART

1. S.NO
2. Name
3. Age
4. Sex – M-Male, F-Female
5. Marital status –M-Married, Um-Unmarried
6. O-Occupation -St-Student, C- Coolie, P- Private, F-Farmer, Hw House wife, Nw-Not working,
7. Route of ingestion-O-Oral
8. Quantity
9. Intention – S-Suicide
10. Type of poison
11. Time interval
12. Miosis
13. Fasciculation
14. Respiration

15. Heart Rate

16. Consciousness

17. Seizures

18. Total Score

19. Serum CPK – Creatine Phosphokinase

20. Ventilatory support – Yes - Y, No – N

21. Outcome – I - Improved, E – Expired

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